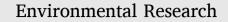
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Perfluoroalkyl substances exposure in firefighters: Sources and implications

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ABSTRACT

Firefighters are at risk of occupational exposure to long-chain per- and poly-fluoroalkyl substances (PFASs), most notably from PFASs present in Class B aqueous film-forming foam (AFFF). Firefighters have been found to have elevated serum levels of long-chain PFASs. Due to the persistence of PFAS chemicals in the human body and their ability to bioaccumulate, firefighters experience the latent and cumulative effects of PFAS-containing AFFF exposure that occurs throughout their careers. This article summarizes the history of AFFF use by firefighters and current AFFF use practices. In addition, this paper describes PFAS levels in firefighter serum, PFAS serum removal pathways, PFAS exposure pathways, and occupational factors affecting PFAS levels in firefighters. International, national, and state agencies have concluded that PFOA, a long-chain PFAS, is potentially carcinogenic and that carcinogens have an additive effect. From the cancer types that may be associated with PFAS exposure, studies on cancer risk among firefighters have shown an elevated risk for thyroid, kidney, bladder, testicular, prostate, and colon cancer. Thus, exposure to PFAS-containing AFFF may contribute to firefighter cancer risk and warrants further research.

1. Introduction

Per- and polyfluoroalkyl substances (PFASs) are a group of over 5000 different chemicals, many of which are included in AFFF formulations for Class B flammable fuel fires due to their effectiveness as surfactants (Hall et al., 2020; Interstate Technology Regulatory Council, 2022). Firefighters who use aqueous film-forming foam (AFFF) have been found to have elevated levels of long-chain PFASs in their serum, the clear, yellowish fluid that remains after separating whole blood into its solid and liquid components (Nilsson et al., 2020).

Buck et al. (2011) define perfluoroalkyl and polyfluoroalkyl substances (PFASs) as highly fluorinated aliphatic substances that contain one or more carbon atoms on which all the hydrogen substituents have been replaced by fluorine atoms, in such a manner that they contain the perfluoroalkyl moiety C_nF_{2n+1}-. Polyfluoroalkyl substances have multiple sites where hydrogen has been substituted with fluorine, while all sites have been substituted with fluorine in perfluoroalkyl substances (Lindstrom et al., 2011). Due to the fluorinated region of the molecule, these compounds possess numerous unique physical and chemical properties such as water and oil repellency, thermal stability, and surfactant characteristics that make them useful for many different industrial and consumer-use applications. The carbon-fluorine bond makes these compounds extremely strong and stable. This chemical and thermal stability, in addition to the hydrophobic and lipophobic nature of PFASs, allows these substances to persist in the environment without breaking down. For instance, under typical soil conditions, it can take over 1000 years for some PFASs to fully degrade in the environment (Russell et al., 2008; Washington et al., 2009).

Some PFASs bioaccumulate and biomagnify in the food chain and ecosystems through exposure and intake (Liu et al., 2018). Acidic PFASs (e.g., PFOA, PFOS) have been found to be associated with proteins like serum albumin and phospholipids rather than storage lipids. As a result,

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acidic PFASs primarily accumulate in the serum, liver, kidney, and brain of non-human organisms rather than adipose tissue (De Silva et al., 2021). Due to the persistence of PFAS chemicals and their ability to bioaccumulate (Liu et al., 2018), firefighters may experience the cumulative effects of occupational exposure to PFASs throughout their careers. One occupational exposure pathway for firefighters involves exposure to Class B AFFF, which can contain perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) (Interstate Technology Regulatory Council, 2022). Class B firefighting foams are designed to extinguish flammable liquids, whereas Class A foams are used for structural and vegetation fires (Dobraca et al., 2015; Interstate Technology Regulatory Council, 2022). Mentions of "AFFF" in this review exclusively refer to Class B AFFF.

The World Health Organization (WHO), the United States (U.S.) Environmental Protection Agency (EPA), the California Office of Environmental Health Hazard Assessment (OEHHA), and the International Agency for Research on Cancer (IARC) reported that PFOA is possibly carcinogenic to humans (International Agency for Research on Cancer, 2017; U.S. Environmental Protection Agency, 2016; California Office of Environmental Health Hazard Assessment, 2022; International Agency for Research on Cancer, 2020). In 2021, OEHHA added PFOS along with its salts, transformation, and degradation precursors to Proposition 65, the list of chemicals known to the state of California to cause cancer for the purposes of the Safe Drinking Water and Toxic Enforcement Act of 1986 (California Office of Environmental Health Hazard Assessment, 2021). Regulation and understanding of the health effects of PFASs are continually evolving, and this review is constrained by the current state of knowledge and available evidence for these chemicals. In the recently published National Academies of Science publication on PFAS, PFOA and PFOS are recognized as the most studied PFAS chemicals. The science about PFOA and PFOS is thus treated as a proxy for the entire class of PFAS chemicals, and this widely accepted view is presumed in this paper (National Academy of Science, 2022).

EPA methodology supports that carcinogens have an additive effect (U.S. Environmental Protection Agency, 2005). In this context, PFOA is a potential carcinogen that may confer its own cancer risk or potentially interact with other occupational carcinogens for firefighters. Various studies have shown firefighters may have an elevated risk of cancers including malignant melanoma and cancers of the thyroid, kidney, bladder, testicles, prostate, and colon (Jalilian et al., 2019; LeMasters et al., 2006). As PFOA is a potential carcinogen, occupational exposure to PFOA may be an important contributor to the elevated cancer risk for firefighters. There are a variety of non-carcinogenic effects associated with PFAS exposure, however, these are outside the scope of this review.

