Outdoor Occupational History and Risk of Parkinson Disease: a Case-Control Study

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A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2012

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Program Authorized to Offer Degree:

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Abstract

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Introduction: A role for antioxidants in prevention of Parkinson disease has been proposed, however, epidemiologic evidence supporting this assertion has been inconclusive. Ninety percent of vitamin D in adults is produced *in vivo* related to ultraviolet type B exposure. This creates a plausible role for outdoor work as a strong surrogate for vitamin D in studies related to neurodegenerative disease.
Design and Setting: We investigated this association among non-Hispanic Caucasians in Washington state using 447 incident Parkinson disease cases diagnosed between 1992-2008, and 578 neurologically normal controls, frequency matched by age and sex.
Material and Methods: Subjects' work histories were obtained by in-person interviews, and a validated method was used to classify each occupation up to 10 years prior to diagnosis (cases)/reference (controls) according to relative time spent outdoors. Research participants were categorized as having exclusively indoor, a combination of indoor/outdoor, or exclusively outdoor occupations using job title. Length of time employed in each occupation was also used to estimate the lifetime duration of any outdoor work, and the maximal and typical levels of outdoor work.
Results: Classified by job title and without the inclusion of a 10-year lag time, Odds ratios and 95% confidence intervals from unconditional logistic regression adjusting for age, sex, and smoking were as follows: (> 0 - < 50% of work day outdoors) 0.79 (0.50-1.22), (50%-75% workday outdoors) 0.81 (0.52-1.25), and (> 75% workday outdoors) 0.86 (0.60-1.23), compared to workers who labored exclusively indoors. Classified by job title and incorporating a 10-year lag time, Odds ratios and 95% confidence intervals from unconditional logistic regression adjusting for age, sex, and smoking were as follows: (> 0 - < 50% of work day outdoors) 0.85 (0.54-1.32), (50%-75% workday outdoors) 0.83 (0.54-1.29), and (> 75% workday outdoors) 0.85 (0.60-1.22), compared to workers who labored exclusively indoors.
Conclusions: Our findings suggest that workers who spend at least part of their day outdoors have a lower risk of Parkinson disease as compared to workers who labor exclusively indoors. This supports the hypothesis that ultraviolet type B exposure acting as an ecological surrogate for vitamin D may provide a protective effective for the development of Idiopathic Parkinson Disease.

ACKNOWLEDGMENTS

The author wishes to express sincere appreciation to the Department of Environmental and Occupational Health Sciences for their extended guidance and support, especially to Harvey Checkoway PhD, MPH, Gary Franklin MD, MPH, Susan Searles Nielsen PhD, MS and Lisa Gallagher DSc, MPH. I would also like to thank the Department of Preventive Medicine at Madigan Healthcare Center, specifically, LTC Christopher Littell DO, MPH, for his mentorship and continued patience and oversight during this project. Finally, this thesis would never have been completed without the devotion and encouragement of my family and friends.

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INTRODUCTION

Parkinson disease (PD) is a progressive neurodegenerative movement disorder estimated to affect at least 1% of the U.S population.[1,2] The disease can be treated symptomatically, however, there is no cure.[3] Initial response to PD treatment can be dramatic. Over time, however, the benefits of medication frequently diminish or become less consistent.[3] This has focused attention on modifiable risk factors, such as the role of environment, in influencing PD risk. [1,4-7] Inadequate vitamin D levels have been linked to decreased incidence of neurodegenerative disease, including Parkinson disease.[7] The vulnerability of fragile brain cells to intracellular damage related to accumulation of Reactive Oxygen Species (ROS) and formation of hydroxyl-free radicals resulting in oxidative stress has been proposed as one plausible mechanism in which vitamin D aids the nervous system. During oxidative stress, the brain tissue's own cellular defenses are overwhelmed and cannot counter the rapidly accumulating ROS. Given the fact that vitamin D is an antioxidant it acts to regenerate vital glutathione reductase decreasing intracellular damage and limiting the toxic effects of ROS and hydroxyl-free radical accumulation. Vitamin D has also been shown to have immunomodulatory effects including reduced generation of pre-inflammatory CD4+ T helper 1 (TH1) cells and an ability to increase the levels of the CD4 + T helper 2 (TH2) subset.[8] Therefore, multiple potential pathways exist through which vitamin D may mediate PD risk. Thus, the role for antioxidants in mediation of PD is broad, and perhaps a result of a complex interplay of several factors. As such, the promise of not one, but perhaps several modifiable pathways that may reduce Parkinson disease incidence, makes this an important research topic particularly in a disease with a sporadic pattern of heritability which appears to affect the population at random.

