Firefighters and Parkinson's Disease Risk

Report to the Legislature regarding inclusion of Parkinson's disease into RCW 51.32.185

Washington State Advisory Committee on Firefighter Presumption

SHARP Technical Report 101-03-2023

July/2023

Contents

Tables

ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
L&I	Washington State Department of Labor and Industries
NIOSH	National Institute for Occupational Safety and Health
NOMS	National Occupational Mortality Surveillance
NR	Not reported
OR	Odds ratio
PD	Parkinson's disease
PMR	Proportionate mortality ratio
RR	Risk ratio
SHARP	Safety and Health Assessment and Research for Prevention
SIR	Standardized incidence ratio
SRR	Standardized rate ratio
WA	Washington State

SUGGESTED CITATION

Washington Department of Labor and Industries [2023]. Firefighters and Parkinson's Disease Risk: Report to the Legislature regarding inclusion of Parkinson's disease into RCW 51.32.185. By LaSee, CR; Bonauto, DK; Cohen, MA; Wasserman, CR; Friedman, LS; Harrison, RJ; Zhang, C; Nam, JY. Olympia, WA: Washington State Department of Labor and Industries, Safety and Health Assessment and Research for Prevention Program, L&I SHARP Publication #101-03-2023.

KEYWORDS

SHARP, Parkinson's disease, Firefighter, Firefighting, Presumption

EXECUTIVE SUMMARY

In Washington State (WA), certain medical conditions diagnosed in career firefighters are presumed to be occupational diseases according to the firefighter presumption law (RCW 51.32.185). In a 2019 amendment, the law established the creation of the Firefighter Presumption Advisory Committee, a committee comprised of experts from various occupational safety and health disciplines, to provide a scientifically based recommendation to state lawmakers about whether additional diseases or disorders should be added to the firefighter presumption law. The committee is chaired by the research director of the Washington State Department of Labor and Industries' (L&I) Safety and Health Assessment and Research for Prevention (SHARP) program and is supported by SHARP research staff.

On February 1, 2023, two Washington State legislators requested that the Firefighter Presumption Advisory Committee review the scientific literature related to Parkinson's disease (PD) among firefighters. L&I mobilized the Firefighter Presumption Advisory Committee and facilitated their review of the best available research. The Firefighter Presumption Advisory Committee reviewed scientific evidence about the PD burden in firefighters compared to other occupations, workplace exposures associated with PD, and whether firefighter-related workplace exposures are associated with PD. The purpose of this study was to (1) determine if firefighters are at a higher risk of developing PD compared to other workers and (2) provide a recommendation about whether PD should be included in the firefighter presumption law.

Key Findings

Parkinson's disease by occupation

- Epidemiologic studies reporting risk of PD by occupation did not report estimates for firefighters specifically, but rather included firefighters within broader occupational groups, such as "protection workers" or "service workers." None of these published, peer-reviewed studies reported a statistically significant increased risk of PD among protection or service workers compared to other workers.
- Evaluation of two occupational mortality databases yielded proportionate mortality ratio (PMR) estimates based on relatively few deaths. The WA Occupational Mortality Data from 1950-2010 had two PD deaths in firefighters aged 20-64 years, with a PMR of 117 that was not statistically significantly elevated. NIOSH's National Occupational Mortality database aggregated multiple years of national data, reporting 8 deaths in firefighters aged 20-64 years, with a statistically significantly elevated PMR of 241.

Occupational exposures associated with Parkinson's disease

- Occupational and environmental exposures to pesticides and chlorinated solvents have been associated with elevated risk of PD. Other research has demonstrated associations between PD and metals (such as lead, manganese, mercury, and iron), though results have been mixed.

However, there is little evidence to suggest that firefighters are routinely exposed to pesticides, solvents, or metals.

- There is growing evidence to suggest that air pollution, specifically exposure to fine particulate matter ($PM_{2.5}$), may be associated with PD. Firefighters' exposure to $PM_{2.5}$ may occur during a fire response, and such occupational exposures reflect the excess risk firefighters may have for PD relative to the general population. Such elevated exposures have not resulted in elevated risk estimates for PD in firefighters in occupational epidemiology studies.

Firefighter exposures and their associations with Parkinson's disease

- Per- and polyfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs), and shiftwork are common workplace hazards for firefighters. However, there is little to no data suggesting that these exposures are linked to an increase in PD risk.

Advisory Committee Recommendation

This report and the subsequent recommendation only address the risk of PD in firefighters as a collective group under the presumption law. The content of this report and the recommendation presented here are not intended to and should not be used for a causal determination of PD in an individual firefighter. In such instances individual susceptibility and occupational exposures can be assessed to explore causality.

Based on a review of the current scientific literature, the committee has not found sufficient evidence for an association between firefighting and PD to warrant inclusion of PD into WA's presumption law. Scientific inquiry is not static, and additional research will broaden our understanding of environmental, occupational, and genetic risks for PD. As more research evidence regarding these risks for PD emerges, a subsequent request for a review of PD for inclusion into Washington presumption law may be necessary.

INTRODUCTION

Washington State Presumption Law

In Washington State, workers seeking workers' compensation benefits must provide evidence to demonstrate that their injury or illness was caused by work. This can be complicated for certain workers, such as career firefighters, who are at risk of developing chronic illnesses years after hazardous workplace exposures. As a result, WA has enacted a law establishing a prima facie presumption that certain illnesses among firefighters are occupational diseases (RCW 51.23.185). First passed in 1987, this law has been expanded several times and now includes: respiratory diseases; any heart problems experienced within 72 hours of exposure to smoke, fumes, or toxic substances or experienced within 24 hours of strenuous physical exertion due to firefighting activities; certain types of cancers for firefighters after serving at least 10 years; select infectious diseases; and posttraumatic stress disorder for firefighters after serving at least 10 years.

Starting in 2019, the law also established an advisory committee to review the scientific evidence and make recommendations to the legislature on whether additional diseases and disorders should be presumed to be occupational diseases. Ranking members of appropriate WA legislative committees may initiate a request for the advisory committee to review a specific disease or disorder. Once formally initiated, the advisory committee is tasked with reviewing the '*scientific literature on the disease or disorder, relevant exposures, and strength of the association between the specific occupations and the disease or disorder proposed for inclusion in this section*' (RCW 51.32.185). The committee must consider the relevance, quality, and quantity of the scientific literature and may consult nationally recognized subject matter experts if necessary. The advisory committee recommendation is made by a majority of voting members and summarized in a written report documenting the relevant scientific literature and rationale for their recommendation. Individual advisory committee members may provide a written dissent if desired.

The advisory committee is composed of five voting members who are not employed by L&I (two epidemiologists, two preventive medicine physicians, and one industrial hygienist) and is chaired by the research director of L&I's Safety and Health Assessment and Research for Prevention (SHARP) program. The current advisory committee members are as follows:

Dr. Cathy Wasserman

Cathy Wasserman, PhD, MPH, is the State Epidemiologist for Policy and Practice at the Washington State Department of Health, where she provides leadership, oversight and technical assistance regarding disease surveillance, epidemiologic methods and standards, non-infectious disease cluster investigations, population surveys and related policy. She is an Affiliate Assistant Professor in Epidemiology at the University of Washington School of Public Health, and completed her graduate studies at the University of California, Berkeley.

Dr. Lee Friedman

Professor Lee Friedman, PhD, MSc, is faculty at the University of Illinois Chicago School of Public Health in the Division of Environmental and Occupational Health Sciences. He has a PhD in occupational epidemiology with more than 20 years of experience in the field of occupational health and safety. His occupational health research principally covers occupational health surveillance, injury prevention at work, and precarious employment. He specializes in analyses of large population-based datasets, longitudinal cohorts, surveillance systems, data linkage and multi-center projects. He currently leads the CDC-NIOSH funded state occupational surveillance program in Illinois.

Dr. Chunbai Zhang:

Dr. Zhang, MD, MPH, is the Director of Employee Occupational Health at the Veterans Affairs Puget Sound Health Care System in Seattle. He also serves as an Assistant Professor at the University of Washington School of Medicine and an Adjunct Professor at the University of Washington School of Public Health. Dr. Zhang received his medical degree from Geisel School of Medicine at Dartmouth and is board certified in internal medicine, occupational medicine, and sleep medicine.

Dr. Robert Harrison:

Dr. Harrison, MD, MPH, is a Public Health Medical Officer with the California Department of Public Health Occupational Health Branch and Clinical Professor at the University of California, San Francisco in the Division of Occupational and Environmental Medicine. He established the UCSF Occupational Health Services, where he has diagnosed and treated thousands of work and environmental injuries and illnesses. He has designed and implemented numerous medical monitoring programs for workplace exposures, and has consulted widely with employers, health care professionals, and labor organizations on the prevention of work-related injuries and illnesses. Dr. Harrison has led many work and environmental investigations of disease outbreaks. He has served as a technical and scientific consultant to Federal OSHA and CDC/NIOSH, and was a member of the California Occupational Safety and Health Standards Board. His research interests include the collection and analyses of California and national data on the incidence of work-related injuries and illnesses. Dr. Harrison has authored or co-authored more than 50 peer-reviewed journal articles, and more than 40 book chapters/contributed articles/letters to the editor. He is the co-editor of the most recent edition of the textbook Occupational and Environmental Medicine (McGraw-Hill Education, New York, NY, 2021).

Dr. Martin Cohen:

Martin Cohen is a Teaching Professor, Assistant Chair for Stakeholder Engagement, and Director of the Field Research and Consultation Group at the University of Washington's Department of Environmental and Occupational Health Sciences. He is a Certified

Industrial Hygienist and Certified Safety Professional and holds a Doctorate of Science (ScD) degree from the Harvard University School of Public Health in Exposure Assessment. He specializes in the assessment of workplace exposures and the development of new assessment methods.

Dr. David Bonauto (Non-voting chair):

David Bonauto, MD, MPH, is the Research Director for the Washington State Department of Labor and Industries' Safety and Health Assessment and Research for Prevention (SHARP) program. He has 23 years of experience in occupational safety and health research, has published numerous peer reviewed articles, and has served on national, regional, and state groups and committees focused on preventing workplace injuries and illness and improving occupational safety and health research and prevention activities.

The advisory committee is supported by one dedicated SHARP epidemiologist, Ms. Claire LaSee, MPH/MSW, and is further assisted by other L&I staff members as needed.

Request for Review: Parkinson's Disease

On February 1, 2023, the Department of Labor and Industries (L&I) received a letter from two WA state legislators proposing PD for inclusion into the WA workers' compensation law as a presumed occupational disease for firefighters (See Appendix A: Legislative Request). This request resulted in the mobilization of the expert advisory committee on firefighter presumption.

PD is the second most common neurodegenerative disorder and is strongly associated with age. Symptoms of PD result from progressive loss of dopaminergic neurons in the midbrain, mostly in the substantia nigra pars compacta. PD presents clinically with motor symptoms such as resting tremor, cogwheel rigidity, and slowed movements and non-motor symptoms such as sleep disorders and mood and affect disorders. Pathological and experimental studies indicate that oxidative stress, proteolytic stress, and inflammation contribute to the pathogenesis of PD (Alexander, 2004).