This paper evaluates the occupational exposure to PFASs among firefighters and considers such exposure capable of contributing to the cancers associated with firefighting (Demers et al., 2022; National Academy of Science, 2022). The paper begins with a brief review of AFFF exposure among firefighters, the history of AFFF usage, and current usage practices in the U.S. This is followed by a review of studies examining PFAS serum concentrations in firefighters, the half-life and elimination pathways of PFAS in the body, PFAS exposure pathways, and occupational factors affecting firefighter PFAS levels. Next, results from medical and epidemiological studies are summarized which evaluate the association between PFAS chemicals and different cancers. Lastly, the EPA's methodology for carcinogen risk assessment is detailed to support the additive effect of PFASs as potential carcinogens.

2. Methods

From June 2021 through November 2022, we reviewed studies about firefighters and their exposure to PFASs through Google Scholar. To refine our search, we used the key terms "firefighters," "PFAS," "AFFF," "cancer," "blood" and the names of different types of PFAS to identify the most relevant literature. In the studies reviewed for this paper that lack information about their analytical methods, it is assumed that serum matrices were used for analyzing PFASs using liquid chromatography-tandem mass spectrometry techniques. It is further assumed that 'background' body burdens of PFASs impact those in the fire service comparably and that occupational exposures add to the overall body burden of firefighters beyond what is experienced from non-occupational sources such as water, non-stick cookware, and food packaging. Through this search, we aimed to identify and assess studies evaluating firefighter exposure to AFFF, PFAS half-life studies, and epidemiological studies of the association between PFAS exposure and various cancers.

3. Results

3.1. PFAS exposure in firefighters

3.1.1. Aqueous film-forming foam

Firefighters are occupationally exposed to many carcinogens and hazardous chemicals through exposures to combustion products, fire station dust, diesel exhaust, and contaminated fire equipment and gear (Clarity et al., 2021). PFASs are another recurrent toxic occupational exposure for firefighters. AFFF is a fire-extinguishing surfactant used to extinguish oil fires and other liquid fuel fires. AFFF produces an aqueous film that works by suppressing flammable liquid vapor, suffocating a fire hazard, and preventing re-ignition (Filipovic et al., 2015). The hydro-, oleo-, and lipophobic properties of PFASs make them an effective addition to AFFF formulations, as such properties are highly effective at extinguishing liquid fuel fires. Smoke and turnout gear are additional sources of occupational PFAS exposure for firefighters (Tao et al., 2008; Peaslee et al., 2020). Historically, however, AFFF has been a more significant source of PFAS exposure for firefighters (Interstate Technology Regulatory Council, 2022). PFAS exposure pathways for firefighters include dermal exposure, incidental ingestion of contaminated dust, AFFF, or degraded firefighter textiles, smoke inhalation, and ingestion of contaminated food and water.

Firefighters can be exposed to AFFF during fire events and routine training. Through these activities, both professional and volunteer firefighters with increased exposure to AFFF have elevated serum levels of various PFASs (Graber et al., 2021; Leary et al., 2020; Dobraca et al., 2015; Trowbridge et al., 2020). Serum levels escalate in firefighters with increasing time served on the firefighting force (Nilsson et al., 2020).

3.1.2. AFFF history and current use practices in the U.S.

The U.S. Navy collaborated with 3M in the 1960s to develop AFFF to suppress liquid fuel fires (3 M, n.d, 2022). 3M used the electrochemical fluorination (ECF) process to produce AFFF, and this type of AFFF is referred to as legacy PFOS AFFF (Darwin, 2004). AFFF is the most effective and efficient liquid fire-suppressing agent, and it quickly became adopted in a variety of industries, including military, aviation, oil and gas, and firefighting (Darwin, 2004). By 1969, the U.S. Department of Defense (DoD) created a military specification (MilSpec) for AFFF, MIL-F-24385, that required all military installations to use the PFAS-containing product for firefighting and training exercises (Interstate Technology Regulatory Council, 2022). The military was the largest user of firefighting foams and AFFF in particular, using 29 percent of all AFFF concentrate used in the U.S. in 2004 (Place and Field, 2012; Darwin, 2004). 75 percent of all AFFF stored in U.S. military bases was produced using ECF and thus contained PFOS (Darwin, 2004). Non-aviation fire departments and civil aviation utilized around 14 percent and 16 percent of all AFFF concentrate in the U.S. in 2004, respectively (Darwin, 2004). Most fire departments have a small inventory of AFFF to use in the event of a flammable liquid fire, and AFFF is the standard firefighting agent at airports in the U.S. (Interstate Technology Regulatory Council, 2022).

Following rising concerns about the impacts of long-chain PFASs on human health and the environment in the early 2000s, the U.S. implemented various initiatives to decrease or eliminate the use of PFAS chemicals (Leary et al., 2020). The EPA created the PFOA Stewardship Program in 2006 to reduce PFOA use within the PFAS industry and raise awareness about its health risks (Buck et al., 2011; U.S. Environmental Protection Agency, 2022a). As a part of the program, eight major companies within the PFAS industry were asked to commit to a 95 percent reduction in PFOA facility emissions compared to baseline emissions in 2000 b y 2010.3M, the leading manufacturer of AFFF in the U.S. from the 1960s until 2002, was included in the program (Buck et al., 2011; International Agency for Research on Cancer, 2020). All companies reported that they had met this goal by phasing out the production and importation of long-chain PFAS chemicals or leaving the industry as a whole. Those that remained in the industry transitioned from legacy PFOS and fluorotelomer AFFF to predominantly modern fluorotelomer AFFF, which contains short-chain PFAS (Interstate Technology Regulatory Council, 2022). The telomerization process used to produce fluorotelomer AFFF does not involve PFOS or products that could degrade into PFOS (Darwin, 2004). In the general U.S. population, PFAS serum concentrations measured by the CDC Control National Health and Nutrition Examination Survey (NHANES) declined by more than 70% since 1999 likely due to the phase-out of PFOA, PFOS, and PFHxS (Khalil et al., 2020).

In January 2016, the U.S. Department of Defense issued a policy to remove and properly dispose of all PFOS-based AFFF at its military installations where "practical" (U.S. Department of Defense, 2018). In addition, the 2022 National Defense Authorization Act mandates that the DoD create a MilSpec for PFAS-free foams by January 2023 to facilitate the transition away from PFAS-based AFFF. These initiatives serve to address the signification association between the number of military fire training areas and public airports with AFFF training and the detection of PFAS above minimum reporting levels (Hu et al., 2016).