Ninety percent of vitamin D in adults is produced *in vivo* when ultraviolet radiation type B (UVB) strikes the skin. Specifically, photoconversion of dehydrocholesterol to pre-vitamin D is directly correlated to dose of UVB radiation. Also, it has been recognized for some time that at temperate latitudes serum 25-hydroxyvitamin D exhibits cyclic variation. This annual cyclic variation results in a peak in late summer and a nadir in late winter. Furthermore, it should be considered that

as a dietary supplement vitamin D is poorly absorbed and has limited bioavailabity,[9-11] After taking into account the evidence listed above, this creates a plausible role for outdoor work as a strong surrogate for vitamin D in studies related to neurodegenerative disease.[7]

As previously described by Kenborg et al. [12] job title can be used to estimate average percentage of workday subject's spend outdoors. This in turn can be utilized as an ecological surrogate for amount of UVB exposure. This paper builds on prior research[12] by carefully examining this association in a new study venue; utilizing data gathered from residents of western Washington State. Strengths of this study include ability to verify date of onset for PD cases, establishing temporal association between exposure and outcome. Also, this study included a strict case definition which was rigorously verified by a panel of three trained neurologists. Also, ability to directly control for important confounders such as smoking improves the validity of the data. Finally, where other studies have only included men, our study includes women, as well[12]. This leads to improved generalizability of study finding, as well as, ability to examine the extent that gender influences the association between PD and outdoor work.

METHODS

SUBJECTS

Data were obtained from a case-control study in western Washington State. Incident PD cases were diagnosed between 1992-2008 at the University of Washington Neurology Clinic or Group Health Cooperative. Prior publications have described methods of recruitment and subject enrollment.[11,13-15] Briefly, eligible PD cases were identified by one of three separate sources (1) provider referrals from both facilities, (2) ICD-9 primary diagnosis search (ICD-9 code 332.0) utilizing the computerized database of both facilities, and (3) pharmacy database searches for medications most commonly prescribed to PD patients (e.g., Carbidopa/Levadopa, and Levadopa). For cases which were not referred by a neurologist, diagnosis of Parkinson disease was confirmed by

an abstracted review of the subject's medical record conducted by one of the study's panel of three independent neurologists. This panel required at least two of the four cardinal signs of PD (bradykinesia, cogwheel rigidity, postural reflex impairment and resting tremor)[3,16] be documented in the research participant's chart in order to meet study inclusion criteria.

Cases in which a known cause of Parkinsonism had been established (e.g., head trauma, encephalitis, cerebrovascular event, or brain tumor) were excluded from the study. Exclusion criteria also included use of specific medications whose adverse affects may include Parkinsonism during the 12 months preceding PD diagnosis (e.g., Haloperidol, Metoclopramide, and Phenothiazines). No exclusions were made with respect to gender, race, or ethnicity.

Eligible control subjects were randomly selected from the enrollees of Group Health Cooperative without history of Parkinson disease or other progressive neurological disorder. Controls were frequency matched to cases by age, sex, race/ethnicity, clinic and length of enrollment in Group Health Cooperative.[13,14] The Human subjects committees at the University of Washington and Group Health Cooperative reviewed and approved the study, and all subjects provided written informed consent, prior to study conduct.

EXPOSURE ASSESSMENT

Research participants underwent a structured in-person interview with a nurse practitioner. The same nurse practitioner interviewed all research participants. Subjects were provided information describing the purpose, risks, and benefits of the research, and written consent was obtained for participation. The Mini-Mental Status Exam was then administered on each potential subject to establish cognitive competence. During the in-person interview subjects provided demographic information, family, residential, and exposure history. Occupational history was obtained as subjects examined a questionnaire listing 60 specific job titles and indicated whether they had worked at each

of these jobs for more than six months (yes/no), and if so the start and end year. Subjects were to consider their entire occupational history. An open-ended section at the end of the occupational history questionnaire enabled subjects to report up to five additional job titles not previously listed. Participants were asked to include part-time employment and multiple jobs held during the same time period. Detailed job descriptions provided by the *Dictionary of Occupational Titles* were used to standardize self-reported job titles. Occupational histories were sufficiently complete for 438 (97.9%) of cases and 561 (96.8%) of controls.

