

Association between PFAS and Pancreatic Cancer in Firefighters

Washington State Advisory Committee on Firefighter Presumption

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Background

Per- and poly-fluoroalkyl substances (PFAS) are a group of man-made chemicals used in a variety of applications since the 1950s (NIEHS, 2023). Characterized by multiple strong carbon-fluorine bonds, PFAS are able to withstand high temperatures and are slow to degrade (NSTC, 2023). PFAS are defined using a variety of methods and the number of estimated individual PFAS chemicals depends on the definition used (US Joint subcommittee 2023). Currently, the US Environmental Protection Agency (EPA) lists 12,034 individual PFAS and regularly adds more (CompTox, 2024). In 2018, The Organisation for Economic Co-operation and Development (OECD) published a report listing 4,730 PFAS-related chemicals with Chemical Abstracts Service (CAS) registry numbers. A subsequent study has determined that only 6% of these are commercially relevant on a global scale (Buck, 2021). Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) are two of the most widely used PFAS (US EPA, 2023).

PFAS are used broadly in commercial and industrial applications. In 2020, Glüge et al. compiled a non-exhaustive list of 200 uses for PFAS in nearly every industry. PFAS are commonly used as a protective coating in consumer products (water- and stain-proofing), such as in clothing, furniture, paint, and food packaging and in industrial products such as firefighting foam (CDC, 2019; NSTC, 2023). Concerns about the health effects of PFAS exposure and bioaccumulation were heightened in 2001 when researchers detected PFAS in wildlife blood samples (Buck, 2011). While most people in the US are exposed to PFAS (NASEM, 2022) via contaminated water, soil, or in consumer products, those with the highest exposure levels are typically exposed to PFAS in occupational settings (NIOSH, 2023).

Firefighters have possible exposures to per- and poly-fluoroalkyl substances (PFAS) through use of aqueous film forming foams (AFFF), which were most commonly used in airport and military firefighting operations (Barzen-Hanson, 2017). Although by the early 2000's, environmental and human health concerns led to diminished production and use of long chain PFAS, including PFOS and PFOA, in AFFF (Rosenfeld, 2023). Other sources of PFAS exposure include through use and degradation of PFAS containing turnout gear (Peaslee, 2020), and potential contamination of dusts or other particulate airborne exposures in the fire station and on the fire ground (Hall, 2020; Young, 2021). Products enhanced with PFAS for water and oil resistance, e.g. home furnishings and carpeting, on combustion may release smoke, fumes containing PFAS and contaminate gear or work spaces (Tao, 2008). Firefighters are also subjected to the environmental background levels of PFAS in their communities.

PFAS routes of exposure for firefighters are through inhalation and ingestion of: AFFF, degraded or contaminated turnout gear, smoke from combustion of PFAS containing furnishing or other PFAS containing products, and ingestion of contaminated food and water (Rosenfeld, 2023). Dermal absorption from contact with PFAS is considered a less common route of exposure (Rotander, 2015; De Silva, 2021).

Request for Review: Association between PFAS and pancreatic cancer in firefighters

On February 1, 2023, the Department of Labor and Industries (L&I) received a letter from two WA state legislators asking for an evaluation and recommendation for inclusion of the numerous conditions under the WA's firefighter presumption law (Appendix A – Legislative Request). The request included pancreatic cancer, and specifically a link between PFAS exposure and the occurrence of pancreatic cancer in firefighters. The Advisory Committee on Firefighter Presumption considered the relevance, quality, and quantity of the scientific literature and data about pancreatic cancer in firefighters and ultimately determined that, at the time of their review, there was not sufficient evidence to suggest that firefighters were at an increased risk of developing pancreatic cancer. This review of pancreatic cancer was not limited to those related to PFAS exposure.

The purpose of this addendum is to explore if there is an association between PFAS exposure and pancreatic cancer in firefighters.

Methods

The committee framed their review of the relevant literature with pancreatic cancer by addressing two main questions:

1. What is known about the association between PFAS exposure and pancreatic cancer?
2. Is there evidence of increased exposure to PFAS among firefighters (compared to the general public) based on biomonitoring data?
3. Does the epidemiologic data suggest that firefighters are at an increased risk of pancreatic cancer?

To identify additional articles assessing the association between PFAS and pancreatic cancer in firefighters, we searched *scholar.google.com* and *pubmed.ncbi.nlm.nih.gov/* using various combinations of relevant search terms. We also reviewed non-peer reviewed sources, such as governmental websites and reports. The methods for how we assessed the risk of pancreatic cancer in firefighters have been published previously in "Firefighters and Cancer Risk" (Washington State Department of Labor and Industries, 2024).