In June 2021, the EPA issued three new actions to control PFAS use (U.S. Environmental Protection Agency, 2022c; U.S. Environmental Protection Agency, 2021). These actions include issuing a proposed Toxic Substances Control Act (TSCA) rule with new reporting

requirements for more than 1000 PFASs manufactured in the US, withdrawing guidance that weakened the EPA's July 2020 Significant New Use Rule (SNUR) restricting certain long-chain PFASs, and publishing a final rule that officially incorporates three additional PFAS chemicals into the Toxics Release Inventory (TRI). The EPA aims to increase transparency among manufacturers, reduce health and environmental risks associated with PFAS exposure, and ultimately prevent the release of PFAS into the environment through these recent actions and its roadmap of proposed actions and policies to address PFAS through 2024 (U.S. Environmental Protection Agency, 2022b). See Fig. 1 for a timeline visualizing the history of AFFF use and relevant actions to address it in the U.S.

3M voluntarily halted production of all AFFF products, including its PFOS-based "LightWater" AFFF, in 2002 (Buck et al., 2011), but the U.S. government does not restrict the use of stockpiled 3M AFFF (Place and Field, 2012). While there has been some success with voluntary controls for some PFAS through the EPA Stewardship Program, companies have limited incentive to join these voluntary agreements. They are often motivated to increase the production of long-chain PFAS to meet continuing international market demands (Lindstrom et al., 2011).

3.2. PFAS exposure pathways for firefighters

Firefighters are exposed to PFAS from AFFF and contaminated turnout gear through dermal exposure, inhalation and ingestion of AFFF and turnout gear textiles, ingestion of contaminated water and food, dust ingestion, and smoke inhalation.

3.2.1. Dermal exposure

Direct skin contact to turnout gear, AFFF, and contaminated dust can expose firefighters to PFAS (Rotander et al., 2015; De Silva et al., 2021). Gear worn by firefighters are made from PFAS-containing textiles that make the textiles water and oil-resistant (Peaslee et al., 2020). PFAS from the gear can potentially be taken up by the skin or shed and

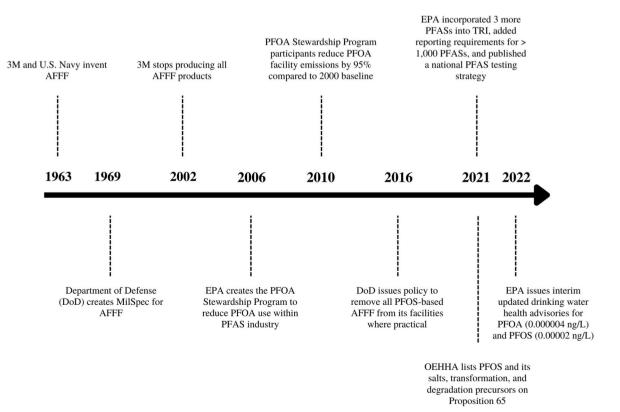


Fig. 1. Timeline of AFFF use in the U.S.

accumulate in dust (Peaslee et al., 2020). Peaslee et al.'s (2020) study highlights firefighter textiles are a potential source of dermal exposure to PFAS, although they do not assess the magnitude of this exposure pathway. Rotander et al. (2015) find that dermal contact is not an important pathway of PFAS exposure for firefighters working with AFFF. In agreement with Rotander et al.'s findings, De Silva et al. (2021) synthesis of PFAS exposure assessments confirms that dermal contact is not as significant of a contributor to PFAS exposure compared to other routes of exposure.

3.2.2. Ingestion and inhalation of AFFF and turnout gear

Firefighters have the potential to expose themselves to PFAS via incidental ingestion and inhalation of AFFF and degraded textiles from their gear (De Silva et al., 2021; Peaslee et al., 2020). Contact with contaminated PPE can result in hand-to-mouth transfer of AFFF and other PFAS-containing substances and droplets likely settling in the oral pharynx (Leary et al., 2020). Aerosolized AFFF can enter the lungs and be absorbed into the bloodstream through pulmonary capillaries or move to the upper respiratory system and transfer onto food, where it then enters the digestive tract (Horn et al., 2022). According to several studies (Peaslee et al., 2020; Tao et al., 2008), inhalation of AFFF is one of the main exposure pathways of PFAS for firefighters. Peaslee et al. present ingestion and inhalation of PFAS shed from turnout gear as a potential source of PFAS in the body and acknowledge the lack of information available to validate the significance of this form of exposure (Peaslee et al., 2020).

3.2.3. Ingestion of contaminated water and food

AFFF use during fire training and fire suppression activities releases PFASs into the environment, which can contaminate groundwater and drinking water supplies (Hu et al., 2016; Filipovic et al., 2015; Xu et al., 2020). Water sampling around airports and fire training areas have identified groundwater and surface water sources with PFAS concentrations up to 4 times higher than EPA's 2016 drinking water health advisory level of 70 ng/L PFOA and PFOS (Hu et al., 2016). With the EPA's announcement of interim updated health advisories of 0.000004 ng/L PFOA and 0.00002 ng/L PFOS in 2022, these contaminated water sources can contain PFAS concentrations millions of times higher than the advisory levels (U.S. Environmental Protection Agency, 2022d). Hu et al. (2016) found that watersheds with detectable levels of PFOA have more military fire training areas, AFFF-certified airports, industrial sites, and wastewater treatment plants than watersheds with PFOA concentrations below the detection limit. PFAS detection frequency was found to increase by 17.8 percent with the presence of a military fire training area in a watershed. The presence of facilities with personnel trained to use AFFF is a significant predictor of PFAS detection above minimum reporting levels. Ingestion of contaminated water can therefore cause an accumulation of PFAS in the body.