It is generally accepted that the cause of PD within the general population is unknown, although there may be specific occupational exposures linked to the development of Parkinson-like symptoms. Risk for PD is generally considered to have a genetic link, with possible associations with environmental exposures. Older age is a strong risk factor for PD. Young onset PD occurs in people younger than 50 years and is generally considered to be associated with genetics, especially those with a family history of PD (Post, 2020).

Criteria for causation

While the legislature did not provide specific criteria to be used to weigh the scientific evidence regarding whether a condition should be included in the law, the committee's general approach is to use Sir Austin Bradford Hill's observations regarding how a causal relationship between an exposure and a disease might be considered (Hill 1965). Hill's nine considerations include the following:

1. **Strength of association:** The association between the exposed population and the disease or injury outcome is of a sufficient magnitude. The stronger the association the more likely it is that its relation is causal.
2. **Consistency:** The association is consistent across a number of studies in different populations and study designs. Evidence of an association may occur due to statistical chance in any one study, whereas this is reduced if there are multiple studies demonstrating a statistically significant increased risk.
3. **Specificity:** There is a specificity in the association of the exposure with the disease or outcome.
4. **Temporality:** The chemical, physical and biologic exposure precedes the disease.
5. **Biological gradient:** There is an exposure-response relationship, such that an increasing amount of exposure increases the risk.
6. **Plausibility:** There is biologic plausibility that the chemical, physical, or biological occupational exposures are associated with the disease.
7. **Coherence:** The association is coherent with what is known about the disease, existing theory or knowledge of causation.
8. **Experiment:** Alternative explanations of the potential relationship between the disease and the exposure are eliminated or controlled for. Additional factors related to both the exposure and the disease are accounted for either in the study design or analysis.
9. **Analogy:** When strong evidence suggests a causal relationship between a specific exposure and a disease, then other similar exposures may lead to analogous outcomes.

We evaluated the body of evidence using these nine considerations as a framework upon which to base our recommendation. We primarily used epidemiological studies to assess **strength of the association**, **consistency**, **specificity**, **temporality**, **biological gradient**, and **analogy,** and we looked to relevant exposure data when assessing **plausibility**. Both epidemiological studies and exposure studies were used to assess **coherence**. Due to the nature of the occupational exposure and severity of the disease, we anticipated that it would be unlikely any evidence would allow for complete consideration of **experiment**.

This report is organized into two components. The first component presents our search and summarization of evidence from epidemiologic studies evaluating whether firefighters and Emergency Medical Services (EMS) workers are at higher risk of PD compared to workers in other occupations. We searched publication databases to identify peer-reviewed, scientific publications that estimate risk by occupation for PD, and specifically for firefighters and emergency response workers. Such epidemiologic studies included case-control, retrospective or prospective cohort studies, and meta-analyses.

The second component of the evaluation describes the review of existing scientific literature to determine if 1) firefighters have workplace exposures currently associated with PD, and 2) whether known firefighter chemical and physical exposures have been evaluated as risks for the development of PD. The committee used this information to assess the biologic plausibility of firefighting as a cause of PD, and whether such an association is consistent with the current knowledge of risks for PD.

METHODS

Occupational Mortality Databases

We described the number of deaths and proportional mortality ratios (PMRs) of PD in firefighters using two different databases assessing the usual occupation and cause of death listed on the death certificate. The WA Occupational Mortality Database (WA DOH 2011) includes deaths over a 60-year span. The National Occupational Mortality database (NIOSH 2019) reports deaths from 26 US states over two different time periods, the latter of which (a combination of 1999, 2003-2004, 2007-2014) includes WA data. Queries were restricted to working-aged adults.

Identifying Epidemiologic Studies

In March 2023, we searched the PubMed Central online database for peer-reviewed research articles about PD in firefighters using the following search terms:

((Parkinson OR “Parkinsonian Disorders” [mh]) AND*

(Firefighter OR firefighting))

We did not limit the search by study design or any other factors. This query yielded two results, and the titles and abstracts of these articles were reviewed to determine their relevance to our research question.

To identify additional articles assessing the risk or prevalence of PD in firefighters, we searched *scholar.google.com* and *google.com* using various combinations of previously used search terms as well as more general search terms such as “Parkinson*” and “Occupation.” We reviewed non-peer reviewed sources, such as website and discussion boards related to PD in firefighters looking for additional references to peer-reviewed research articles. Through this ad hoc search strategy, an additional 52 articles were identified (Appendix B).

All relevant articles identified in the initial and secondary search were read and reviewed. When an article reported an estimate related to PD in firefighters, data about study design and the study results were extracted and organized into tables. Elements of study design, such as length of study, number of subjects, and data sources, were included to characterize the quality and relevance of the study.

Review of Exposure Data

In the context of the review of the existing scientific literature, we considered two questions to aid in the recommendations of the presumption advisory committee.

1. What workplace exposures are suspected to be associated with PD? Are these exposures related to firefighting?
2. Are known chemical and physical exposures to firefighters (e.g. shift work) associated with PD?

Literature searches to evaluate the relationships between chemical exposures and PD were conducted in PubMed Central and Google Scholar. Generally, search terms included:

Parkinson's disease AND *<Exposure Name>*

Parkinson's disease/etiology AND *<Exposure Name>*

Parkinson's diseases/epidemiology AND *<Exposure Name>*

There are many and varied approaches to conducting animal, toxicological, and human studies evaluating environmental or occupational etiologies for PD. Thus, the results from various queries were filtered to identify recent meta-analyses and literature reviews summarizing a possible relationship between the exposure and PD. Due to time and resource constraints, the reviews were not intended to be comprehensive and exhaustive. The approach was to detect meaningful signals for an association between firefighting exposures and the risk for developing PD. This review was restricted to PD exposures and did not include studies related to drug-induced or toxin-induced parkinsonism, e.g. following acute carbon monoxide poisoning.

RESULTS

Epidemiological Studies

Literature search

In total, we identified 54 references to review. After reviewing the title and abstracts of the two articles captured in the initial PubMed Central search, one article was deemed not relevant to our research question (Rami, 2009) and was not reviewed further. One article (Ye, 2017), was published in Korean, so we were unable to review the manuscript, aside from the title, abstract, tables, and references that were all provided in English. For the secondary search, we were able to obtain full text for all articles except Minerbo 1990, as this reference was for an in-person academic conference presentation. For all other articles, the full text was read and reviewed.

Magnitude of association

We identified one study assessing the risk of PD in firefighters (Minerbo 1990), which implied a nearly 10x increase in PD among firefighters in Houston, Texas. Despite extensive searches, we were not able to find the published results of this study in any peer-reviewed journals. As such, the study's methodology, results, and conclusion were not peer-reviewed. To our knowledge, this conference abstract reference is the sole source of information that states firefighters are at a 10x increased risk of developing PD.

Table 1 describes the PMR of PD in firefighters from WA-specific and national mortality databases for adults of working ages. Table 2 summarizes ten case-control studies assessing odds of people in firefighting-related occupations developing PD versus people in other occupations developing PD. Table 3 summarizes the two cohort studies assessing risk of PD in firefighting-related occupations compared to other adults who had not worked in firefighting-related occupations. Studies summarized in Tables 2 and 3 did not report risk or odds of developing PD in firefighters specifically, but instead reported results for more broad occupations, such as "protection workers", which includes all other community protection workers, or even more broadly, "service workers." Three case-control studies (Kirkey 2001, Park 2004, Park 2005) also assessed odds of developing PD in public administration industry workers, which is the broader industry group that includes firefighters, law enforcement officers, and others who manage public programs. None of the studies summarized in Table 2 or Table 3 reported that people working in firefighting-related occupations are at a statistically significant increased risk or odds of developing PD.

Table 1. National and WA-State specific Parkinson's disease deaths among firefighters.

Source	Years	Firefighter Deaths	PMR (95% CI)	p-value
WA Occupational Mortality Database (males, ages 20-64) (WA DOH 2011)	1950-2010	2	117*	0.69084
NOMS (all races/sexes combined, ages 18-64) (NIOSH 2019)	1985-1998	<5		
NOMS (all races/sexes combined, ages 18-64) (NIOSH 2019)	1999, 2003-2004, 2007-2014	8	241 (104, 474)	

*95% CI not reported

Dose response

In a convenience survey of FFs from Massachusetts, Kotwani et al. (2022) found that the number of years as a firefighter, the number of days per week worked, and number of fire calls were positively associated with several PD-related symptoms, such as hyposmia (decreased ability to detect odor), micrographia (small handwriting), and decreased walking pace. However, the three main PD symptoms assessed are not specific to PD and have a variety of other possible etiologies, including the natural aging process. Additionally, the study was advertised to FFs as a PD study, which may have contributed to a reporting bias as well as confirmation biases among participants. No other studies have assessed whether an increase in firefighting related exposures lead to an increased risk of PD or PD-related symptoms.

Parkinson's disease in other occupations

The association between occupation and PD remains elusive. Of the eighteen studies investigating odds or risk of developing PD by occupation, six studies found no elevated risk of developing PD in any of the occupational groups studied. Twelve studies reported at least one occupational group with a statically significant increase in risk or odds of developing PD. However, there was little consistency among

Table 2. Case-control studies reporting on Parkinson's Disease among firefighting-related occupations and injuries.

First Author, year	Region and Study Years	Sample size	Cases	Controls	Data Sources/definitions: Occupation	Data Sources/definitions: Parkinson's Disease	Cofactors	Subpopulation of interest	Point estimate (95% CI)
Beard, 2017	US, 30 states; 1985-1999, 2003-2004, 2007-2011	N= 12,128,774 deaths; n= 115,262 total PD deaths; n= 148,058 deaths among protective services; n=1,295 PD deaths among protective services	Decedents in the National Occupational Mortality Surveillance (NOMS) collaborative	All causes of deaths in NOMS	NOMS coded 'usual occupation' from death certificates: Protective Services	NOMS: PD defined as those having an ICD-9 (332) or ICD-10 (G20) code listed as an underlying or contributing cause of death on death certificate	Age, sex, race, calendar year	N/A	PMR=0.86 (0.81, 0.91)
Firestone, 2010	US, Pacific Northwest; 1992-2006	N=930; n=404 cases, n=526 controls	Patients newly diagnosed idiopathic PD from Group Health Cooperative (GHC) and UW	GHC enrollees with no history of PD, matched by sex and age	Self-report from patient interview: Military or Protective Services	Neurologist panel confirming PD from medical chart review	Age, ethnicity, smoking status	Military or Protective services Males (n=46 cases, n=60 controls) Females (n=4 cases, n=1 control)	OR=0.9 (0.61, 1.45) OR=8.3 (0.80, 85.96)
Goldman, 2005	New York City, Atlanta, Sunnyvale CA	NR	Movement disorder clinic patients at 3 clinics	Bureau of Labor Statistics Metro Area Cross-Industry Occupational Employment Estimates (1998)	Clinic intake questionnaire; job category= Protection	Clinic diagnosis of PD or parkinsonism	Geographic area	"Protection" job category, risk of onset ≤50; n= NR	OR= 2.5 (NR); *P* >.05
Kirkey, 2001	Metro Detroit; 1991-1995	N=608; n=144 cases and n=464 controls	Patients 50 years old or older with PD who received primary care services in the last 5 years from Henry Ford Health System (HFHS). Patients were excluded if they (1) had a diagnosis of secondary parkinsonism or other neurologic disorder, (2) had PD symptoms for 10+ years,	Patients 50 years old or older without PD receiving primary care services from HFHS within the last 5 years; matched to cases on age, sex, and race.	Occupation from patient questionnaire, job held for at least 6 months since the age of 18	Presence of PD ICD-9CM code (332.0), reviewed by neurologist	Age, race, sex	Occupation= Protective Services[1], n=16 cases, n=63 controls Industry= Public Administration[2], n=68 cases, n=216 controls	OR=0.80 (0.44, 1.43) OR=1.03 (0.71, 1.49)

[1] Protective services (according to the Dictionary of Occupational Titles) includes: crossing tenders and bridge operators, security guards and correctional officers, firefighters, police officers and detectives, sheriffs and bailiffs, armed forces, and other protective service occupations

[2] Public Administration industries (defined by the Standard Industrial Classification [SIC] codes) includes government, law enforcement, public finance, human resources, Housing programs, environmental quality, economic programs, national security, international affairs, etc.