DATA CODING AND REVIEW

Primary analysis was restricted to non-Hispanic Caucasians. Given the fact that only 7% of the study population was of a racial/ethnic minority, non-Hispanic Caucasians represented the predominate racial group (93%) at the time the study was conducted. Scientific literature has cited a significant difference in UVB absorption related to skin color[17]. This suggests that this population would be most vulnerable to UVB exposure related to the fact that lighter skinned individuals absorb UVB radiation at a faster rate that individuals with dark pigmented skin.

Self-reported job title was used as the primary indicator for assignment into one of four occupational exposure categories. Job titles grouped by occupational exposure category are listed in **Table 2**. This method has been previously applied in a large study of 23,101 Danish workers conducted in 2011 by Kenborg et. al.[12,18]. The four occupational exposure categories were: indoor exclusively, moderate (< 50% workday outdoors), frequent (50-75% of workday outdoors), and maximal outdoor work (> 75% of workday outdoors). Among the 481 cases and 627 controls with sufficiently complete occupational histories, 71 cases and 85 controls had job title(s) for which > 25% of work years could not be classified according to level of outdoor work. Following the method of Kenborg, we retained these subjects in our analyses as an "unclassified" group, to help ensure that

results were not biased by exclusion of cases and controls. However, keeping them as a separate category allowed us to minimize exposure misclassification and put greatest emphasis on results for cases and controls for which there was more complete exposure data.

To account for time between symptom onset and time to diagnosis in PD patients a 10-year lag time was incorporated into the exposure assessment from date of diagnosis. Incorporation of a 10-year lag time addresses the period of the occupational history most likely to be influenced by job choices related to limitations secondary to undiagnosed PD symptoms, therefore, causing this portion of the occupational history to be not representative of a cases' overall occupational history. Controls' occupational history was discounted similarly, 10 years from the reference date. Results incorporating this 10-yr lag time were compared to study results prior to incorporating the 10-year lag time in order to assess for bias.[3]

Multiple methods were used to assign job titles in occupational exposure categories. These methods were as follows: Method 1) research subject assigned to occupational exposure categories based on job title with the highest degree of outdoor work, Method 2) research subject assigned to occupational exposure category based on job held for longest duration, Method 3) Based solely on number of years employed as an outdoor worker (considers any outdoor work). These multiple methods were utilized in order to examine different aspects of the exposure with the hope being that this would help us capture information unavailable for study participants such as variability between job title and actual job duties.

STATISTICAL ANALYSIS

Statistical analysis was conducted using STATA 11.1 (StatCorp LP, College Station, Tex). A preliminary assessment of outdoor work was conducted as a binary variable (ever/never) examining whether subjects had worked indoor only, a combination of indoor and outdoor or outdoor jobs over the duration of their entire occupational history. Categorical variables were also used to examine frequency of research participant's outdoor exposure. The categories were as follow: indoor work only, < 50% of workday mandated outdoors, 50%-75% of workday mandated outdoors, and > 75% workday mandated outdoors. Relative risk estimates (odds ratios [OR]) were estimated using unconditional logistic regression with subjects grouped according to their four occupational exposure categories. The analysis controlled a priori for age (continuous), sex,[26,27] ever smoking (yes/no) and pack-years,[28] as these are strongly related both to PD case status and outdoor work.[21,23,26,27,29,30] Factors such as having a first degree relative with PD[3,31] and use of vitamin D supplements[16,17,21,32] were also considered as potential confounders[15,16,20,27,32,33], were only included in models if ORs were changed by > 10% by their inclusion. Statistical significance was set at alpha= 0.05.

RESULTS

POPULATION DEMOGRAPHICS

Demographic characteristics of the research participants are summarized in Table 1.

Cases included 291 men (56%) and 165 women (64%); of median age 67 (range= 22-88). The controls included 377 men (56%) and 218 women (37%); of median age range 70 (43-86). Both groups had a high level of education, with the majority attending "at least some college" (87% of cases and 81% of controls)

The Demographic data do exhibit a difference in the percentage of cases and controls who ever had smoked cigarettes; 202 Cases (44%) were ever smokers as compared to 336 (56%) of controls. Ever smoker cases reported a mean of 25.0 pack-years, while controls reported a mean of 28.4 pack-years. This is consistent with often observed inverse relation between smoking and Parkinson disease[23].