Ingestion of contaminated food represents another significant PFAS exposure pathway (De Silva et al., 2021; Tefera et al., 2022). PFASs are found in food packaging and non-stick cookware, which can contaminate food and then enter the body via ingestion (Young et al., 2021). Consumption of meat, fish, and other animal products can expose people to PFASs due to their bioaccumulation and biomagnification in food webs (De Silva et al., 2021). The exposure assessments reviewed by De Silva et al. (2021) generally agree that dietary exposure is a major contributor to PFOS and PFOA exposure. Tefera et al. (2022) found that the consumption of food grown on fire stations is another relevant PFAS exposure pathway for firefighters. Consumption of food cultivated on fire stations contributed more significantly to firefighters' PFAS exposure (82% of intake) than incidental ingestion and dermal absorption of PFAS in dust (15%) (Tefera et al., 2022). However, this study does not compare the contribution of foods not grown on fire stations to those grown on fire stations, which is not the primary source of food for most firefighters.

3.2.4. Dust ingestion

To measure the difference between PFAS levels in homes and fire stations, a study compared indoor dust samples from 184 North Carolina homes and 49 fire stations across the U.S. and Canada (Hall et al., 2020). Dust collected in living areas of fire stations had median levels of PFAS fifteen times higher than homes, and median levels of PFHxS three times higher than homes. Considering adults ingest around 30 mg of dust per day, dust ingestion is a possible exposure route for firefighters who work indoors with AFFF (Hall et al., 2020).

Young et al. (2021) assessed PFAS concentrations and sources within fire stations in Massachusetts and found that dust in turnout gear locker rooms had higher levels of total fluorine, PFHxA, PFHpA, and PFOA than fire station living rooms. Over 92 percent of dust samples in the fire station had detectable levels of PFAS. In their study, AFFF use was not a significant predictor of PFAS concentrations in dust, suggesting that turnout gear contributes more significantly to indoor dust PFAS concentrations.

3.2.5. Smoke inhalation

According to the EPA, smoke often contains combustion byproducts and contaminants that are harmful to human health (U.S. Environmental Protection Agency, 2019). PFASs are one such group of contaminants that can be released into the air through smoke (Tao et al., 2008; Young et al., 2021). In particular, PFASs are used in various building materials like upholstery, carpets, and flooring, which can release PFAS into soot and smoke during a fire (Tao et al., 2008). Studies have linked elevated cancer rates in firefighters in part to their increased exposure to dangerous compounds found in smoke during fire responses, despite routine use of self-contained breathing apparatuses (Tsai et al., 2015; Crawford et al., 2017). A study of World Trade Center responders by Tao et al. (2008) found higher concentrations of PFOA and PFHxS in responders exposed to smoke than those exposed to dust. PFNA and PFHxS concentrations were 39.3% and 12.4% higher, respectively, in a subgroup of first responders exposed to more smoke than a subgroup exposed to less smoke (Tao et al., 2008). Additionally, exposure to turnout gear contaminated by PFAS from encounters involving smoke or AFFF use can pose risks (Young et al., 2021). Still, further research is needed on the links between smoke inhalation and PFAS exposure from PFAS-containing consumer products.

3.3. Factors affecting firefighter PFAS levels

AFFF exposure, occupational duties, length of employment, and the use of personal protective equipment (PPE) have been found to affect PFAS levels in firefighters.

3.3.1. Background PFAS exposure

PFASs are persistent in the environment and have been detected in humans around the world (Trowbridge et al., 2020). PFASs are commonly found in consumer products like furniture fabrics and carpets, indoor dust and air, and contaminated food and drinking water sources. These factors contribute to background exposure levels of these compounds for firefighters and non-firefighters globally. While there are many identified PFAS exposure pathways, some firefighters experience above-background PFAS exposures due to their occupational PFAS exposures.

3.3.2. AFFF exposure

Several studies support an association between the amount of direct AFFF exposure and elevated PFAS serum levels. Nilsson et al. (2020) found that PFOS and PFHxS were positively correlated with length of employment working with AFFF (n = 799). Participants who started work before 2005, the year that all Airservices sites replaced 3M LightWater AFFF with Ansulite AFFF, showed average concentrations of PFHxS, PFHpS, and PFOS higher than the general population, while those who started working after 2005 had average concentrations

similar to those of the general population. This suggests that the substitution of 3M LightWater AFFF was successful in reducing PFAS exposure in participants who started working after 2005. Similarly, a history of AFFF use correlated significantly with serum PFOS, PFOA, and PFHxS concentrations (n = 36) (Leary et al., 2020). Firefighters who reported AFFF use had elevated serum levels compared to those who did not, as did those who reported a PFAS-contaminated drinking water supply at home.

A study of Finland firefighters who used AFFF in training sessions (n = 8) found that PFHxS and PFNA serum levels increased by 17% and 10%, respectively, after three training sessions over a three-month period compared to individual baseline concentrations, despite firefighters wearing PPE and full-face masks (Laitinen et al., 2014). Due to heavy protection against respiratory exposure, results suggest that dermal exposure could be a significant pathway. The other possible exposure route is the transfer from contaminated PPE to hands and hands to mouth, leading to gastrointestinal exposure (Fent et al., 2013).

In the U.S., firefighters who reported AFFF use had significantly higher PFHpA concentrations than those who did not use AFFF (n = 101) (Dobraca et al., 2015). Trowbridge et al. (2020) found that firefighters who reported using firefighting foams during their career (n = 77) had elevated PFAS levels compared to those who reported never using firefighting foams before (n = 9).

Even 10 years after Australia phased out 3M's AFFF products, PFOS serum levels remained above 100 ng/mL and 200 ng/mL in 27% and 3% of participating firefighters (n = 799), respectively (Nilsson et al., 2020).