First Author, year	Region and Study Years	Sample size	Cases	Controls	Data Sources/definitions: Occupation	Data Sources/definitions: Parkinson's Disease	Cofactors	Subpopulation of interest	Point estimate (95% CI)
			(3) had dementia or did not speak English.						
Park, 2004	South Korea; 2001-	N= 335; n=105 PD cases, n=129 control group 1, n=101 control group 2	PD patients diagnosed in 2001 or later from a university neurological clinic in Busan. Exclusions included patients diagnosed with Parkinsonism plus, secondary Parkinsonism, and essential tremor.	Two groups: (1) cerebrovascular disease (CVD) patients from the same clinic (2) healthy individuals who were examined at the same university hospital	In-person interviews, longest held occupation and industry	Physician diagnosis[3]	Age, sex, smoking	Industry: Public Administration[4] (n=7 cases, n=3 CVD controls) Occupation: Service workers[5] (n=7 cases, n=11 CVD controls) Industry: Public Administration[4] (n=7 cases, n=1 healthy control) Occupation: Service workers[6] (n=7 cases, n=8 healthy controls)	OR=3.74 (0.90, 15.56) OR=0.86 (0.31, 2.43) OR=5.15 (0.59, 44.77) OR=0.75 (0.24, 2.34)
Park, 2005	South Korea; 2001-	N=676; n=367 cases, n=309 controls)	Patients under 70 years old diagnosed with PD in 2001 or later from 5 neurology clinics in Seoul and Busan. Exclusions included patients diagnosed with Parkinsonism plus, secondary Parkinsonism, and essential tremor	Cerebrovascular disease patients without PD	Patient questionnaires and interviews, longest held industry and occupation	Physician diagnosis[3]	Sex, age, smoking status, education level	Industry: Public Administration[4] (n=18 cases, n=8 controls) Occupation: Personal and protective service workers (n=3 cases, n=1 control)	OR=1.71 (0.66, 4.43) OR=1.81 (0.17, 19.21)

[3] Diagnosis according to the UK PD Society Brain Bank Clinic diagnostic criteria

[4] Public Administration industries (according to Korean Standard Industrial Classifications) includes executive, legislative, and general government support; administration of industrial and social policy of community, foreign affairs and defense activities, public order and safety activities, and compulsory social security activities

[5] Service worker occupations (according to the Korean Standard Classification of Occupations) include police, fire fighting and security related service occupations; caregiving, health and personal service workers; transport and leisure services occupations; cooking and food service occupations

[6] Service worker occupations (according to the Korean Standard Classification of Occupations) include police, fire fighting and security related service occupations; caregiving, health and personal service workers; transport and leisure services occupations; cooking and food service occupations

First Author, year	Region and Study Years	Sample size	Cases	Controls	Data Sources/definitions		Cofactors	Subpopulation of interest	Point estimate (95% CI)
					Occupation	Parkinson's Disease			
Schulte, 1996	US, 27 states; 1982-1991	N=614 PD cases among black females; n=2 cases among black female protection workers; total deaths among black females NR	Decedents in the National Occupational Mortality Surveillance (NOMS) collaborative, black women	All causes of deaths in NOMS	NOMS coded 'usual occupation' from death certificates: Protection workers	NOMS data (PD defined an ICD-9 code [332] as an underlying or contributing cause of death on the death certificate)	Age	N/A	PMR=3.11 (0.38, 11.23)
Tanaka, 2011	Japan; 2006-2008	N=618; n=249 cases, n=369 controls	Patients from 11 hospitals who experienced PD onset within last 6 years	Patients without previous neurodegenerative diseases recruited from 4 of the 11 hospitals	Patient questionnaires (mailed and telephone follow-ups if needed), longest held occupation	Physician Diagnosis[7]	Gender, age, region of residence, education level, pack-years of smoking	Occupation: Protective services (n=4 cases, n=3 controls)	OR=2.73 (0.56, 14.86)
Tanner, 2009	US and Canada; 2004-2007	N=1,030; n=519 cases, n=511 controls	Patients from 8 North American movement disorders centers diagnosed with PD in last 8 years and who did not have of dementia	Non-blood associates of patients from the same clinics and individuals recruited through commercial telephone number lists. People with neurodegenerative disorders were excluded. Controls were matched to cases on age, sex, and location.	Telephone interviews, occupation held for at least 3 months	Physician diagnosis[8]	age, sex, race/ethnicity, cigarette pack years, caffeine use, alcohol use, head injury, duration of job	Occupation: Protective Services (n=36 cases, n=50 controls)	OR=0.71 (0.44, 1.15)
Teschke, 2014		N=808; n=403 cases, n=405 controls	Individuals 40-69 years of age who had an anti-parkinsonian	Individuals from the BC Ministry of Health Client	In-person interviews,	In-person physical assessing PD-related	Gender, birth year (5	Occupation: Protective service (n=20, n=11 controls)	OR=1.37 (0.63, 2.96)

[7] Diagnosis according to the UK PD Society Brain Bank Clinic diagnostic criteria

[8] Parkinsonism of no known cause defined by at least two signs (resting tremor, bradykinesia, rigidity, and postural reflex impairment) and one of the signs must be resting tremor or bradykinesia

First Author, year	Region and Study Years	Sample size	Cases	Controls	Data Sources/definitions		Cofactors	Subpopulation of interest	Point estimate (95% CI)
					Occupation	Parkinson's Disease			
	BC, Canada: 1995-2002		prescription medication reimbursed by PharmaCare. Exclusion criteria: long-term care facility residents, patients who filled a prescription for an antipsychotic drug, or took anti-parkinsonian medications for other purposes.	Registry without PD; matched to cases on age, sex, and geographic location.	occupation held for at least 6 months	symptoms conducted and reviewed by a neurologist	year groups), smoking (cumulative pack-years)	Occupation (held for at least 6 months 10 years prior to diagnosis): Protective service	OR=1.18 (0.53, 2.60)

Table 3. Cohort studies reporting on Parkinson's Disease among firefighting-related occupations and injuries.

First Author, year	Region	Years of F/U	Study Population	n	Data Source		Reference Population	Cofactors	Subpopulation of interest	obs	Risk estimate (95% CI)
					Occ	Disease					
Burstyn, 2019	US	average follow-up: 11.4 years	Women, ages 50-79, with a 3+ year life expectancy from 40 clinics across the US enrolled between 10/1/93 to 12/31/98 ;	80,646 women	self-report (occupational history questionnaire), coded to SOC 2010 codes	PD diagnosis reported as baseline, yearly patient questionnaires, if death was attributed to PD, or if they took meds consistent with PD diagnosis	all other women in the cohort (including those never employed, n=974)	Age at baseline, years of living on a farm, pack-years of smoking, coffee and alcohol consumption, region of the US, ethnicity, education, income, marital status	Protective service (SOC: 33-0000), n=640	22	RR=1.13 (0.75, 1.71)
Li, 2009	Sweden								Public Safety and Protection Workers By Sex:		

First Author, year	Region	Years of F/U	Study Population	n	Data Source: Occ	Data Source: Disease	Reference Population	Cofactors	Subpopulation of interest	obs	Risk estimate (95% CI)
		1987-2004	People over 30 years of age		Census Data (1960, 1970, and 1980)	Swedish Hospital Discharge Register (ICD-9: 332; ICD-10: G20, G21)		Age, region, education	Males (1960 census)	128	SIR=1.02 (0.85, 1.22)
									Women (1970 Census)	4	SIR=0.80 (0.21, 2.07)
									Public safety and Protection workers (males only) reporting same occupation in repeat censuses:		
									Census 1960 and 1970	84	SIR=1.01 (0.81, 1,26)
									Census 1960, 1970, 1980	55	SIR=1.17 (0.88, 1.52)

studies. See Appendix C for studies assessing association between risk of PD and occupation. The occupational groups found to have a statistically significant increase in odds of developing PD were variable, representing jobs with vastly different work environments and workplace hazards and are dissimilar to the expected workplace exposures of firefighters.

Exposure Studies

Firefighters are known to have workplace exposures that can adversely impact their health. These exposures include mixed chemical exposures in the context of a fire response or physical stressors associated with shift work and sleep deprivation. The relationship between firefighting chemical and physical exposures and the risk for developing PD has not been extensively studied. We therefore framed the review to address two questions:

1. What workplace exposures are suspected of being associated with PD? Are these exposures related to firefighting?
2. Are known chemical and physical exposures to firefighters (e.g. shift work) associated with PD?

Exposures associated with Parkinson's disease

Pesticides, solvents, metals, and air pollution are considered possible causative agents for PD. Although there is likely significant variation across the fire service regarding exposure, a general literature review was conducted for each exposure. The goal was to affirm suggestive evidence of an association between the exposure and PD, and if affirmed, to consider if most firefighters are routinely exposed to such agents.

Pesticides

Pesticides have been extensively studied as causative of PD. There is recognition of an increased risk of PD with exposure to pesticides (NINDS, 2023), and recognition of their neurotoxicological properties in the pathogenesis of neurodegenerative disorders.

Experimental models broadly implicate oxidative stress and mitochondrial inhibition (Tanner, 2011; Weed, 2021) as biologically plausible pathways causing PD. PD has been associated with exposure to pesticides causing oxidative stress (OR = 2.0; 95%CI: 1.2-3.6) and those which inhibit mitochondrial complex one (OR = 1.7; 95%CI: 1.0-2.8) (Tanner, 2011). Multiple meta-analyses reporting summary risk estimates for exposure to pesticides and PD have been published. A meta-analysis by Gunnarsson and Bodin (2023) reviewing 23 studies of multiple designs (case-control, cohort, or cross-sectional) reported a weighted relative risk estimate of 1.67 (95% CI: 1.42-1.97) for exposure to any pesticide. Ahmed et al. (2017) published a meta-analysis of case-controlled studies reporting a pooled odds ratio of 1.46 (95% CI: 1.21 – 1.77) for pesticides and PD although there was significant heterogeneity among included studies.