Results

Association between PFAS exposure and pancreatic cancer

In 2020, The National Institute of Environmental Health Sciences' National Toxicology Program (NTP) published a comprehensive review of studies evaluating the carcinogenicity of PFAS in rats. Such studies allowed researchers to control the type, amount, timing, and duration of PFAS exposure, something that is nearly impossible to do in human subjects. Researchers reported increases in pancreatic acinar cell adenoma and adenocarcinoma in rats exposed to PFOA over a two-year span, leading them to conclude that there is clear evidence of an association between PFOA and pancreatic cancer in male rats and

some evidence of an association between PFOA and pancreatic cancer in female rats (NTP, 2020). Others researchers have suggested that the specific mechanisms by which PFOA is thought to cause pancreatic tumors in rats is less present in humans (Steenland, 2021).

The International Agency for Research on Cancer (IARC) periodically assembles to assess and identify agents that may be carcinogenic to humans. A group of 30 scientists from 11 countries met in November 2023 to evaluate the impact of PFOA and PFOS in humans. After reviewing the best available evidence for all types of cancer, the group classified PFOA as “carcinogenic to humans (Group 1)” and PFOS as “possibly carcinogenic to humans (Group 2B),” noting that there was strong mechanistic evidence supporting carcinogenesis, but limited or inadequate evidence regarding cancer in humans (Zahm, 2024). The classification relates to carcinogenicity when looking all types of cancers combined, but does not necessarily apply to individual cancer types or sites. The authors noted that there is limited evidence of an association between PFOA and renal cell carcinoma and testicular cancer, but they did not address pancreatic cancer. At the time of this writing, the full assessments are slated to be published in Volume 135 of the IARC Monographs later in 2024.

The association between PFAS and pancreatic cancer has been evaluated in few epidemiological studies. In a meta-analysis of 16 epidemiological studies measuring the association between PFAS, mostly PFOA and PFOS, and various types of cancers, researchers were unable to establish an association between PFAS and pancreatic cancer (Steenland, 2021). It is unclear if methodological limitations, such as small number of cases, left-truncation, and selection bias have impeded researchers from detecting an association or if the association does not exist (Steenland, 2021). In a cohort study following 57,053 Danish individuals who were 50-65 years old with no previous cancer diagnoses, researchers identified 128 subsequent pancreatic cancer diagnoses (Eriksen, 2009). PFAS and PFOA plasma concentrations were measured among the 128 individuals diagnosed with pancreatic cancer and a subcohort of 772 randomly selected individuals representing the approximate male-to-female ratio of the full cohort. The PFOS plasma concentrations for the individuals with pancreatic cancer (32.7 ng/mL; 5-95% percentiles: 15.2-56.4ng/mL) were similar to the plasma concentrations for both men (35.0 ng/mL; 5-95% percentiles: 16.8-62.4 ng/mL, n=680) and women (29.3 ng/mL; 5-95% percentiles: 14.2-55.6 ng/mL, n=92) in the subcohort. There were no observed differences for PFOA plasma concentrations as well. The researchers further analyzed pancreatic cancer incidence rate ratios (IRR) by quartile of PFOA/PFOS plasma concentration, and report a statistically non-significant “positive association between plasma concentrations of PFOA and risk for pancreatic cancer (for the lowest vs. the fourth quartiles, IRR for pancreatic cancer = 1.55, 95% CI = 0.85 to 2.80)” (Erikson, 2009).

The synthesis and polymerization of tetrafluoroethylene involves the use of ammonium perfluorooctanoate and thus a study of workers exposed to TFE is commonly referenced in assessing mortality risk from PFOA (Consonni, 2013). Reported standardized mortality ratio (SMR) for cause of death from pancreatic cancer among 4,773 male production workers was 1.15 (95% CI: 0.61, 1.97). There were also no significant increases in the risk of pancreatic cancer mortality based on cumulative years of exposure to TFE, length of exposure to TFE, or time since first exposure.