3.3.3. Occupational duties

Occupational sources do not exhaustively encompass firefighters' PFAS exposures. However, based on the findings in this review, they contribute to higher than background exposure in firefighters. Two studies discussed in section 3.2 support a correlation between firefighter occupational duties and PFAS serum levels. In Trowbridge et al. (2020), higher levels of five specific PFASs were associated with the assigned firefighter position (n = 86). The position of firefighter or officer (versus driver) was associated with higher average levels of PFOA, PFOS, PFNA, PFDA, and PFUnDA. Leary et al. (2020) compared firefighters assigned to an airport who reported AFFF exposure to suburban firefighters in Southwest Ohio (n = 36). Those assigned to the airport had 21%–62% higher levels of total PFASs than those assigned to other stations. However, when evaluated for specific PFAS chemicals, only PFOS was significantly elevated. Additionally, Nilsson et al. (2022a) found higher levels of PFAS in emergency vehicle technicians (EVTs) compared to firefighters. EVTs may be directly exposed to AFFF concentrate when repairing and maintaining fire engines. Limited use of protective equipment compared to firefighters, as discussed later in section 3.3.5, may also explain higher levels of PFAS.

3.3.4. Employment length

Two studies support a correlation between length of employment and elevated PFAS. Graber et al. (2021) found that PFDA and PFDoA are positively associated with years of firefighting and the yearly number of calls (n = 135). For every 10-year increase in firefighting experience, expected levels of PFDA and PFDoA increased respectively by 8% and 19%. Nilsson et al. (2020) found higher concentrations of PFHxS, PFHpS, and PFOS in firefighters with longer employment lengths (n =799). Additionally, Nilsson et al.'s (2022b) findings indicate that chloro-substituted-PFOS (Cl-PFOS) is likely bioaccumulative, suggesting that elevated levels of the compound increase with employment length.

3.3.5. Personal protective equipment

Appropriately cleaning personal protective equipment (PPE) gear may reduce occupational exposure to PFAS (Dobraca et al., 2015). Contaminated PPE may increase the chance of hand-to-mouth PFAS transfer and ingestion (Leary et al., 2020). Because of this, professional

cleaning of PPE turnout gear has been associated with lower PFNA and PFOA levels (Dobraca et al., 2015). Although firefighters are encouraged to wash their uniforms frequently, using contaminated PPE and uniforms may be a common practice because the cleaning process can be inconvenient (Leary et al., 2020). Frequency of PPE use may also affect the extent of PFAS exposure, considering PPE provides firefighters with protection from smoke and direct contact with AFFF. Nilsson et al. (2022a) found that 74% of emergency vehicle technicians (n = 39) and 27% of firefighters (n = 679) did not wear PPE "most days" when in contact with AFFF.

While wearing proper PPE provides important protection to firefighters in direct contact with AFFF, firefighter turnout gear may be another source of PFAS exposure. Turnout gear is manufactured from textiles made from fluoropolymers or extensively treated for oil and water resistance with PFAS in the form of side-chain fluoropolymers. A recent study assessed 30 sets of used and unused turnout gear manufactured by six primary U.S. companies with textiles made by four different manufacturers (Peaslee et al., 2020). The study found very high total fluorine levels in both the moisture barrier and outside shell layers of every sample. They also found that used gear showed lower levels of PFAS, indicating that PFAS degrades and wears off with time. Additional observations of fluorine in untreated layers of gear suggest that PFAS migrates from the highly fluorinated layers and collects in untreated layers of clothing against the skin, increasing the risk of direct dermal exposure. However, the significance of Peaslee et al.'s findings require more research, as little evidence exists to support that degraded PPE textiles contribute significantly to PFAS exposure. Shaw et al. (2013) found no significant relationship between PPE use and contaminant concentrations, although they had a small sample size (n = 12). Despite the potential for turnout gear to shed PFAS, the use of PPE is still recommended to protect firefighters against various occupational contaminant exposures.

3.4. PFAS in firefighter serum

Ten published studies were reviewed which show that firefighters have elevated serum levels of PFAS including PFOA, PFOS, perfluorononanoic acid (PFNA), perfluorohexane sulfonic acid (PFHxS), perfluoroheptane sulfonic acid (PFHpS), perfluorodecanoic acid (PFDeA), perfluorododecanoic acid (PFDoA), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA). Table 1 identifies the studies and reports the serum findings by PFAS type.

Rotander et al. (2015) studied 149 firefighters working with AFFF at training facilities in Australia's Airservices Aviation Rescue Fire Fighting Service. They report that compared to general populations in Australia and Canada, firefighter PFOS serum levels were 6–10 times higher and PFHxS levels 10 to 15 times higher. Nilsson et al. (2020) conducted a larger follow-up study on 799 current and former Airservices staff, with 130 staff from the earlier Rotander study. PFOA, PFOS, PFNA, PFHxS, and PFHpS were detected in more than 90% of participants, with PFOS, PFHxS, and PFHpS above the 95th percentile for the general Australian population. The geometric mean of both the control and study groups dropped between 2015 and 2018, suggesting that the 2005 phase-out of PFAS-containing AFFF from Airservices facilities caused the decrease in PFAS serum levels.

Four studies used NHANES biomonitoring data as a measure of PFAS blood levels in the general U.S. population. The Firefighter Occupational Exposures (FOX) Project assessed 101 Southern California firefighters and found that they had elevated PFOS concentrations in their serum and PFDeA concentrations roughly 3 times higher than NHANES general population levels (Dobraca et al., 2015). A study of 38 Arizona firefighters found elevated PFHxS and PFOS levels compared to levels in NHANES (Khalil et al., 2020). One study looked specifically at volunteer firefighters, which comprise about two-thirds of U.S. firefighters (Graber et al., 2021). Of 135 New Jersey volunteers, almost half had detectable PFDeA (LOD = 0.10 ng/mL), compared to less than 3% of NHANES

Table 1

PFAS blood serum levels in firefighter and control populations.