Ohlander et al. (2022) reported that summary risk estimates of pesticide exposure were significantly elevated regardless of exposure assessment methods. Summary risk estimates were significantly elevated when assessing by: 1) job titles or through self-reported work exposures (sRR=1.34; 95%CI 1.16, 1.54); 2) questionnaires, interviews, or through expert level assessments (sRR=1.45; 95% CI: 1.18, 1.76); or 3) expert case-by-case assessments or job-exposure matrices JEMS (sRR=1.56; 95% CI: 1.21, 2.01). Regardless of how occupational exposure was assessed, the summary risk estimates were significantly elevated.

Further, studies have identified elevated risk of PD from exposure to specific pesticides, such as 2,4-Dichlorophenoxyacetic acid (OR = 2.59; 95%CI: 1.03-6.48) (Tanner, 2009) and organochlorine pesticides (OR=2.4; 95% CI: 1.2-5.0) (Elbaz, 2009; Goldman, 2014). There is a need to further determine which specific pesticide or which class of pesticides may lead to an elevated risk of PD (Breckenridge, 2016). Finally, exposure to pesticides is associated with significantly elevated risk of gene alterations for genes associated with increased risk for PD, and these observations support the hypotheses of gene-environment interactions as an etiology for PD (Ahmed, 2017).

If an association between pesticides and PD exists, to use such information to support a presumption would require that firefighters as a group are exposed to pesticides as a part of their work activity. However, there is limited available evidence that firefighters are routinely exposed to pesticides. An analysis of six urinary biomarkers for organophosphate pesticide exposure demonstrated significantly elevated median exposure levels for firefighters after a fire response (Jayatilaka, 2019). A recent review of biomonitoring in firefighting found evidence of exposure to pyrethroid insecticides, phenoxyacetic acid herbicides, and organophosphorus insecticide metabolites in the urine and organochlorine pesticides in the blood, although the toxicologic relevance of these observations are not known (Barros, 2023). However, a study using silicone wrist bands to assess semi-volatile organic chemical exposure in 43 firefighters in North Carolina reported there were no meaningful differences in pesticide exposure levels when off-duty or on duty (Levasseur, 2022). A case series of acute exposure to pesticides with subsequent symptoms as reported through poison control centers have been published, although long term follow-up for these cases has not been studied (Calvert, 2006).

Solvents

Research demonstrating the association between solvent exposure and PD is growing although there are mixed assessments of such an association (Lock, 2013; Pezzoli, 2013). The most suggestive literature involves chlorinated liquid hydrocarbons which were mostly used in industrial applications but have come to be broadly distributed contaminants in ground water supplies. Case reports and an evaluation of PD occurrence in twins suggest chlorinated solvents, specifically trichloroethylene (TCE) and tetrachloroethylene (PERC), are associated with elevated risk of PD (Dorsey, 2023; Goldman, 2012). Resident exposure to TCE contaminated ground water at Camp Lejeune was associated with a 70% higher risk of PD relative to Camp Pendleton residents who were not exposed to TCE contaminated groundwater (Goldman, 2023). Experimental studies have demonstrated significant damage to the nigrostriatal dopamine system in rats following TCE administration (Gash, 2008; Liu, 2010).

However, similar to pesticides, it seems unlikely that firefighters have significant excess exposure to chlorinated solvents compared to the general population. Such solvents may be used in specific industrial applications but are unlikely products of combustion as TCE and PERC are non-flammable. Environmental monitoring studies reported non-detectable levels of PERC in a pre- and post-structural fire training exercise (Jahnke, 2021). Personal air sampling for TCE during structural fires reported exposure levels of 0.112-0.181 ppm (0.6 mg/m^3 – 0.97 mg/m^3) (Jahnke, 2021), while the current WA Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit is an 8 hour time-weighted average of 50 ppm (WAC 296-841). Additional biomonitoring and environmental sampling on the fire ground would be helpful to assess exposures to trichloroethylene and tetrachloroethylene.

Metals

Lead, manganese, mercury, and iron have underlying mechanistic pathways that may lead to neurotoxicity and PD (Caudle, 2012; Goldman, 2014; Pyatha, 2022). A recent meta-analysis reported summary odds ratios of 1.04 (95% CI: 1.01, 1.06) for manganese, 1.14 (95% CI: 0.64, 2.01) for lead, and 1.22 (95% CI: 0.70-2.14) for non-specified metal exposure, while there were inconclusive impacts of copper, iron, mercury, and zinc (Zhao, 2023). Similarly, a systematic review and meta-analysis of 24 articles reported a pooled risk ratio of 1.07 (95% CI 0.92-1.24) for metal exposure and PD (Chambers-Richards, 2023).

Like other possible PD exposures, it seems unlikely that firefighters are routinely exposed to metals. Biomonitoring results suggest low level exposure. For example, a convenience sample of 101 participating southern California firefighters revealed geometric mean blood levels for cadmium (0.19 ug/L; 95% CI 0.18-0.21) and lead (0.96 ug/dl; 95% CI 0.87-1.05) (Dobraca, 2015; Jahnke, 2021) which were below the blood cadmium levels and geometric mean adult blood lead levels (BLL) in healthy, non-exposed, nonsmokers according to the CDC (CDC 2005, CDC 2023).

Blood lead levels collected from firefighters as part of the World Trade Center response found statistically elevated BLLs in firefighters who were exposed at the WTC site, including subgroups present at the collapse, who arrived the day following the collapse, or worked in special operations relative to controls. However, none of the reported BLL in FFs were greater than 5 µg/dL, which is considered elevated according to the CDC (2023).

Air pollution/polycyclic aromatic hydrocarbons

As air pollution represents a mix of particulate matter and gases (nitrogen dioxide, sulfur dioxide, ozone, lead, carbon monoxide, etc.) and may have similarities to exposures during a fire response, this relationship is of interest. Comprehensive reviews of the health effects of air pollution, specifically of exposure to particulate matter less than 2.5 microns ($PM_{2.5}$), are presented in the United States Environmental Protection Agency's *Integrated Science Assessment for Particulate Matter* (2019) and the *Supplement to the 2019 Integrated Science Assessment for Particulate Matter* (2022). From the supplement –

'There was strong evidence for biologically plausible pathways that may underlie nervous system effects resulting from long-term exposure to $PM_{2.5}$. …. Although the loss of dopaminergic neurons in the substantia nigra, which is a hallmark of Parkinson's disease, was demonstrated in animals, epidemiologic studies did not report associations with Parkinson's disease' (US EPA, 2022, p. 2-11).

Biologic plausibility rests on pathways in which air pollutants are neurotoxic to the dopaminergic system, induce neuroinflammation, and cause oxidative stress (US EPA, 2019). Epidemiologic studies are inconsistent regarding an association between $PM_{2.5}$ and PD. The variability is reported to originate from 1) how outcome measures for PD are defined, e.g. incident cases, hospitalization, and death; 2) differences in lag between exposure and disease onset and the short durations of the observation period for the outcome; 3) variation in diagnostic certainty related to clinical confirmation or billing records; and 4) control of confounders, e.g. smoking, age (Murata, 2022). Despite these limitations, there have been multiple meta-analyses of epidemiologic studies of air pollution and PD. Kasgadali et al (2018) reported the pooled relative risk for the incidence of PD from six studies with long term exposure to $PM_{2.5}$ of 1.06 (95% CI: 0.99 – 1.14) per 10 mcg/m^3 increase. Gong et al (2023) reported a pooled odds ratio for PD from eight qualifying studies of 1.17 (95% CI: 1.00-1.33) for long-term $PM_{2.5}$ exposure. Fu et al. (2019) assessed human studies associated with the long-term effects of $PM_{2.5}$ and observed an increased risk of PD (RR= 1.34, 95% CI 1.04-1.73).

While further research will likely clarify the association between $PM_{2.5}$ exposure and PD, firefighters would need to be exposed to $PM_{2.5}$ in excess of the background exposures to the general population to have elevated risk. While the use of self-contained breathing apparatuses (SCBAs) provide respiratory protection factors of 10,000, use may not be consistent throughout a fire response. Historically, during the overhaul phase of a fire response, SCBAs may be removed. Measurements by Baxter (2014) reported an average $PM_{2.5}$ mass concentration during overhaul events of 5178 µg/m^3. Elevated exposures to $PM_{2.5}$ in the fire station, specifically the kitchen and firetruck bay added to the exposure. The study estimated a 24-hour time weighted average for $PM_{2.5}$ at 143 µg/m^3. It is also worth noting that the observed average time in exposure to overhaul was 33.5 minutes. The calculation of the 24-hour time weighted average for $PM_{2.5}$ showed that firefighters' exposure during a 24-hour work shift can exceed the EPA National Ambient Air Quality Standards 24-hour average of 35 µg/m^3, although exposure over any individual shift will be highly variable (Baxter, 2014).

Further, $PM_{2.5}$ exposures may occur at the firehouse and when on the fireground, outside of fire suppression and overhaul. Fent, et al. (2018) conducted controlled residential fires and measured elevated particle counts and respirable mass concentrations that exceeded background exposures but were below any applicable occupational exposure limits. The location of incident command also influenced such exposure with an upwind location mitigating exposure levels. Further, the study by Baxter (2014) highlights additional excess exposure to particulate matter while in the firehouse, specifically in the kitchen and firetruck bays. Similar excess exposures to particulate matter and volatile organic compounds in firehouses following a fire response have been reported in other studies (Rakowska, 2022).

In summary, there is growing evidence of a relationship between air pollution and PD (US EPA, 2019; US EPA, 2022). Excess risk for firefighters would derive from exposures to combustion products of fires during a fire response and in other workplace settings, e.g. firehouse. While this supports some biologic plausibility and excess risk of PD in firefighters, the absence of elevated risk in the epidemiologic studies suggests these exposures may not be sufficient to manifest in excess disease.

Assessing common firefighter exposures and their relationship to Parkinson's disease:

The combustion products of fires vary tremendously based on the fire size and intensity, the chemistry of the materials involved, and the ventilation conditions of the fire (Underwriters Laboratories, Inc., 2010). Firefighter exposure and internal dose to particulates and chemicals likely depends on the use respiratory protection, dermal exposure and use of other PPE. Many exposures likely encountered by firefighters are neurotoxic, including air pollution/diesel exhaust particles (Costa, 2017; Shkirkova, 2022), polycyclic aromatic hydrocarbons (Olasehinde, 2022), polychlorinated biphenyls and polybrominated diphenyl ethers (Pessah, 2019). A broad review of all possible chemical, biological and physical exposures a firefighter may face is beyond the capacity of the staff support for the committee. Below, we report specific known chemical (e.g. PFAS and PCBs) and physical exposures (e.g. shiftwork) likely experienced universally by firefighters and discuss the evidence related to whether these exposures are associated with PD.