Residents living near a naval air station in Pennsylvania have long expressed concern about health problems due to contaminated drinking water in the area. In 2014, samples of both public and private drinking water showed elevated levels of PFAS, e.g. PFOS and PFOA, likely a result of firefighting foam that was used for decades at the naval air station (PA DOH, 2017). Subsequently, The Pennsylvania

Department of Health assessed pancreatic cancer rates in the three zip codes around the naval base from 1985-2013. From 1985-1994, pancreatic cancer incident rates were lower among men (SIR=0.50, 95%CI: 0.3-0.77) and women (SIR=0.57, 95%CI: 0.37-0.84) in the three zip codes than the statewide pancreatic cancer incidence rates. From 1995-2004, the pancreatic cancer incidence rate in the study area were not statistically different than the state-wide rate. However, from 2005-2013, the pancreatic cancer incidence rate for both men (SIR=1.60, 95%CI: 1.21-2.08) and women (SIR=2.30, 95%CI: 1.81-2.89) in the study area were statistically higher than the statewide pancreatic cancer incidence rates. However, the researchers cautioned that the calculations in the earlier cohorts were based on a small number of pancreatic cancer cases (averaging fewer than 10 incident pancreatic cancer cases per year), which resulted in wide confidence intervals. Furthermore, the authors noted the absence of additional information regarding possible risk factors for cancer, e.g. smoking, diabetes, pancreatitis, obesity, and certain genetic risk factors which might limit the interpretation of the pancreatic cancer results. (PA DOH, 2017).

In Sweden, researchers studied the cancer incidence among individuals who ever lived in the Ronneby municipality during a period of time in which the local drinking water was contaminated with PFAS from AFFF used at a nearby military airfield (Li, 2022). The cohort included everyone who ever lived in the area between 1985 and 2013, and address data was further used to stratify individuals by exposure level. Age and sex adjusted cancer incidence was then compared to the county population, excluding the individuals in the cohort. Neither males nor females of either exposure group were found to have an increased risk of pancreatic cancer when compared to the county population (Li, 2022). Numerous governmental agencies and task forces have provided official statements based on their review of the scientific evidence, but none noted a specific risk of pancreatic cancer from PFAS exposure. The National Cancer Institute has launched a series of studies to identify specific cancers associated with PFAS at exposure levels typically found in the general population, but it did not include pancreatic cancer among the cancers being studied (NCI, 2020). According to the Environmental Protection Agency, PFAS exposure may lead to increased risk of some cancers including prostate, kidney, and testicular cancers (US EPA, 2023). Similarly, the Agency for Toxic Substances and Disease Registry noted that “high levels of certain PFAS may lead to increased risk of kidney and testicular cancer” in humans (ATSDR, 2020). To date, no governmental or regulatory agency has suggested that PFAS exposures are specifically associated with pancreatic cancer.

Firefighters and PFAS Exposure

PFAS are manufactured, non-naturally occurring chemicals. Manufacture and use of PFAS has diminished over time. The various PFAS, such as PFOA and PFOS, have different half-lives in humans, thus measured levels are influenced by the time of exposure to PFAS relative to the timing of serum PFAS testing. Further, there is evidence that blood donation (Gasiorowski, 2022) and blood loss through menstruation may lower PFAS levels (Trowbridge, 2020).

Serum levels of PFAS in individual firefighters will be influenced by individual occupational and non-occupational exposures. Firefighters’ serum levels of PFAS relative to various control populations have been summarized by IARC (2023) and more recently by Rosenfeld, et al. (2023) and Mazumder, et al. (2023). Evidence supports elevated PFAS levels, i.e. PFOS and perfluorohexane sulfonic acid (PFHxS), in association with firefighters’ exposure to AFFF.

Rotander et al., 2015 reported that when 149 Australian firefighters with AFFF exposure were compared to the general Australian and Canadian populations, the serum PFOS levels in firefighters were six to 10 times higher than in the control population, and serum PFHxS levels were 10 to 15 times greater in firefighters than in the control population. Serum PFOA levels in firefighters were in the same range as in the Australian and Canadian populations. The authors attributed the elevated levels of PFOS and PFHxS to the likely exposure to AFFF manufactured by 3M, which has perfluorinated sulfonates as their major components (Rotander, 2015). Further there was a positive association between years on the job and serum levels of PFOS. Firefighters who had less than 10 years on the job, which correlated to a time when PFOS-containing 3M AFFF were phased-out from use, had PFOS levels similar to that of the general population controls. The median concentration of PFOS for FF with 20 years of exposure or more was greater than 5 times that of firefighters with less than 10 years of exposure (Rotander, 2015). A follow-up study with an expanded population of firefighters, confirmed that elevated serum concentrations of PFOS/PFHxS associated with the historical use of PFOS/PFHxS-based AFFF (Nilsson, 2022). Further, in the longitudinal analysis of firefighters who had serum samples in both 2013-2014 and in 2018-2019, calculated annual significant decreases in serum concentrations of PFOA, PFHxS, PFHpS and PFOS (Nilsson, 2022). The authors suggest these findings support that discontinued use of the AFFF products likely contributed to the decline in serum PFAS levels of previously exposed FF.