OUTDOOR WORK AND PARKINSON DISEASE

Main Results

Odds ratios for Parkinson disease (PD) and outdoor work are summarized in **Table 3.** These results show that outdoor work confers a modest protective effect on incidence of PD. The rudimentary model which identifies workers as having indoor only, a mixture of indoor and outdoor, or outdoor only jobs throughout their entire occupational history[1] showed a dose-response effect. Odds ratios (OR) for Parkinson disease were found to be 0.87 (95% CI 0.64-1.18) in research subjects with "indoor and outdoor jobs" compared to indoor workers, and 0.74 (95% CI 0.44-1.25) in "outdoor only" workers as compared to indoor workers.

Greatest risk reduction for PD was observed when subjects were classified into outdoor exposure categories **(Table 2)** according to job title which required them to spend the greatest proportion of the workday outdoors[22]. Using job title [longest job], ORs and 95% confidence intervals from unconditional logistic regression adjusting for age, sex and smoking were as follows: (< 50% of workday outdoors) 0.85 (0.54-1.32), (50-75% workday outdoors) 0.83 (0.54-1.29) and (> 75% workday outdoors) 0.85 (0.60-1.22) as compared to workers who labored exclusively indoors.

Utilizing job title which subject held for the longest duration [2] to place research participants into occupational exposure categories **(Table 2)** also indicated a reduction in PD risk for outdoor workers, but there was no evidence of dose-response. In fact ORs calculated using job title with

[1] Up to 10 years prior to diagnosis (cases) or reference (controls)
[2] Considers job titles held over subject's entire occupational history

longest duration[2] were inverse of those predicted based on occupational exposure category **(Table 2)**. This may be related to two primary factors. First, though occupational UVB exposure is important, encompassing 40-50 hours of an individual's exposure per week, other factors which were not accounted for in this model may be influential, as well. These factors include recreational and residential UVB exposure. Finally, though job held for longest duration accounts for a significant portion of an individual's occupational history, it may introduce bias by failing to factor in occupational UVB exposure that occurred prior to or after an individual held their job of longest duration.

Using cumulative number of years employed in any outdoor occupation as a method of exposure assessment did show a protective effect of outdoor work in relation to risk of PD. Utilizing this model, greatest reduction in PD risk was observed in individuals who had spent greater than 10 years laboring outdoors.

Results stratified by gender

Research participants were stratified by gender. This is particularly important given the reported 2:1 male to female predominance of PD in the scientific literature[18]. Odds ratios for Parkinson disease and outdoor work are summarized for males in **Table 4** and females in **Table 5.** In comparing male to female participants there were significant discrepancies. Upon examining the rudimentary model, , Odds Ratios (OR) for Parkinson disease in males were found to be 1.00 (95% CI 0.62-1.60) in research subjects with "indoor and outdoor jobs" compared to indoor workers, and 0.72 (95% CI 0.40-1.30) in "outdoor only" workers as compared to indoor workers. OOR) for Parkinson disease in females were found to be 1.23 (95% CI 0.74-2.04) in research subjects with "indoor and outdoor jobs" compared to indoor workers, and 0.60 (95% CI 0.16-2.21) in "outdoor only" workers as compared to indoor workers. This may be partially attributable to the fact that only 92/253 (36.3%) female research subjects reported occupations involving any outdoor work, as compared to 361/524 (68.8%) male participants.

All study methods utilized to capture outdoor work exposure did support a protective effect of outdoor work in terms of incidence of Idiopathic Parkinson disease. Our study results seems to illustrate that males have a sharper decline in Parkinson's risk than females when exposed to UVB light for the same length of time. However, these findings may be biased given the fact that only 23/322 (7%) of female, as compared to, 170/356 (47.7%) of males reported laboring outdoors for greater than 50% of their workday.

Finally, these study results also highlight that males may receive a more profound protective effect from PD after 10 years of primarily outdoor employment: < 10 years0.84 (95%CI 0.53-1.32); 10-<20 years 0.45 (95% CI 0.24-0.86). Females do not seem to experience this profound reduction in PD risk until they have spent greater than 20 years in an occupation that requires primarily outdoor employment: 10-<20 years (95% CI 0.51-3.08); > 20 years 0.44 (95%CI 0.11-1.71).

Effects of smoking were examined in all models, given the fact that smoking is known to be protective for PD. However, the interaction term was not statistically significant in any of the above models.