Per- and polyfluoroalkyl substances (PFAS)

Per- and polyfluoroalkyl substances (PFAS) commonly used in firefighting foams and turnout gear are known to cross the blood-brain barrier and accumulate in the brain. PFAS neurotoxicity relates to the disruption of neurotransmission, particularly of the glutamate and dopaminergic systems, and thus there is some speculated association to PD (Brown-Leung, 2022). Human studies demonstrating an association between exposure to PFAS and PD are sparse. In an ecological study comparing communities with higher levels of PFAS contaminated drinking water to communities with lower levels of PFAS contamination, researchers reported an elevated risk of PD mortality in communities with more contaminated drinking water, but this was not statistically significant (RR=1.18; 95% CI: 0.93-1.50) (Mastrantonio, 2018).

Polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs)

Polychlorinated biphenyls (PCBs) are recognized biopersistent, non-flammable chemicals used in electrical equipment, and polybrominated diphenyl ethers (PBDEs) are flame retardants used in many consumer products. While there is a dearth of epidemiological data regarding PCB exposure and PD risk, PCB concentrations in human brain tissue were higher in women with PD than for controls, although this was not observed for men (Hatcher-Martin, 2012). Researchers of one of the few epidemiologic studies assessing PCB exposure in a working population reported a significant excess of PD among the most highly exposed women workers in a manufacturer of electrical capacitors (SMR = 2.95; 95% CI = 1.08-6.42; 6 deaths) (Steenland, 2006). Alternatively, in a Finnish study, PCB exposure measured in blood did not correspond to an increased risk of PD, but may actually suggest a protective effect of PCBs for PD (Weisskopf, 2012).

A second cohort of capacitor manufacturing workers did not have an elevated standardized mortality ratio for PD, nor was there a positive association between cumulative exposure and PD (Ruder, 2014). Since PBDEs have a similar chemical structure , one may question the relationship between PBDE exposure and PD. PBDE mixtures have been shown to be neurotoxic to the nigrostriatal dopamine system in both vitro and in vivo models (Bradner, 2013), but human studies assessing PBDE exposure and PD are limited. More research on an association between PBDEs and PD is warranted.

Shift work

Shift work is common in the fire service. Current research suggests that shift work is not a risk factor for PD (Chen, 2006; Jorgenson, 2020). From the US Nurses' Health Study, nurses with 15 or more years of night shift work had a 50% lower risk of PD after adjustment for age and smoking (Chen, 2006). In a similar cohort study of Danish nurses, no significant difference in PD risk was reported in nurses working rotating shifts as compared to permanent daytime shifts (Jorgenson, 2020).

SUMMARY

Epidemiologic evidence supporting an association between firefighting and PD are sparse. In general, the literature did not consistently show that firefighters are at a higher risk of developing PD compared to other workers. Similarly, there was no sufficient evidence to suggest that other workers with exposures similar to firefighting are at an increased risk of developing PD. The epidemiologic evidence does not show clear evidence that firefighting is a specific risk factor for developing PD.

Support for causal associations between the myriad of potential chemical and physical exposures firefighters encounter and potential neurologic outcomes are limited. Exposures currently considered to possibly be associated with PD, i.e. pesticides, chlorinated solvents, and heavy metals, do not appear to be exposures that are commonly encountered by most firefighters. Increasing exposure to $PM_{2.5}$ is plausibly associated with increased risk of PD, although the evidence of such elevated risk in firefighters as a result of excess exposure to $PM_{2.5}$ is not apparent in occupational epidemiology studies. Chemical and physical exposures linked to firefighting at this time do not appear to be associated with PD. Scenarios in which firefighters may be chronically exposed to pesticides, chlorinated solvents, or other specific exposures linked to increased risk for PD may best be evaluated individually for causation.

Advisory Committee Recommendation

This report and the subsequent recommendation only address the risk of PD in firefighters as collective group under the presumption law. The content of this report and the recommendation presented here are not intended to and should not be used for a causal determination of PD in an individual firefighter with varying susceptibility and occupational exposures.

Based on a review of the current scientific literature, the committee has not found sufficient evidence for an association between firefighting and PD to warrant inclusion of PD into WA's presumption law. Scientific inquiry is not static, and additional research will broaden our understanding of environmental, occupational, and genetic risks for PD. As more research evidence regarding these risks for PD emerge, a subsequent request for a review of PD for inclusion into Washington presumption law will be necessary.

Estimated Burden and Cost of Parkinson's Disease in WA Firefighters

As defined in the firefighting presumption law (RCW 51.32.185), the advisory committee's recommendation must be accompanied by the estimated number of WA firefighters at risk of developing PD and estimated cost of treating PD in firefighters. The advisory committee did not consider these estimates while developing their recommendation as to whether there is an association between firefighters in PD.

Due to rarity of disease and lack of population-based disease registries, few researchers have been able to calculate PD incidence rates. The most recent study attempting to establish PD incidence rates in the

U.S. by sex and age was conducted using data from a large health insurance company in northern California from 1994-1995 (Van Den Eeden et al. 2003). These age-adjusted PD incidence rates per 100,000 person-years are presented in Table 4.

Table 4. U.S. Parkinson's disease incidence rates by age and sex, 1994-1995 (Van Den Eeden et al. 2003).

Age Group	PD Incidence Rate per 100,000 (95% CI)	
	M	F
0 to 29	0	0
30 to 39	0.5 (0.0, 1.2)	0.5 (0.0, 1.2)
40 to 49	3.4 (1.5, 5.2)	1.6 (0.4, 2.9)
50 to 59	11.1 (7.1, 15.1)	8.6 (5.2, 12.0)
60 to 69	49.5 (39.5, 59.5)	29.0 (21.6, 36.3)
70 to 79	140.7 (118.7, 162.7)	78.4 (63.2, 93.6)
80 to 89	190.5 (143.1, 237.8)	70.7 (46.9, 94.4)
90+	Not reported	Not reported
Total	**19.0 (16.1, 21.8)***	**9.9 (7.6, 12.2)***

Table 5 describes number of current and former WA firefighters and PD case estimates by age and sex. The number of firefighters is based on the total number of WA firefighters enrolled in WA's Law Enforcement Officer and Fire Fighter retirement plan. To emulate the eligibility criteria required for firefighter seeking presumptive coverage for cancer, we also describe the number WA firefighters with at least ten years of experience who are currently working or within five years of separation or retirement. Estimated number of PD cases among this subset of firefighters is also presented in Table 5. From these data and applying the ten-year employment requirement, summing the estimated cases for age groups from 30-69, we estimate at most, one PD case per year. This is likely an overestimate given a portion of firefighters in the 60-69 age group would likely not qualify given how the presumption is phased out in retirement.

Table 5. Estimated burden of Parkinson's disease among WA Firefighters by age, sex, and experience.

Age Group	All Current and Former Firefighters[1]				Current and Former Firefighters in WA with 10+ years of experience[2]			
	N		Average Annual PD cases		N		Average Annual PD cases	
	M	F	M	F	M	F	M	F
0 to 29	425	55	0	0	0	0	0	0
30 to 39	2,456	245	0.0123	0.0012	605	39	0.0030	0.0002
40 to 49	3,021	228	0.1027	0.0036	2,110	112	0.0717	0.0018
50 to 59	3,241	292	0.3598	0.0251	2,552	156	0.2833	0.0134
60 to 69	2549	173	1.2618	0.0502	911	49	0.4509	0.0142
70 to 79	1754	31	2.4679	0.0243	41	1	0.0577	0.0008
80 to 89	434	2	0.8268	0.0014	0	0	0	0
90+	23	1	0.0000	0.0000	0	0	0	0
Total	**13903**	**1027**	**5.0311**	**0.1059**	**6219**	**357**	**0.8667**	**0.0304**

Estimating potential costs of a PD workers' compensation claim remains difficult given the rarity of the disease and what is currently known about occupational exposures leading to PD. We identified seven accepted worker's compensation claims filed in WA between 1990 and 2022 for PD or secondary parkinsonism. When adjusted to the 2022 consumer price index, medical costs for these claims ranged from $11,503 to $1,538,111 and averaged $281,069 per claim. Claims costs, including both medical and non-medical costs, averaged $573,194 per claim. It should be noted that these seven claims are not typical workers' compensation claims, and are not necessarily representative of future workers' compensation claims for PD.

In a study assessing the economic burden of PD in Medicare recipients, Albarmawi et al (2022) compared the yearly medical costs of people diagnosed with PD to individuals without PD. The first year of a PD diagnoses was observed to be the most costly, and people newly diagnosed with PD incurred an average of $9,625 in direct medical costs compared to these without PD. These results are similar to previously observed average annual PD costs. Dohodwala et al (2020) and Huse et al (2005) reported annual PD medical costs of $9,924 and $10,349, respectively. Additionally, people younger than 65 years old with PD tend to have higher 1-year, 3-year, and 5-year costs compared to older PD patients (Albarmawi 2022). These cost estimates, however, do not account for indirect costs associated with PD, which researchers have found surpass PD-related medical costs (Yang 2020). PD cost estimates are primarily derived from Medicare beneficiaries, who are generally older than the typical working

[1] Includes all living firefighters (current and former) as defined by enrollment in WA's Law Enforcement Officer and Fire Fighter Retirement program as of 2022.
[2] Includes all current firefighters and former firefighters (who have retired or separated within the last 5 years) with 10+ years of firefighting experience
*Age adjusted to 1990 US census population

population. Therefore, these cost estimates do not necessarily represent the potential cost of a PD workers' compensation claim among a firefighter in WA, specifically the exclusion of wage replacement costs from lost work time, the potential of total permanent disability and associated pension costs.

REFERENCES CITED

Ahmed H, Abushouk AI, Gabr M, Negida A, Abdel-Daim MM. Parkinson's disease and pesticides: A meta-analysis of disease connection and genetic alterations. Biomed Pharmacother. 2017; 90:638-649.

Albarmawi H, Zhou S, Shulman LM, Gandhi AB, Johnson A, Myers DE, et al. The economic burden of Parkinson disease among Medicare beneficiaries. Journal of Managed Care & Specialty Pharmacy. 2022;28(4):405-14.

Alexander GE. Biology of Parkinson's disease: pathogenesis and pathophysiology of a multisystem neurodegenerative disorder. Dialogues Clin Neurosci. 2004; 6(3):259-280.

Barros B, Oliveira M, Morais S. Biomonitoring of firefighting forces: a review on biomarkers of exposure to health-relevant pollutants released from fires. J Tox Env Health, Part B. 2023; 26(3):127-171.

Baxter CS, Hoffman JD, Knipp MJ, Reponen T, Haynes EN. Exposure of firefighters to particulates and polycyclic aromatic hydrocarbons. J Occup Environ Hyg. 2014; 11(7):85-91.