	First	Sample	Cohort Size			PFAS	Blood Serum Levels [ng/mL]	
	Author	Year	Cases Controls		AFFF Use ds		Geo. Mean Cases	Geo. Mean Controls
Southeast Queensland Population in Australia	Nilsson et al., 2020	2018	799	2400	Some	PFOS	27	5.7
						PFHxS	14	2.1
	Rotander et al., 2015 ^a	2013	149	-	Yes	PFOS	74	12
						PFHxS	33	3.2
National Health and Nutrition Examination	Graber et al., 2021	2019	135	_	No	PFOA	2.1	1.7
Survey ^b	Khalil et al., 2020	2009-2010	38	-	No	PFHxS	11.8	1.1
	Dobraca et al., 2015	2010-2011	101	-	No	PFOA	3.8	3.6
						PFHxS	2.3	2.2
						PFOS	12.5	12.1
	Shaw et al., 2013	2009	12	-	No	PFOA	7	3.9
						PFNA	2	1
Suburban Firefighters in Ohio	Leary et al., 2020	2018-2019	36	9		PFOS	10.7	4
					Yes	PFOA	2.2	1.7
						PFHxS	6.5	3.2
General Employed Ohio Population	Jin et al., 2011	2005-2006	36	5373	No	PFOS	24.4	22.1
						PFHxS	4.8†	3.6
City and County of San Francisco Office Workers	Trowbridge et al., 2020	2014–2015	86	84	Some	PFHxS	3.8†	1.7
American Red Cross Blood Donors	Tao et al., 2008	2002-2003	458	645	No	PFOA	8.9–13.4 [°]	4.6
						PFHxS	3.7–4.4 ^c †	1.9

^a 130 of these individuals later participated in the Nilsson et al., 2020 study. Also, the control population uses additional data from Health Canada 2013).
 ^b Khalil et al. (2020) and Dobraca et al. (2015) use the 2009–2010 NHANES dataset, Shaw et al. (2013) uses the 2003–2004 dataset, and Graber et al. (2021) uses

both 2015–2016 and 2017–2018 datasets.

^c Range of means from multiple cohorts in the study.

 † Statistically significant value compared to the control value.

^{††} "Yes" means that case participants used AFFF before. "Some" means that the study did not require AFFF use, although some participants did use it. "No" means the study did not specify AFFF use.

[‡] Nilsson et al. (2020) and Rotander et al. (2015) use arithmetic means rather than geometric means.

subjects. Participants also had elevated PFNA and PFDA levels. Shaw et al. (2013) collected samples from 12 San Francisco firefighters within 24 h of responding to a fire and found PFOA and PFNA concentrations twofold higher than reported in 2003–2004 NHANES samples. All four of the studies using NHANES data found that firefighters have higher levels of various PFAS chemicals in their serum compared to the general American population.

An Ohio study assessed PFAS levels in 47 airport and suburban firefighters and found that firefighters had PFAS serum concentrations 18%–74% higher than NHANES blood level samples (Leary et al., 2020). They also found that airport firefighters, who are more likely to work with AFFF, had 21%–62% higher PFAS serum concentrations than civilian firefighters. Specifically, PFHxS serum levels were 74% higher in firefighters than non-firefighters, and 51% higher in airport firefighters than civilian firefighters. Similarly, PFOS serum levels were 29% higher in firefighters than in controls. Airport firefighters have a greater body burden of PFAS than other types of firefighters and the general population.

Another study of 36 firefighters from Ohio and West Virginia found significantly higher levels of PFHxS and slightly higher levels of PFOS and PFNA in firefighters compared to workers in other industrial jobs and unemployed participants (Jin et al., 2011). Trowbridge et al. (2020) assessed a cohort of 86 San Francisco female firefighters, comparing their serum levels to a cohort of female office workers. PFNA, PFHxS, and PFUnDA concentrations were significantly higher in firefighters than in office workers. A study with 458 World Trade Center (WTC) first responders found elevated serum levels of PFOA and PFHxS, roughly twice as high as levels in American Red Cross blood donors in various metropolitan cities across the country (Tao et al., 2008).

3.5. PFAS half-life and removal pathways

The residence time of PFAS in the human body depends on the specific PFAS congener half-life, or the time for a quantity to reduce to half of its initial value, and blood removal pathways. Summarizing the results of eight studies performed using human serum and urine samples, Table 2 shows that the half-life of PFAS in the human body varies widely (Nilsson et al., 2022a; Fu et al., 2016; Zhang et al., 2013; Li et al., 2018; Xu et al., 2020; Olsen et al., 2007; Worley et al., 2017; Bartell et al., 2010).

In addition to the PFAS congener half-life, removal pathways impact the residence time of the chemicals in the human body. At 300 nM in length, PFOS and PFOA are too large to filter through the kidney glomerulus (26–600 nM) (Zhang et al., 2013; Li et al., 2018) and thus cannot be readily removed from the body. Han et al. (2012) found that humans have "extremely low renal elimination of PFOA," allowing the compound to accumulate in the blood. Further increasing their size, some PFAS bind to albumin, a protein in blood serum. Blood removal is therefore a viable elimination pathway for these compounds (Jones et al., 2003; Han et al., 2003; Rotander et al., 2015).

Blood removal via blood donation or menstruation has been found to reduce PFAS levels in serum. Rotander et al. (2015) found that PFOS, PFHxS, and PFOA levels were negatively associated with blood donation (n = 149). Although the number of females in the Rotander study was small, female participants had lower PFAS levels. This is consistent with studies showing that menstruation can function as a PFAS elimination pathway (Wong et al., 2014; Zhang et al., 2013). Trowbridge et al. (2020) found lower levels of most PFAS congeners in the female firefighters sampled by the Women Firefighters Biomonitoring Collaborative (n = 86) compared to the firefighters in the FOX Study (n = 101), 98 percent of which are men (Dobraca et al., 2015). This difference in PFAS blood levels again could be explained by the increased excretion of PFASs during menstruation. Nilsson et al. (2020) expanded on Rotander et al.'s results (2015) and found that participants who donated blood had lower average PFOA, PFHxS, PFHpS, and PFOS concentrations compared to those who did not report donating (n = 799). Lower PFAS concentrations were also associated with increased blood donation frequency (Nilsson et al., 2020; Nilsson et al., 2022a). Apparent half-lives for PFHxS, PFHpS, and PFOS were shorter among blood donors, according to Nilsson et al. (2022a). Hence, it is likely that firefighters who

Table 2 PFAS half-life in occupationally exposed individuals.