Leary et al. (2020) compared PFAS levels in 38 male municipal airport firefighters to nine male suburban mostly volunteer firefighters and then compared all 47 municipal airport and suburban firefighters to general population levels of PFAS as estimated from the National Health and Nutrition Examination Survey (NHANES). Serum levels of PFOS, PFHxS and PFOA were higher in firefighters than the general population. PFOS levels in the municipal airport firefighters were significantly higher than suburban firefighters but statistical significance was not reached for PFHxS, PFOA, and perfluorononanoic acid (PFNA). Serum levels of PFHxS were significantly elevated in firefighters who reported a history of use of AFFF compared to those who did not report its use.

Laitinen et al. (2014) evaluated serum PFAS levels of eight firefighters following three training periods in which AFFF were used. Baseline samples were taken two weeks prior to the initial training period and then two weeks after each of the three training sessions. Measured levels of PFHxS and PFNA increased 17% and 10% respectively after the third training session and exceeded baseline measures, although statistical testing was not performed due to the small number of study participants.

Several research studies reported elevated PFAS levels in municipal and volunteer firefighter populations with no reported exposures to AFFF. Khalil et al (2020) reported serum PFAS results from 38 Arizona firefighters and compared them to PFAS levels in 49 participants in the 2009 to 2010 NHANES. Serum levels of PFHxS were significantly elevated in firefighters relative to the NHANES participants. PFOS levels were elevated in the firefighter population, but the difference was not statistically significant from the NHANES subjects. PFNA and perfluoroundecanoic acid (PFUA) were significantly lower in the firefighter population, and serum levels of eight other PFAS were not significantly different between the firefighter population and NHANES referents. The authors noted that records of AFFF use in firefighters participating in the study were not available (Khalil, 2020). Background PFAS levels for Arizona firefighters were not reported or may have been unknown.

Dobraca et al (2015) reported results from biomonitoring of 101 Southern California firefighters with measurement of 12 serum perfluorinated chemicals (PFCs) and compared the results to calculated

geometric means from men 20 years or older from the 2009 to 2010 NHANES. Of the 12 PFCs measured, perfluorodecanoic acid (PFDA) was significantly elevated in firefighters. Geometric means for the FF participants in the study were similar to the NHANES values for the remaining measurable PFCs, including PFHxS, PFOS, and PFNA.

The California biomonitoring study of firefighters, Firefighter Occupational Exposure (FOX) study (Dobraca, 2015), also completed an exposure assessment survey which collected data on firefighting experience, recent incident response, occupational duties, personal protective equipment (PPE) use and maintenance, exposure to firefighting foam, selected dietary intake, and demographic information. Multivariate analyses results reported by Dobraca (2015) included:

- Higher concentrations of perfluorooctane sulfonamide (PFOSA) in firefighters aged 50 years or older compared to younger firefighters.
- Monthly or more frequent responses to commercial fires were associated with higher perfluoroheptanoic acid (PFHpA) concentrations.
- Those who responded to hazardous materials incidents at least monthly had higher concentrations of 2-(N-methyl-perfluorooctane sulfonamido) (N-MeFOSAA) than those who did not.
- Those who had responded to any hazardous materials response was associated with higher PFNA values.
- PFNA and PFOA were also significantly higher in firefighters whose turnout gear had not been professionally decontaminated within the last year.
- FF who used Class A firefighting foam had significantly higher PFHpA concentrations than those who did not use any class of foam.

Shaw et al. (2013) measured serum PFAS levels in 12 San Francisco FFs. Blood samples were drawn within 24 hours of a fire response. PFOS and PFHxS concentrations were two-fold lower and PFOA and PFNA concentrations were two-fold higher in the firefighters when compared to concentrations in the general US populations from the 2003-2004 NHANES. The authors suggest that elevated PFNA levels may be associated with high smoke exposure, and is consistent with observations from firefighters exposed to smoke during the World Trade Center response (Tao, 2008).