SUMMARY OF STUDY FINDINGS

Study results evidenced a modest protective effect for outdoor work and Parkinson disease. Furthermore, there is preliminary evidence that men receive greater benefit from UVB exposure in terms of reduction of PD risk. Furthermore, most notable reduction of risk of Parkinson Disease occurs in men after 10 yrs. of outdoor labor as compared to females who do not experience sharp decline in PD risk until they have spent greater than twenty years in an outdoor occupation. The interaction term for smoking, which is known to be protective for PD, was not statistically significant.

SCIENTIFIC LITERATURE REVIEW

A previous study has examined the association between outdoor work and idiopathic Parkinson disease[13] noting that job title can be used to estimate proportion of workday mandated outdoors. This is turn can serve as an ecological surrogate for sunlight, specifically UVB exposure. Also applicable, are other scientific studies which have examined the association between Squamous

Cell Carcinoma (SCC) and occupation[29]. Risk of Squamous Cell Cancer has been shown to be increased in individuals with chronic (e.g.,occupational) UVB exposure.[5] Providing further evidence that job title may indeed be a valid surrogate that can be used to estimate occupational UVB exposure.

STUDY STRENGTHS

Strengths of this study include ability to verify date of onset for Parkinson disease cases, as well as, a strict case definition which was rigorously verified by a panel of three trained neurologists. Furthermore, ability to directly control for important confounders, such as smoking, improves the validity of the data. Finally, previous studies[13] have only included men, whereas our study also includes women. This leads to improved generalizability of study findings, as well as, the ability to examine the extent that gender influences the association between PD and outdoor work.

STUDY LIMITATIONS

It is encouraging that our study evidenced a modest protective association between outdoor work and Parkinson disease. Particularly in area with limited UVB exposure throughout the year. Especially in light of the fact that Webb et. al has reported that at latitudes above 40 degrees [Seattle= 46 degrees] photoconversion of dehydrocholesterol to pre-vitamin D does not occur during winter months[30]. This further limits research subject's exposure to UVB radiation and ability of outdoor work to influence Parkinson disease risk within this study setting. However, in the future increasing number of study subjects, or conducting the study in an area of the state with a greater amount of UVB exposure may lead to results that are statistically significant.

Other study limitations include use of an occupational exposure questionnaire leading to information bias. This can be mitigated by verification of research subject's job title with their employers. Furthermore, requiring detailed job descriptions from study participants may be helpful in order to eliminate bias in determining actual percentage of workday subjects spend outdoors.

Information regarding research participant's residential UVB exposure, and outdoor hobbies would be helpful in developing a more comprehensive picture of an individual's total UVB exposure burden. Other important information includes detailed residential history, and occupational history including location of all jobs, and amount time employed in each job title (giving starting and ending month and year).

Furthermore, information detailed dietary data would be helpful in developing a comprehensive picture of vitamin D status. As well as, other important factors such as family history of neurodegenerative disease, particularly Parkinson disease are essential in evaluating an individual's risk.

FUTURE RESEARCH

Future PD research is essential given the fact that the standard of care, medication, is only efficacious for a finite period of time and may cause serious extra-pyramidal effects. New avenues of PD research focusing on modifiable environmental pathways show promise. This study highlights that work in an outdoor environment offers a modest protective effect in terms of Parkinson disease incidence. With refinement of its methodology using advanced technologies such as Geographic Information System (GIS), the method of occupational exposure classification detailed in the paper above could be refined providing higher quality of data. The prospect that a natural resource, such as the sun, has the potential to provide a therapeutic role to assist patients with a progressive neurodegenerative disease is definitely encouraging.

TABLE 1 Demographic Characteristics of Parkinson's Disease (PD) Cases and Controls[1]

	Cases	Controls
	N=456	N=595
	n (%)	n (%)
Age at diagnosis/reference years		
<60	116 (25)	106 (18)
≥ 60	340 (75)	489 (82)
Mean (std. deviation)	66 (10.1)	68 (8.5)
Median (range)	67 (28-88)	70 (43-86)
Gender		
Female	165 (36)	218 (37)
Male	291 (64)	377 (63)
Smoking Status[2]		
Never	254 (56)	259 (44)
Ever	202 (44)	336 (56)
Pack-years (mean (std. dev))[2]	25.0 (24.2)	28.4 (25.5)
Education		
< High School	16 (4)	35 (6)
High School	42 (9)	79 (13)
Some College	177 (39)	251 (42)
College Degree	74 (16)	74 (13)
Graduate Degree	147 (32)	156 (26)
First Degree Relatives with PD		
Yes	40 (9)	23 (4)
No	321(70)	436 (73)
Unknown	95 (21)	136 (23)
Birth year (median (range))	1932 (1908-1976)	1930 (1911-1957)
Number of years worked (median (range))[3]	3 (1-18)	3 (1-15)
Years worked (median (range))[3]	35 (2-56)	36 (2-58)

[1] Non-Hispanic Caucasian subjects only; excludes 34 cases and 49 controls with other race/ethnicity
[2] Includes cigarette smokers only
[3] Calculated with 10 year lag from diagnosis/reference year. Excludes 9 cases and 17 controls with missing occupational history .