PFAS Chemical	Half-Lives from Referenced Literature [years]										
	Fu et al., 2016	Zhang et al., 2013 [1]	Zhang et al., 2013 [2]	Li et al., 2018	Li et al., 2022	Xu et al., 2020	Olsen et al., 2007	Worley et al., 2017	Bartell et al., 2010	Nilsson et al., 2022a	
PFOS	1.9	5.8	18	3.4	-	2.9	4.8	3.3	-	5.7	
PFOA	1.7	1.5	1.2	2.7	2.5	1.8	3.5	3.9	2.3	2.0	
PFHxS	3.6	-	-	5.3	4.5	2.9	7.3	15.5	-	6.0	
PFHpS	-	_	_	_	4.6	1.5	_	-	-	5.6	

Zhang et al. (2013) [1] & [2] are different groups reported in the same study. [1] is data from women under the age of 50, while [2] is data from women over the age of 50 as well as men of any age.

Li et al. (2018) and Li et al. (2022) are two different studies based on study populations exposed to the same contaminated drinking water in Ronneby, Sweden. Li et al. (2018) used blood samples collected from 2014 to 2016 from 106 participants, and Li (2022) used blood samples collected from 2014 to 2018 from 114 participants.

donate blood or menstruate have been exposed to higher levels of PFAS than can be extrapolated from current blood levels.

While the results of Table 2 are largely consistent with PFAS half-life values used by various public health entities, it should be noted that half-lives do not elucidate the full extent of exposure. The biological half-life of PFAS in the human body can range from months to decades depending on several factors (e.g., menstruation, dialysis, blood donation). As such, it can be difficult to determine a true half-life value for each of the PFAS chemicals discussed in this review. Fig. 2 demonstrates the theoretical decay of PFAS chemicals in human blood serum for halflife values ranging from 1 to 10 years assuming a PFAS concentration of 100 ppt and no further exposure to PFAS after year zero. As shown, PFAS levels in blood decrease significantly over time with increasing years after exposure. This trend would not be observed, however, if PFAS exposure were to continue over time. Retroactively analyzing blood samples for PFAS concentration in firefighters years after the time of their occupational exposure may only provide a limited underestimation and should not be considered reflective of their historical concentrations. Fig. 2 provides a model to extrapolate past concentrations for understanding cumulative exposure over time; however, it does not consider other factors affecting serum PFAS levels.

3.6. PFAS cancer risk

Epidemiological studies have found elevated rates of several cancers among firefighters including thyroid, kidney, testicular, and prostate cancer. In fact, IARC recently declared the occupation of firefighting as a Class 1 known carcinogen (Demers et al., 2022). PFASs are one group of many chemicals and contaminants to which firefighters are exposed occupationally that may cause cancer. PFOS and PFOA have been linked to a multitude of cancers including kidney cancer (Li et al., 2022a; C8 Science Panel, 2012), testicular cancer (C8 Science Panel, 2012), prostate cancer (Vieira et al., 2013; Demers et al., 2022; Steenland and Winquist, 2021), bladder cancer (Messmer et al., 2022; Olsen et al., 2004; New York State Department of Health, 2017), thyroid cancer (Messmer et al., 2022) colon cancer (Olsen et al., 2004; Grice et al., 2007; Messmer et al., 2022) and pancreatic cancer (Consonni et al., 2013).

Messmer et al. (2022) analyzed the cancer risk of residents from Merrimack, New Hampshire, whose public water supply was contaminated by PFAS from a plastic coating plant in the area. Residents who used the public water supply were found to have PFOA blood serum levels twice the mean level in the U.S. Compared to national average cancer risks, residents of Merrimack faced a significantly higher risk of thyroid cancer, bladder cancer, and esophageal cancer. In addition, residents faced a significantly higher risk of thyroid cancer, colon cancer, and prostate cancer than residents of New England communities with similar demographics.

In an assessment of cancer risks from six water districts contaminated with PFOA in Ohio and West Virginia, Vieira et al. (2013) found that all combined PFOA-contaminated water districts faced a 20 to 30 percent excess risk of lung cancer and significantly higher site-specific cancer

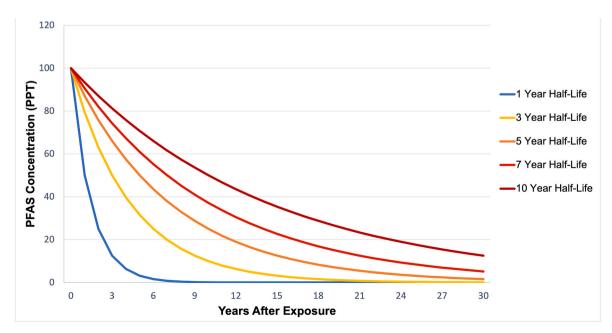


Fig. 2. Theoretical decay of PFAS chemicals in human blood serum with varying half-lives.

odds ratios for lung cancer compared to non-contaminated water districts in the same regions. Study participants faced a fivefold excess testicular cancer risk in Little Hocking, the most contaminated water district. Vieira et al. also found an association between very high PFOA exposure and prostate cancer, ovarian cancer, and non-Hodgkin lymphoma. Evidence in their study contributed to the C8 Science Panel's conclusion of a probable link between PFOA exposure and cancer of the kidneys and testicles.