Graber et al (2021) measured PFAS levels in 135 volunteer New Jersey firefighters in 2019, and compared results to two sets of NHANES data. In comparison of the PFAS results to the 2017-2018 NHANES data, volunteer firefighters had significantly lower geometric mean serum concentrations of PFOS and MeFOSAA; volunteer firefighters had significantly higher mean serum concentrations of PFNA, PFDA, and perfluorododecanoic acid (PFDoA) (as compared to the 2015–2016 NHANES). In multivariate analyses, higher serum levels of both PFDA and PFDoA were positively and significantly associated with years of firefighting service after controlling for age, educational level, and occupation. For every increase of 10 years of firefighting, the expected value of PFDA increased by 8% (95% CI: 1%, 15%) and the expected value of PFDoA increased by 19% (95% CI: 9%, 30%). The authors noted (Graber, 2021) that PFAS sampling of waterways adjacent to the town where the study was conducted contained

detectable levels of PFOA and PFOS but not of PFDoA or PFNA, suggesting these exposures are less likely to be influenced by environmental or community exposures.

Trowbridge et al (2020) measured PFAS levels in 86 female firefighters and 84 female office workers in San Francisco. In regression models comparing PFAS levels by occupation and adjusting for potential confounders, female firefighters had significantly higher geometric mean concentrations of PFHxS and PFNA than female office workers (Trowbridge, 2020). By occupation, firefighters and officers had higher PFNA, PFOA, PFDA, and PFUnDA levels compared to drivers (Trowbridge, 2020). The study design used a community based comparison group of female office workers and adjusted for possible similar environmental and background exposures to PFAS.

Burgess et al (2023) compared PFAS levels in 290 firefighters from four municipal fire departments and matched three NHANES participants to each firefighter based on sex, ethnicity, age and PFAS collection year. This study included 31 women from two different fire departments. Serum PFHxS, the sum of branched perfluoromethylheptane sulfonate isomers (Sm-PFOS), PFOS, PFOA, and PFNA concentrations were increased in at least two of four fire departments in comparison to NHANES (Burgess, 2023). In the two departments with female firefighters, PFHxS and Sm-PFOS concentrations were elevated as compared to controls (Burgess, 2023). Other PFAS concentrations were elevated and/or reduced in only one department or not significantly different from NHANES in any department (Burgess, 2023).

From these exposure and biomonitoring studies, it appears that firefighters are likely exposed to PFAS in excess of the general population. The most obvious source would be AFFF but even for firefighters who are likely less exposed to AFFF, elevated levels of specific PFAS have been observed.

Pancreatic Cancer in Firefighters

The advisory committee previously reviewed the association between firefighting and pancreatic cancer, which is described in full in "Firefighters and Cancer Risk" (Washington State Department of Labor and Industries, 2024). In short, the committee identified six meta-analyses, 35 cohort studies, seven case-control studies, and two PMR studies describing pancreatic risk in firefighters. Most of these studies, including five of the meta-analyses, did not find that firefighters had an increased risk of pancreatic cancer. The committee concluded that the epidemiologic evidence did not provide sufficient supportive evidence of an increased risk of pancreatic cancer in firefighters at the point of their review. Therefore, the committee did not recommend pancreatic cancer to be included in the WA firefighter presumption law, but acknowledged that additional review of the evidence may be necessary as more research evidence emerges.

Conclusion

The International Agency for Research on Cancer (IARC) has classified PFOA as "carcinogenic to humans (Group 1)" noting that there is an observable association between PFOA and certain types of cancer and PFOS as "possibly carcinogenic to humans (Group 2B)" (Zahm, 2024). However, there is insufficient evidence to suggest that PFAS is specifically associated with pancreatic cancer in the general public.

Biomonitoring studies have observed elevated PFAS levels in firefighters compared to non-firefighters, likely due to occupational use of AFFF. However, epidemiological studies of pancreatic cancer in firefighters have not demonstrated that firefighters are at an increased risk of developing pancreatic cancer compared to non-firefighters.

Based on a review of the current scientific literature, the committee found sufficient evidence to support that firefighters are regularly exposed to PFAS at work, but did not find evidence that firefighters have an increased risk pancreatic cancer incidence or mortality. Therefore, the committee has not found sufficient evidence for an association between PFAS exposure and pancreatic cancer in firefighters. Subsequent requests for a review of the association between PFAS and pancreatic cancer in firefighters may be necessary as more research evidence emerges.

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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,

Handwritten signature of Karen Keiser in black ink.

Karen Keiser
State Senator
33rd Legislative District

Handwritten signature of Liz Berry in black ink.

Liz Berry
State Representative
36th Legislative District