Table 2- Occupational Exposure Categories

Exposure category	% of work day spent outdoors	Job title
Indoor work	None	-Administrators -College Professors -Factory Workers -Healthcare Workers Laboratory Workers -Manufacturing Trades -Secondary (middle and high school) Teachers -Warehouse/Wholesale Workers
Moderate outdoor work	<50%	-Agricultural Consultants -Electrical Contractors -Electricians -Ferry Operators Gas Station Attendants -Iron Shipyard Workers -Miners -Movers -Nursery and Kindergarten Teachers -Public Building and Planning Workers -Policeman Real Estate Agents -Rescue Squad Workers (Paramedics and Firefighters) Stone Cutters
Frequent outdoor work	50-75%	-Bricklayers -Building Painter -Clay and Gravel Pit Workers -Fishery and Sailing Vessel Workers (Seamen) -General Construction Contractor Horticultural Personnel -Joiner -Laborer in the Extraction of Oil or Natural Gas Landscapers -Miller -Postmen -Public Building and Planning Workers -Sewer Department Workers -Shipbuilders -Window Washers -Zoological Workers
Maximal outdoor work	>75%	-Agricultural Workers -Animal Husbandry Workers -Chimney Sweeps Employees who work on scaffolding -Farmers -Fresh Water and Pond Fishery Workers -Forestry Personnel -Gardeners -Ocean and Coastal Fishery Workers -Orchard Workers -Paving Experts -Plant Nursery Workers -Roofers -Scuba Divers -Well Diggers
Not Classified	N/A	-Airline industry employees -Housewives -Military Personnel -Newspaper Employees - Other Service Connected with Transport -Part-Time Workers Prisoners -Railroad Workers -Retirees -Self-employed Individuals -Students Truck Drivers -Unemployed -Workers in Transport Services

TABLE 3 - Risk of Parkinson's Disease and Outdoor Work[a]

	Cases	Controls	OR (95% CI)[b] w/ 10 yr. lag time	Cases	Controls[e]	OR (95% CI)[b] w/o 10 yr. lag time
	N= 447	N=578		N= 447	N= 579	
	n (%)	n (%)		n (%)	n (%)	
Occupational Classification						
Types of Jobs						
Indoor job(s) only	188 (42)	228 (39)	1.0 (reference)	184 (41)	224 (39)	1.0 (reference)
Indoor and outdoor jobs[c]	159 (36)	218 (38)	0.87 (0.64-1.18)	163 (36)	226 (39)	0.85 (0.62-1.15)
Outdoor job(s) only	29 (6)	47 (8)	0.74 (0.44-1.25)	25 (6)	44 (8)	0.71 (0.41-1.24)
Unclassified[d]	71 (16)	85 (15)	1.00 (0.67-1.49)	75 (17)	85 (15)	1.06 (0.71-1.56)
% workday outdoors, maximum ever						
Indoor only	188 (42)	228 (39)	1.0 (reference)	184 (41)	224 (39)	1.0 (reference)
< 50%	44 (10)	61 (11)	0.85 (0.54-1.32)	42 (9)	63 (11)	0.79 (0.50-1.22)
50-75%	54 (12)	76 (13)	0.83(0.54-1.29)	54 (12)	77 (13)	0.81 (0.52-1.25)
> 75%	90 (20)	128 (22)	0.85 (0.60-1.22)	92 (21)	130 (23)	0.86 (0.60-1.23)
Unclassified[d]	71 (16)	85 (15)	1.00 (0.67-1.49)	75 (17)	85 (15)	1.06 (0.72-1.57)
Indoor only	300 (67)	378 (65)	1.0 (reference)	302 (68)	375)65)	1.0 (reference)
< 50%	30 (7)	44 (8)	0.88 (0.53-1.45)	27 (6)	45 (8)	0.80 (0.48-1.34)
50-75%	33 (7)	55 (9)	0.75 (0.47-1.21)	33 (7)	58 (10)	0.70 (0.43-1.12)
> 75%	13 (3)	16 (3)	0.97 (0.45-2.10)	10 (2)	16 (3)	0.72 (0.31-1.65)
Unclassified[d]	71 (16)	85 (15)	1.05 (0.73-1.52)	75 (17)	85 (15)	1.10 (0.76-1.57)
Years						
Indoor only	188 (42)	228 (39)	1.0 (reference)	184 (41)	224 (39)	1.0 (reference)
< 10	95 (21)	110 (19)	0.99 (0.69-1.41)	91 (20)	107 (19)	0.97 (0.68-1.39)
10-<20	30 (7)	53 (9)	0.64 (0.38-1.06)	26 (6)	46 (8)	0.69 (0.41-1.18)
≥ 20	63 (14)	102 (18)	0.79 (0.52-1.18)	71 (16)	117 (20)	0.73 (0.49-1.07)
Unclassified[d]	71 (16)	85 (15)	0.99 (0.67-1.48)	75 (17)	85 (15)	1.05 (0.71-1.55)