Beard JD, Steege AL, Ju J, Lu J, Luckhaupt SE, Schubauer-Berigan MK. Mortality from amyotrophic lateral sclerosis and Parkinson's disease among different occupation groups—United States, 1985–2011. Morbidity and Mortality Weekly Report. 2017;66(27):718.

Bradner JM, Suragh TA, Wilson WW, Lazo CR, Stout KA, Kim HM, Wang MZ, Walker DI, Pennell KD, Richardson JR, Miller GW, Caudle WM. Exposure to the polybrominated diphenyl ether mixture DE-71 damages the nigrostriatal dopamine system: role of dopamine handling in neurotoxicity. Exp Neurol. 2013 Mar;241:138-47.

Breckenridge CB, Berry C, Chang ET, Sielken Jr RL, Mandel JS. Association between Parkinson's disease and cigarette smoking, rural living, well-water consumption, farming and pesticide use: Systematic review and meta-analysis. Plos One 2016; 11(4): e0151841

Brown-Leung JM, Cannon JR. Neurotransmission targets of per- and polyfluoroalkyl substance neurotoxicity: Mechanisms and potential implications for adverse neurological outcomes. Chem Res Toxicol. 2022; 35(8):1312-1333.

Burstyn I, LaCroix AZ, Litvan I, Wallace RB, Checkoway H. Occupation and Parkinson disease in the Women's Health Initiative observational study. Am J Ind Med. 2019;62(9):766-76.

Calvert GM, Barnett M, Mehler LN, Becker A, Das R, Beckman J, Male D, Sievert J, Thomsen C, Morissey B. Acute Pesticide Illness Among Emergency Responders, 1993-2002. Am J Int Med. 2006; 49:383-393.

Caudle WM, Guillot TS, Lazo CR, Miller GW. Industrial toxicants and Parkinson's disease. Neurotoxicology. 2012; 33(2):178-188.

Centers for Disease Control and Prevention. National Institute for Occupational Safety and Health. Worker Safety and Health Topics: Lead.
https://www.cdc.gov/niosh/topics/lead/referencebloodlevelsforadults.html. Accessed June 26, 2023.

Centers for Disease Control and Prevention. (2005). Third National Report on Human Exposure to Environmental Chemicals. Atlanta, Georgia: National Center for Environmental Health.

Chen H, Schernhammer E, Schwarzschild MA, Ascherio A. A prospective study of night shift work, sleep duration, and risk of Parkinson’s disease. Am J Epidemiol 2006;163:726–30.

Chambers-Richards T, Su Y, Chireh B, D’Arcy. Exposure to toxic occupations and their association with Parkinson’s disease: a systematic review with meta-analysis. Rev Env Health. 2023; 38(1):65-83.

Costa LG, Cole TB, Coburn J, Chang YC, Dao K, Roque PJ. Neurotoxicity of traffic-related air pollution. Neurotoxicology 2017; 59:133-139.

Dick S, Semple S, Dick F, Seaton A. Occupational titles as risk factors for Parkinson's disease. Occupational Medicine. 2007;57(1):50-6.

Dahodwala N, Li P, Jahnke J, Ladage VP, Pettit AR, Kandukuri PL, et al. Burden of Parkinson's disease by severity: Health care costs in the US Medicare population. Movement Disorders. 2021;36(1):133-42.

Dobraca D, Israel L, McNeel S, Voss R, Wang M, Gajek R, Park JS, Harwani S, Barley F, She J, Das R. Biomonitoring in California firefighters; Metals and perfluorinated chemicals. J Occ Med. 2015; 57(1):88-97.

Dorsey ER, Zafar M, Lettenberger SE, Pawlik ME, Kinel D, Frissen M, Schneider RB, Kieburtz K, Tanner CM, DeMiranda BR, Goldman SM, Bloem BR. Trichloroethylene: An invisible cause of Parkinson’s disease? J Parkinson’s Disease 2023; 13:203-218.

Elbaz A, Clavel J, Rathouz PJ, Moisan F, Galanaud JP, et al. Professional exposure to pesticides and Parkinson disease. 2009. Ann. Neurol. 66:494–504

Fall PA, Fredrikson M, Axelson O, Granérus AK. Nutritional and occupational factors influencing the risk of Parkinson's disease: a case-control study in southeastern Sweden. Movement disorders: official journal of the Movement Disorder Society. 1999;14(1):28-37.

Fent KW, Evans DE, Babik K, Striley C, Bertke S, Kerber S, Smith D, Horn GP. Airborne contaminants during controlled residential fires. J Occ Env Hyg. 2018; 15(5):399-412.

Firestone JA, Lundin JI, Powers KM, Smith-Weller T, Franklin GM, Swanson PD, et al. Occupational factors and risk of Parkinson's disease: A population-based case–control study. American journal of industrial medicine. 2010;53(3):217-23.

Frigerio R, Elbaz A, Sanft KR, Peterson BJ, Bower JH, Ahlskog JE, et al. Education and occupations preceding Parkinson disease: a population-based case-control study. Neurology. 2005;65(10):1575-83.

Fu P, Guo X, Cheung FMH, Yung KKL (2019) The association between PM(2.5) exposure and neurological disorders: a systematic review and meta-analysis. Sci Total Environ 2019. 655:1240–1248.

Gash DM, Rutland K, Hudson NL, Sullivan PG, Bing G, Cass WA, Pandya JD, Liu M, Choi DY, Hunter RL, Gerhardt GA, Smith CD, Slevin JT, Prince TS. Trichloroethylene: Parkinsonism and complex 1 mitochondrial neurotoxicity. Ann Neurol. 2008; 63:184-192.

Goldman SM. Environmental toxins and Parkinson's disease. Annu Rev Pharmacol and Toxicol. 2014. 54:141-164.

Goldman SM, Quinlan PJ, Ross GW, Marras C, Meng C, Bhudhikanok GS, Comyns K, Korell M, Chade AR, Kasten M, Priestley B, Chou KL, Fernandez HH, Cambi F, Langston JW, Tanner CM (2012) Solvent exposures and Parkinson disease risk in twins. Ann Neurol 2012; 71: 776-784.

Goldman SM, Tanner CM, Olanow CW, Watts RL, Field RD, Langston JW. Occupation and parkinsonism in three movement disorders clinics. Neurology 2005; 65:1430-1435.

Goldman SM, Weaver FM, Stroupe KT, Cao L, Gonzalez B, Coletta K, Brown EG, Tanner CM. Risk of Parkinson Disease among service members at Marine Base Camp Lejeune. JAMA Neurology. Published Online. May 15, 2023. doi:10.1001/jamaneurol.2023.1168.

Gong Y, Zhang X, Zhao X, Chang H, Zhang J, Gao Z, Mi Y, Chen Y, Zhang H, Huang C, Yu Z. Global ambient particulate matter pollution and neurodegenerative disorders; a systematic review of literature and meta-anaylsis. Env Sci Poll Res. 2023; 30:39418-39430.

Gunnarsson LG, Bodin L. Parkinson's disease and occupational exposures: a systematic literature review and meta-analyses. Scan J Work Environ Health. 2017; 43(3):197-209.

Hatcher-Martin JM, Gearing M, Steenland K, Levey AI, Miller GW, Pennell KD. Association between polychlorinated biphenyls and Parkinson's disease neuropathology. Neurotoxicology 2012; 33(5):1298-304.

Hill AB. The Environment and Disease: Association or Causation? Proc R Soc Med. 1965;58(5):295-300.

Huse DM, Schulman K, Orsini L, Castelli-Haley J, Kennedy S, Lenhart G. Burden of illness in Parkinson's disease. Movement disorders: official journal of the Movement Disorder Society. 2005;20(11):1449-54.

Jahnke S, Jitnarin N, Kaipust CM, Hollerbach BS, Naylor BM, Crisp C. Fireground Exposure of firefighters: A literature review. Center for Fire, Rescue and EMS Health Research NDRI Ventures. Fire Protection Research Foundation. Leawood, Kansas. May 2021.

Jayatilaka NK, Restrepo P, Davis Z, Vidal M, Calafat AM, Ospina M. Quantification of 16 urinary biomarkers of exposure to flame retardants, plasticizers, and organophosphate insecticides for biomonitoring studies. Chemosphere. 2019; 235:481-491.

Jørgensen JT, Schernhammer E, Papantoniou K, Hansen J, Westendorp RGJ, Stayner L, Simonsen MK, Andersen ZJ. Night work and incidence of Parkinson's disease in the Danish Nurse cohort. OEM 2020; 78(6): 419-425.

Kasdagli MI, Katsouyanni K, Dimakopoulou K, Samoli E. Air pollution and Parkinson's Disease: A systematic review and meta-analysis up to 2018. In J Hyg Env Health. 2019. 222:402-409.

Kirkey KL, Johnson CC, Rybicki BA, Peterson EL, Kortsha GX, Gorell JM. Occupational categories at risk for Parkinson's disease. American journal of industrial medicine. 2001;39(6):564-71.

Kotwani R, Clapp AN, Huggins HE, Vaou O, Hohler ADP. Assessment of Parkinsonian Symptoms and Toxin Exposures in Firefighters. Journal of Basic and Clinical Pharmacy. 2022;13(3).

Levasseur JL, Hoffman K, Herkert NJ, Cooper E, Hay D, Stapleton HM. Characterizing firefighter's exposure to over 130 SVOCs using silicone wristbands: a pilot study comparing on-duty and off-duty exposures. Sci Tot Environ 2022; 834:155237.

Li X, Sundquist J, Sundquist K. Socioeconomic and occupational groups and Parkinson's disease: a nationwide study based on hospitalizations in Sweden. International archives of occupational and environmental health. 2009;82:235-41.

Liu M, Choi D-Y, Hunter RL, Pandya JD, Cass WA, Sullivan PG, Kim H-C, Gash DM, Bing G. Trichloroethylene induces dopaminergic neurodegeneration in Fisher 344 rats. J Neurochemistry. 2010; 112:773–783.

Lock EA, Zhang J, Checkoway H. Solvents and Parkinson disease: A systematic review of toxicological and epidemiological evidence. Toxicol Appl Pharmacol. 2013; 266(3):345-355.

Mastrantonio M, Bai E, Uccelli R, Cordiano V, Screpanti A, Crosignani P. Drinking water contamination from perfluoroalkyl substances (PFAS): an ecological mortality study in the Veneto Region, Italy. European J Public Health 2018; 28(1):180-185.

Minerbo G, Jankovic J. Prevalence of Parkinson's disease among firefighters. Neurology. 1990;40(Suppl):348.

Murata H, Barnhill LM, Bronstein JM. Air pollution and the risk of Parkinson's Disease: A review. Movement Disorders. 2022. 37(5): 894-904.

National Institute of Neurological Disorders and Stroke (NINDS). Who is more likely to get Parkinson's disease? https://www.ninds.nih.gov/health-information/disorders/parkinsons-disease?search-term=Pesticide%20parkinsons. Accessed June26, 2023.