Consonni et al. (2013) assessed the cancer risks among a cohort of workers at several European and U.S. polytetrafluoroethylene (PTFE) production sites, which utilize PFOA and its ammonium salt, ammonium perfluorooctanoate (APFO), during the polymerization process. Exposed workers faced a higher risk of liver cancer, kidney cancer, and leukemia compared to national reference rates. Li et al. (2022a) also found a moderately increased risk of kidney cancer among a cohort of former and current residents of Ronneby, Sweden, a municipality that supplied drinking water contaminated with PFAS from the use of firefighting foams at a nearby military airport from the 1980s through 2013.

In their assessment of episodes of care of employees occupationally exposed to PFOS at a chemical production plant in Alabama, Olsen et al. (2004) found a statistically significant increase in bladder cancer compared to employees at a film plant in the same site without any PFOS exposure. Workers at the chemical plant had geometric mean serum PFOS concentrations ranging from 400 (roles with lower PFOS exposure) to 2000 ng/mL (roles with higher PFOS exposure), whereas mean serum PFOS concentrations in film plant workers were approximately 100–200 ng/mL.

3.7. EPA risk assessment methodology for carcinogens

Firefighters are exposed to a range of physical, thermal, ergonomic, chemical, and psychological occupational hazards (Guidotti, 1992), and this paper focuses on their chemical exposures. There are numerous chemical mechanisms of toxicity for firefighters due to the complex chemistry of smoke, AFFF, fire retardants, plastics, and other substances to which firefighters are exposed.

Walter and Holford (1978) and Rothman (1976) detail risk-additive and risk-multiplication models for human health. The risk-additive model is generally applied to agents that cause disease, while the risk-multiplicative model is more appropriate for agents that prevent disease. Among epidemiologic literature, there seems to be a consensus that for public health concerns regarding causative toxic agents, the additive model is most appropriate (Hogan et al., 1978; Kupper and Hogan, 1978; Rothman, 1978; U.S. Environmental Protection Agency, 1986).

In 1986, the EPA published a report outlining their guidelines for health risk assessments of chemical mixtures further explaining additive-risk assessments (U.S. Environmental Protection Agency, 1986). The report states, When little or no quantitative information is available on the potential interaction among the components [of a mixture], additive models are recommended for systemic toxicants. Several studies have demonstrated that dose additive models often predict reasonably well the toxicities of mixtures composed of a substantial variety of both similar and dissimilar compounds. The problem of multiple toxicant exposure has been addressed by the American Conference of Governmental Industrial Hygienists (ACGIH, 1983), the Occupational Safety and Health Administration (OSHA, 1983), the World Health Organization (WHO, 1981), and the National Research Council (National Research Council, 1980a; National Research Council, 1980b). Although the focus and purpose of each group were somewhat different, all groups that recommended an approach elected to adopt some type of dose additive model.

In 1989, the EPA published another report detailing risk assessment methodologies for human health evaluation (U.S. Environmental Protection Agency, 1989). This report explains that two compounds that produce adverse effects on the same organ system (e.g., liver), although by different mechanisms, should be treated as dose-additive. For Superfund risk assessments, cancer risks from various exposure pathways are assumed to be additive if the risks are for the same individuals and time period. Generally, the data available to quantitatively assess interactions between carcinogen risks are lacking. In the absence of adequate information, EPA guidelines indicate that multiple carcinogen risks should be treated as additive when evaluating total incremental cancer risk.

There is a lack of comprehensive data on the complex mixture of carcinogenic chemicals to which firefighters are exposed and their interaction with PFAS congeners. Thus, according to EPA guidelines and recommendations, these concurrent risks should be treated as dose-additive until more information is available on their interactions. PFAS exposure may contribute to firefighters' overall occupational cancer risk and should be treated as additive when assessing firefighter cancer rates.

4. Discussion

Compared to the general population, firefighters have elevated serum levels of certain long-chain PFASs which can reasonably be attributed in large part to AFFF. Specifically, elevated levels of PFOS and PFOA are found in AFFF to which firefighters are occupationally exposed. As discussed, due to the persistence of PFASs in the human body and their ability to bioaccumulate, firefighters experience the latent and cumulative effects of PFAS-containing AFFF exposure throughout their careers, especially with increasing years in the fires service (Fu et al., 2016; Leary et al., 2020). Firefighters are at increased risk of developing thyroid, kidney, testicular, and prostate cancer, all of which are cancers linked to PFOS and PFOA exposure according to several studies (Messmer et al., 2022; C8 Science Panel, 2012; Vieira et al., 2013). The PFAS body burden of firefighters, the toxicological profile of PFAS, and the increased risk of cancers in the fire service are suggestive of the contributory role of PFASs in firefighter cancers. Such contribution may be independent of other occupational exposures to carcinogens or through interactions with these other exposures (Peaslee et al., 2020). Thus, cancer risks caused by occupational exposures to PFASs should be considered in the cumulative cancer risk of firefighters. This review supports that further research is warranted to further evaluate the role of occupational PFAS exposure in causing an elevated cancer risk for firefighters.

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Author contribution

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Paul Rosenfeld and Dr. Ken Spaeth are both testifying experts in AFFF litigation. All other authors have no conflicts of interest to declare. Dr. Rosenfeld is co-founder of SWAPE LLC.

Data availability

No data was used for the research described in the article.

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Not applicable.

List of abbreviations

AFFF	Aqueous film-forming foam
CDC	Centers for Disease Control
EPA	Environmental Protection Agency
FOX	Firefighter Occupational Exposures Project
IARC	International Agency for Research on Cancer
NHANES	National Health and Nutrition Examination Survey
OEHHA	California Office of Environmental Health Hazard Assessment
PFAS	Per and poly-fluoroalkyl substances
PFDA	Perflorodecanoic acid
PFDeA	Perfluorodecanoic acid
PFDoA	Perfluorododecanoic acid
PFHpA	Perfluoroheptanoic acid
PFHpS	Perfluoroheptane sulfonic acid
PFHxS	Perfluorohexane sulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctanesulfonic acid
PFUnDA	Perfluoroundecanoic acid
PPE	Personal protective equipment
U.S.	United States
WHO	World Health Organization
WTC	World Trade Center

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