[a] Outdoor work exposure calculated up to 10 years prior to diagnosis (cases) or reference (controls); excludes 9 cases and 17 controls without occupational history data

[b] Odds ratios and 95% Confidence Intervals adjusted for age (continuous), sex, and smoking (ever/never and pack-years); restricted to non-Hispanic Caucasians

[c] Work history contains both indoor job(s) and job(s) with outdoor work

[d] > 25% of Work Years could not be classified in terms of percentage of workday spent outdoors

[e] Gained one control whose occupational history occurred predominately during the 10 year lag time

TABLE 4- PD and Outdoor Work, males[a]

	Cases	**Controls**	95% CI	**Cases**	**Controls**	95% CI
	N= 285	**N=368**	w/ 10 yr.	**N= 285**	**N= 368**	w/o10 yr.
	n (%)	**n (%)**	Lag time[b]	**n (%)**	**n (%)**	Lag time[b]
Occupational Classification						
Types of Jobs						
Indoor job(s) only	80 (28)	83 (23)	1.0 (reference)	79 (28)	82 (22)	1.0 (reference)
Indoor and outdoor jobs[c]	119 (42)	177 (48)	1.00 (0.62-1.60)	122 (42)	181 (49)	0.73 (0.49-1.08)
Outdoor job(s) only	25 (9)	40 (11)	0.72 (0.40-1.30)	22 (8)	38 (11)	0.69 (0.37-1.28)
Unclassified[d]	61 (21)	68 (18)	0.96 (0.60-1.54)	62 (22)	67 (18)	1.00 (0.62-1.61)
% workday outdoors, maximum ever						
Indoor only	80 (28)	83 (23)	1.0 (reference)	79 (27)	82 (22)	1.0 (reference)
< 50%	30 (11)	39 (11)	0.85 (0.48-1.50)	28 (10)	39 (11)	0.80 (0.44-1.43)
50-75%	51 (18)	71 (18)	0.77 (0.48-1.25)	51 (18)	72 (20)	0.75 (0.46-1.21)
> 75%	63 (22)	107 (29)	0.65 (0.42-1.02)	65 (23)	108 (29)	0.67 (0.43-1.05)
Unclassified[d]	61 (21)	68 (18)	0.96 (0.60-1.54)	62 (22)	67 (18)	1.00 (0.62-1.60)
Indoor only	157 (55)	199 (54)	1.0 (reference)	159 (56)	200 (54)	1.0 (reference)
< 50%	25 (9)	34 (8)	1.06 (0.60-1.88)	24 (8)	32 (9)	1.14 (0.64-2.03)
50-75%	31 (11)	52 (14)	0.77 (0.47-1.27)	30 (10)	55 (15)	0.70 (0.43-1.16)
> 75%	11 (4)	15 (4)	0.92 (0.40-2.09)	10 (4)	14 (4)	0.86 (0.36-2.03)
Unclassified[d]	61 (21)	68 (18)	1.15 (0.76-1.74)	62 (22)	67 (18)	1.19 (0.79-1.80)
Years						
Indoor only	80 (28)	83 (23)	1.0 (reference)	79 (28)	82 (22)	1.0 (reference)
< 10	65 (23)	81 (22)	0.84 (0.53-1.32)	62 (22)	79 (22)	0.82 (0.52-1.31)
10-<20	19 (7)	42 (11)	0.45 (0.24-0.86)	18 (6)	33 (9)	0.60 (0.31-1.17)
≥ 20	60 (21)	94 (26)	0.76 (0.48-1.21)	64 (22)	107 (29)	0.68 (0.44-1.06)
Unclassified[d]	61 (21)	68 (18)	0.96 (0.60-1.54)	62 (22)	67 (18)	1.00 (0.62-1.60)