NIOSH (2019). National Occupational Mortality Surveillance (NOMS). U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Division of Surveillance, Hazard Evaluation and Field Studies, Surveillance Branch. <https://www.cdc.gov/niosh/topics/noms/query.html> Accessed May 6, 2023.

Ohlander J, Fuhrimann S, Basinas I, Cherrie JW, Galea KS, Povey AC, van Tongeren M, Harding AH, Jones K, Vermeulen R, Huss A, Kromhout H. Impact of occupational pesticide exposure assessment method on risk estimates for prostate cancer, non-Hodgkin's lymphoma and Parkinson's disease: results of three meta-analyses. Occup Env Med 2022; 79:566-574.

Olasehinde TA, Olaniran AO. Neurotoxicity of polycyclic aromatic hydrocarbons: a systematic mapping and review of neuropathological mechanisms. Toxics 2022; 10: 417.

Park J, Yoo C-I, Sim CS, Kim HK, Kim JW, Jeon BS, et al. Occupations and Parkinson's disease: a multi-center case-control study in South Korea. Neurotoxicology. 2005;26(1):99-105.

Park J, Yoo C-I, Sim CS, Kim J-W, Yi Y, Jung KY, et al. Occupations and Parkinson's disease: a case-control study in South Korea. Industrial health. 2004;42(3):352-8.

Pessah IN, Lein PJ, Seegal RF, Sagiv SK. Neurotoxicity of polychlorinated biphenyls and related organohalogens. Acta Neuropathol 2019. 138(3):363-367.

Pezzoli G, Cereda E. Exposure to pesticide or solvents and risk of Parkinson disease. Neurology.2013; 80(22):

Post B, van den Heuvel L, van Prooije T, van Ruissen X, van de Warrenburg B, Nonnekes J. Young onset Parkinson's disease: a modern and tailored approach. J Parkinson's Dis. 2020; 10:S29-S36.

Pyatha S, Kim H, Lee D, Kim K. Association of heavy metal exposure and Parkinson's Disease: A review of the mechanisms related to oxidative stress. Antioxidants (Basel). 2022. 11(12):2467

Rakowska J, Rachwal M, Walczak A. Health exposure assessment of firefighters caused by PAHs in PM4 and TSP after firefighting operations. Atmosphere 2022. 13(8):1263.

Revised Code of Washington 51.32.185, Stat. RCW 51.32.185.

Rocca WA, Anderson DW, Meneghini F, Grigoletto F, Morgante L, Reggio A, et al. Occupation, education, and Parkinson's disease: A case-control study in an Italian population. Movement disorders: official journal of the Movement Disorder Society. 1996;11(2):201-6.

Ruder AM, Hein MJ, Hopf NB, Waters MA. Mortality among 24,865 workers exposed to polychlorinated biphenyls (PCBs) in three electrical capacitor manufacturing plants: a ten-year update. Int J Hyg Environ Health. 2014 Mar;217(2-3):176-87.

Savitz DA, Loomis DP, Tse C-KJ. Electrical occupations and neurodegenerative disease: analysis of US mortality data. Archives of Environmental Health: An International Journal. 1998;53(1):71-4.

Schulte PA, Burnett CA, Boeniger MF, Johnson J. Neurodegenerative diseases: occupational occurrence and potential risk factors, 1982 through 1991. American Journal of Public Health. 1996;86(9):1281-8.

Shkirkova K, Lamorie-Foote K, Zhang N, Li A, Diaz A, Liu Q, Thorwald M, Godoy-Lugo J, Ge B, D'Agostino C, Zhang Z, Mack W, Sioutas C, Finch C, Mack W, Zhang H. Neurotoxicity of Diesel Exhaust Particles. J Alzheimer's Dis. 2022; 89(4): 1263-1278.

Steenland K, Hein MJ, Cassinelli RT 2nd, Prince MM, Nilsen NB, Whelan EA, Waters MA, Ruder AM, Schnorr TM. Polychlorinated biphenyls and neurodegenerative disease mortality in an occupational cohort. Epidemiology 2006; 17:8–13

Tanaka K, Miyake Y, Fukushima W, Sasaki S, Kiyohara C, Tsuboi Y, et al. Occupational risk factors for Parkinson's disease: a case-control study in Japan. BMC neurology. 2011;11(1):1-6.

Tanner CM, Kamel F, Ross GW et al. Rotenone, Paraquat, and Parkinson's Disease. Env Health Perspectives. 2011; 119(6):866-872.

Tanner CM, Ross W, Jewell SA, Hauser RA, Jankovic J, Factor SA, Bressman S, Deligtisch A, Marras C, Lyons KE, Bhudhikanok GS, Roucoux DF, Meng C, Abbot RD, Langston W. Occupation and risk of parkinsonism; a multicenter case-control study. Arch Neurol. 2009; 66(9):1106-1113.

Teschke K, Marion SA, Tsui JK, Shen H, Rugbjerg K, Harris MA. Parkinson's disease and occupation: differences in associations by case identification method suggest referral bias. American journal of industrial medicine. 2014;57(2):163-71.

Tsui JK, Calne DB, Wang Y, Schulzer M, Marion SA. Occupational risk factors in Parkinson’s disease. Canadian journal of public health. 1999;90:334-7.

Underwriters Laboratories, Inc. Firefighter Exposure to Smoke Particles. (DHS AFG Grant #EMW-2007-FP-02093). Prepared by Fabian T, Borgerson JL, Kerber SI, Gandhi PD, Baxter CS, Ross CS, Lockey JE, Dalton JM. Northbrook, IL, 2010.

US Environmental Protection Agency. Integrated Science Assessment (ISA) for Particulate Matter (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-19/188, 2019.

US Environmental Protection Agency. Supplement to the 2019 Integrated Science Assessment for Particulate Matter (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-22/028, 2022.

Van Den Eeden SK, Tanner CM, Bernstein AL, Fross RD, Leimpeter A, Bloch DA, et al. Incidence of Parkinson's disease: variation by age, gender, and race/ethnicity. Am J Epidemiol. 2003;157(11):1015-22.

WA DOH (2011). Washington State occupational mortality database, 1950–2010. Washington State Department of Health, Office of Epidemiology. <https://fortress.wa.gov/doh/occmort/OMQuery.aspx> Accessed May 6, 2023.

Washington Administrative Code 296-841, Stat WAC-296-841.

Weed DL. Does Paraquat cause Parkinson’s disease? A review of review. Neurotoxicology. 2021; 86:180-184.

Weisskopf MG, Knekt P, O’Reilly EJ, Lyytinen J, Reunanen A, Laden F, Altshul L Ascherio A. Polychlorinated biphenyls in prospectively collected serum and Parkinson’s disease risk. Mov Disord 2012; 27:1659–1665.

Yang W, Hamilton JL, Kopil C, Beck JC, Tanner CM, Albin RL, et al. Current and projected future economic burden of Parkinson’s disease in the US. npj Parkinson's Disease. 2020;6(1):15.

Zhao Y, Ray A, Portengen L, Vermeulen R, Peters S. Metal exposure and risk of Parkinson’s disease: a systematic review and meta-analysis. American J Epidemiology. April 2023.

APPENDIX A

Legislative Request

Legislative Building **Washington State Legislature** Olympia, WA 98504-0600

February 1, 2023

Mr. Joel Sacks
Director
Department of Labor & Industries
7273 Linderson Way SW
Tumwater, WA 98501

Dear Director Sacks,

In 2019, the Washington State Legislature passed HB 1913 which expanded the occupational disease statute and required you, as the Director of the Department of Labor & Industries, to create an advisory committee on occupational disease presumptions.

As the Chairs of the Senate Labor and Commerce Committee and the House Labor and Workplace Standards Committee, we would like to formally request that the advisory committee on occupational disease presumptions to review the scientific evidence and make recommendations to the legislature for the following diseases: adenocarcinoma, esophageal cancer, buccal cancer, pancreatic cancer, pharynx cancer, heart disease not related to exposure to toxic fumes or exertion and Parkinson's disease. Regarding pancreatic cancer, we would like the committee to also look at a link between PFAS (per- and polyfluoroalkyl) exposure and the occurrence of pancreatic cancer in firefighters.

Thank you for your consideration of this request.

Sincerely,

Karen Keiser
State Senator
33rd Legislative District

Liz Berry
State Representative
36th Legislative District

APPENDIX B

Epidemiologic Studies Captured and Reviewed

	Reference	Notes	Full Text Location
1	Beard, J.D., et al., Mortality from amyotrophic lateral sclerosis and Parkinson's disease among different occupation groups—United States, 1985–2011. Morbidity and Mortality Weekly Report, 2017. 66(27): p. 718.		Free online (link)
2	Brouwer, M., et al., Occupational exposures and Parkinson's disease mortality in a prospective Dutch cohort. Occupational and environmental medicine, 2015. 72(6): p. 448-455.		Free online
3	Burstyn, I., et al., Occupation and Parkinson disease in the Women's Health Initiative observational study. American journal of industrial medicine, 2019. 62(9): p. 766-776.		Free online
4	Coon, S., et al., Whole-body lifetime occupational lead exposure and risk of Parkinson's disease. Environmental health perspectives, 2006. 114(12): p. 1872-1876.		Free online
5	Darweesh, S., et al., Professional occupation and the risk of Parkinson's disease. European Journal of Neurology, 2018. 25(12): p. 1470-1476.		Free online
6	Dhillon, A.S., et al., Pesticide/Environmental Exposures and Parkinson's Disease in East Texas. Journal of Agromedicine, 2008. 13(1): p. 37-48.		Free online
7	Dick, F.D., et al., Environmental risk factors for Parkinson's disease and parkinsonism: the Geoparkinson study. Occupational and environmental medicine, 2007. 64(10): p. 666-672.		Free online
8	Dick, S., et al., Occupational titles as risk factors for Parkinson's disease. Occupational Medicine, 2007. 57(1): p. 50-56.		Free online
9	Elbaz, A., et al., Professional exposure to pesticides and Parkinson disease. Annals of neurology, 2009. 66(4): p. 494-504.		Required subscription
10	Fall, P.A., et al., Nutritional and occupational factors influencing the risk of Parkinson's disease: a case-control study in southeastern Sweden. Movement disorders: official journal of the Movement Disorder Society, 1999. 14(1): p. 28-37.		Requires subscription
11	Feldman, A.L., et al., Occupational exposure in parkinsonian disorders: a 43-year prospective cohort study in men. Parkinsonism & related disorders, 2011. 17(9): p. 677-682.		Free online
12	Firestone, J.A., et al., Occupational factors and risk of Parkinson's disease: A population-based case–control study. American journal of industrial medicine, 2010. 53(3): p. 217-223.		Free online
13	Frigerio, R., et al., Education and occupations preceding Parkinson disease: a population-based case-control study. Neurology, 2005. 65(10): p. 1575-1583.		Free online
14	Goldman, S., et al., Occupation and parkinsonism in three movement disorders clinics. Neurology, 2005. 65(9): p. 1430-1435.		Requires subscription
15	Gorell, J.M., et al., The risk of Parkinson's disease with exposure to pesticides, farming, well water, and rural living. Neurology, 1998. 50(5): p. 1346-1350.		Requires subscription
16	Gorell, J.M., et al., Occupational exposures to metals as risk factors for Parkinson's disease. Neurology, 1997. 48(3): p. 650-658.		Free online
17	Gorell, J.M., et al., Multiple risk factors for Parkinson's disease. Journal of the neurological sciences, 2004. 217(2): p. 169-174.		Requires subscription

18	Gunnarsson, L.-G. and L. Bodin, Parkinson's disease and occupational exposures: a systematic literature review and meta-analyses. Scandinavian journal of work, environment & health, 2017: p. 197-209.		Free online
19	Håkansson, N., et al., Neurodegenerative Diseases in Welders and Other Workers Exposed to High Levels of Magnetic Fields. Epidemiology, 2003. 14(4): p. 420-426.		Free Online
20	Hertzman, C., et al., Parkinson's disease: a case-control study of occupational and environmental risk factors. American journal of industrial medicine, 1990. 17(3): p. 349-355.		Requires subscription
21	Jafari, S., et al., Head injury and risk of Parkinson disease: A systematic review and meta-analysis. Movement disorders, 2013. 28(9): p. 1222-1229.		Requires subscription
22	Kenborg, L., et al., Outdoor work and risk for Parkinson's disease: a population-based case–control study. Occupational and environmental medicine, 2011. 68(4): p. 273-278.		Free online
23	Kirkey, K.L., et al., Occupational categories at risk for Parkinson's disease. American journal of industrial medicine, 2001. 39(6): p. 564-571.		Requires subscription
24	Kirrane, E.F., et al., Associations of ozone and PM 2.5 concentrations with Parkinson's disease among participants in the Agricultural Health Study. Journal of occupational and environmental medicine, 2015. 57(5): p. 509-517.		Free online
25	Kotwani, R., et al., Assessment of Parkinsonian Symptoms and Toxin Exposures in Firefighters. Journal of Basic and Clinical Pharmacy, 2022. 13(3).		Free online
26	Kwon, E., et al., Parkinson's disease and history of outdoor occupation. Parkinsonism & related disorders, 2013. 19(12): p. 1164-1166.		Free online
27	Lai, B., et al., Occupational and environmental risk factors for Parkinson's disease. Parkinsonism & related disorders, 2002. 8(5): p. 297-309.		Requires subscription
28	Lai, C.-Y., et al., Increased risk of Parkinson disease in patients with carbon monoxide intoxication: a population-based cohort study. Medicine, 2015. 94(19).		Free online
29	Li, X., J. Sundquist, and K. Sundquist, Socioeconomic and occupational groups and Parkinson's disease: a nationwide study based on hospitalizations in Sweden. International archives of occupational and environmental health, 2009. 82: p. 235-241.		Requires subscription
30	Minerbo, G. and J. Jankovic, Prevalence of Parkinson's disease among firefighters. Neurology, 1990. 40(Suppl): p. 348.	Abstract only	Requires subscription
31	Noonan, C.W., et al., Occupational exposure to magnetic fields in case-referent studies of neurodegenerative diseases. Scandinavian journal of work, environment & health, 2002: p. 42-48.		Free online
32	Palacios, N., et al., Particulate matter and risk of Parkinson disease in a large prospective study of women. Environmental Health, 2014. 13(1): p. 1-9.		Free online
33	Pals, P., et al., Case–control study of environmental risk factors for Parkinson's disease in Belgium. European journal of epidemiology, 2003. 18: p. 1133-1142.		Free online
34	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.		Free online
35	Park, J., et al., Occupations and Parkinson's disease: a case-control study in South Korea. Industrial health, 2004. 42(3): p. 352-358.		Free online
36	Park, J., et al., A retrospective cohort study of Parkinson's disease in Korean shipbuilders. Neurotoxicology, 2006. 27(3): p. 445-449.		Requires subscription

37	Pennington, S., et al., The cause of death in idiopathic Parkinson's disease. Parkinsonism & related disorders, 2010. 16(7): p. 434-437.		Requires subscription
38	Rami, A., Review: autophagy in neurodegeneration: firefighter and/or incendiarist? Neuropathol Appl Neurobiol, 2009. 35(5): p. 449-61.		Free online
39	Rocca, W.A., et al., Occupation, education, and Parkinson's disease: A case-control study in an Italian population. Movement disorders: official journal of the Movement Disorder Society, 1996. 11(2): p. 201-206.		Requires subscription
40	Röösli, 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.		Free online
41	Savitz, D.A., D.P. Loomis, and C.-K.J. Tse, Electrical occupations and neurodegenerative disease: analysis of US mortality data. Archives of Environmental Health: An International Journal, 1998. 53(1): p. 71-74.		Requires subscription
42	Schulte, P.A., et al., Neurodegenerative diseases: occupational occurrence and potential risk factors, 1982 through 1991. American Journal of Public Health, 1996. 86(9): p. 1281-1288.		Free online
43	Seidler, A., et al., Possible environmental, occupational, and other etiologic factors for Parkinson's disease: a case-control study in Germany. Neurology, 1996. 46(5): p. 1275-1275.		Requires subscription
44	Sullivan, K.L., et al., Occupational Characteristics and Patterns as Risk Factors for Parkinson's Disease: A Case Control Study. Journal of Parkinson's Disease, 2015. 5(4): p. 813-820.		Requires subscription
45	Tanaka, K., et al., Occupational risk factors for Parkinson's disease: a case-control study in Japan. BMC neurology, 2011. 11(1): p. 1-6.		Free Online
46	Tanner, C.M., et al., Occupation and Risk of Parkinsonism: A Multicenter Case-Control Study. Archives of Neurology, 2009. 66(9): p. 1106-1113.		Free Online
47	Teschke, K., et al., Parkinson's disease and occupation: differences in associations by case identification method suggest referral bias. American journal of industrial medicine, 2014. 57(2): p. 163-171.		Free Online
48	Tsui, J.K., et al., Occupational risk factors in Parkinson's disease. Canadian journal of public health, 1999. 90: p. 334-337.		Free Online
49	Valdés, E.G., et al., Occupational complexity and risk of Parkinson's disease. PloS one, 2014. 9(9): p. e106676.		Free Online
50	Van Maele-Fabry, G., et al., Occupational exposure to pesticides and Parkinson's disease: a systematic review and meta-analysis of cohort studies. Environment international, 2012. 46: p. 30-43.		Free Online
51	Wang, A., et al., Parkinson's disease risk from ambient exposure to pesticides. Eur J Epidemiol, 2011. 26(7): p. 547-55.		Free Online
52	Willis, A.W., et al., Metal emissions and urban incident Parkinson disease: a community health study of Medicare beneficiaries by using geographic information systems. American journal of epidemiology, 2010. 172(12): p. 1357-1363.		Free Online
53	Wirdefeldt, K., et al., Epidemiology and etiology of Parkinson's disease: a review of the evidence. European journal of epidemiology, 2011. 26: p. 1-58.		Requires subscription
54	Ye, S., et al., Parkinson's disease among firefighters: a focused review on the potential effects of exposure to toxic chemicals at the fire scene. Korean Journal of Biological Psychiatry, 2017. 24(1): p. 19-25.	Title, abstract, tables, and references in English; manuscript text was written in Korean	Free online

APPENDIX C

Epidemiologic Studies Reporting Parkinson's Disease by Occupation

First Author, Year	Measure	Occupations with statistically significant elevated PD risk
Beard, 2017	PMR	• Management • Business Operations • Financial • Computer and mathematical • Architecture and engineering • Life, physical and social science • Community and social services • Legal • Education, training, and library • Art, design, entertainment, sports, and media • Health care practitioners and technical • Sales • Office and Administrative support
Burstyn, 2019	RR	• Counselors, social workers, and other community and social service specialists
Dick, 2007	OR	*None reported*
Fall, 1999	OR	• Carpenters (males) • Cleaners (females)
Firestone, 2010	OR	*None reported*
Frigerio, 2005	OR	• Physicians
Goldman, 2005	OR	• Farming • Physician/Medical • Teacher • Computer (for individuals ≤ 50 years old) • Technical (for individuals ≤ 50 years old)
Kirkey, 2001	OR	*None reported*
Li, 2009	SIR	In Females • Assistant nurses (1) In males: • Teachers (1,2) • Religious, juridical, and other social-science-related workers (1) • Administrators and managers (1,2,3) • Farmers (1,2,3) • Woodworkers (1,2,3) • Sales agents (2,3) • Painters and wall paperhangers (2,3) 1. In once census (1960 for males; 1970 for females) 2. In 2 consecutive censuses (males only; 1960 and 1970 censuses) 3. In 3 consecutive censuses (males only; '60, '60'80 censuses)
Park, 2005	OR	• Agriculture, hunting, and forestry
Park, 2004	OR	• Clerk (only significant when the controls were other neurology patients, not stat significant when controls were healthy people)
Rocca, 1996	OR	*None reported*
Savitz, 1998	OR	*None reported*
Schulte, 1996	PMR	10 Highest Statistically Significant PMRs for White Males:

First Author, Year	Measure	Occupations with statistically significant elevated PD risk
		(1) Extruding- and forming-machine operators, (2) Stock handlers and baggers under 65, (3) Podiatrists, (4) Counselors, educational and vocational, (5) Pattern makers and model makers, wood, (6) Librarians, archivists, and curators, (7) Biological, life, and medical scientists, (8) Computer equipment operators, (9) Teachers, postsecondary (10) Airplane pilots and navigators 10 Highest Statistically Significant PMRs for White Females: (1) Bookbinders, (2) Textile winding and twisting machine operators, (3) Food counter and fountain-related occupations, (4) Supervisory mechanics and repairers, (5) Dental assistants, (6) Religious workers, (7) Designers, (8) Teachers, (9) Financial officers, (10) Writers, artists, entertainers, and athletes 10 Highest Statistically Significant PMRs for Black Males: (1) Lathe-turning machine set-up operators, (2) Hand molding, casting, and forming occupations, (3) Pest control occupation, (4) Health-diagnosing occupations, (5) Nurses, (6) Supervisors, food prep and services under 65, (7) Baggage porters and bellhops, (8), Furnace kiln, and oven operators, excluding food, (9) Teachers, (10) Clergy 10 Highest Statistically Significant PMRs for Black Females: (1) Writers, (2) Textile winding machine operators, (3) Funeral directors, (4) Material recording, scheduling, and distributing clerks, (5) Protection service occupations, (6) Waiters and waitresses, (7) Precision textile, apparel machine workers, (8) Sales workers, (9) Social workers, (10), Teachers
Tanaka, 2011	OR	*None reported*
Tanner, 2009	OR	• Legal occupations • Construction and extraction
Teschke, 2014	OR	• Farming, horticulture • Social sciences, law, library (only when the job was held 10 years prior to diagnosis)
Tsui, 1999	OR	• Social science, law, library • Teaching • Medicine, health • Other primary: forestry, logging, mining, oil/gas field