[a] Outdoor work exposure calculated up to 10 years prior to diagnosis (cases) or reference (controls); excludes 6 cases and 9 controls without occupational history data

[b] Odds ratios and 95% Confidence Intervals adjusted for age (continuous), and smoking (ever/never and pack-years); restricted to non-Hispanic Caucasians

[c] Work history contains both indoor job(s) and job(s) with outdoor work

[d] > 25% of Work Years could not be classified in terms of percentage of workday spent outdoors

Table 5- Risk of Parkinson Disease and Outdoor Work, females[a]

	Cases N= 162 n (%)	Controlse N=210 n (%)	95% CI w/ 10 yr. Lag time[b]	Cases N= 162 n (%)	Controls N= 210 n (%)	95% Ci w/o10 yr. Lag time[b]
Occupational Classification						
Types of Jobs						
Indoor job(s) only	108 (67)	145 (69)	1.0 (reference)	105 (65)	142 (67)	1.0 (reference)
Indoor and outdoor jobs[c]	40 (25)	41 (20)	1.23 (0.74-2.05)	41 (25)	45 (21)	1.13 (0.68-1.86)
Outdoor job(s) only	4 (2)	7 (3)	0.60 (0.16-2.21)	3 (2)	6 (3)	0.78 (0.18-3.42)
Unclassified[d]	10 (6)	17 (8)	0.83 (0.36-1.92)	13 (8)	18 (9)	1.00 (0.46-2.17)
% workday outdoors, maximum ever						
Indoor only	108 (67)	145 (69)	1.0 (reference)	105 (65)	142 (67)	1.0 (reference)
< 50%	14 (9)	25 (10)	0.75 (0.36-1.56)	14 (9)	23 (11)	0.69 (0.34-1.42)
50-75%	3 (2)	5 (2)	0.84 (0.19-3.70)	3 (2)	5 (2)	0.84 (0.19-3.72)
> 75%	27 (17)	21 (10)	1.62 (0.86-3.04)	27 (17)	22 (10)	1.62 (0.86-3.05)
Unclassified[d]	10 (6)	17 (8)	0.83 (0.36-1.93)	13 (8)	18 (9)	1.00 (0.46-2.17)
% workday outdoors, longest job						
Indoor only	143 (88)	179 (85)	1.0 (reference)	143 (88)	175 (83)	1.0 (reference)
< 50%	5 (3)	10 (5)	0.46 (0.15-1.40)	3 (2)	13 (6)	0.24 (0.07-0.86)
50-75%	2 (1)	3 (1)	0.94 (0.15-6.09)	3 (1)	3 (1)	1.33 (0.25-7.11)
> 75%	2 (1)	1 (1)	2.09 (0.17-25.0)	0 (0)	2 (1)	(omitted)
Unclassified[d]	10 (6)	17 (8)	0.78 (0.34-1.80)	13 (8)	18 (9)	0.92 (0.43-1.98)
Years						
Indoor only	108 (67)	145 (69)	1.0 (reference)	105 (65)	142 (67)	1.0 (reference)
< 10	30 (19)	29 (14)	1.30 (0.73-2.31)	29 (18)	28 (13)	1.28 (0.71-2.31)
10-<20	11 (7)	11 (5)	1.25 (0.51-3.03)	8 (5)	13 (6)	0.93 (0.36-2.39)
≥ 20	3 (2)	8 (4)	0.44 (0.11-1.71)	7 (4)	10 (5)	0.77 (0.28-2.11)
Unclassified[d]	10 (6)	17 (8)	0.83 (0.36-1.93)	13 (8)	18 (9)	1.00 (0.46-2.17)

[a] Outdoor work exposure calculated up to 10 years prior to diagnosis (cases) or reference (controls); excludes 3 cases and 8 controls without occupational history data

[b] Odds ratios and 95% Confidence Intervals adjusted for age (continuous), and smoking (ever/never and pack-years); restricted to non-Hispanic Caucasians

[c] Work history contains both indoor job(s) and job(s) with outdoor work

[d] > 25% of Work Years could not be classified in terms of percentage of workday spent outdoors

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