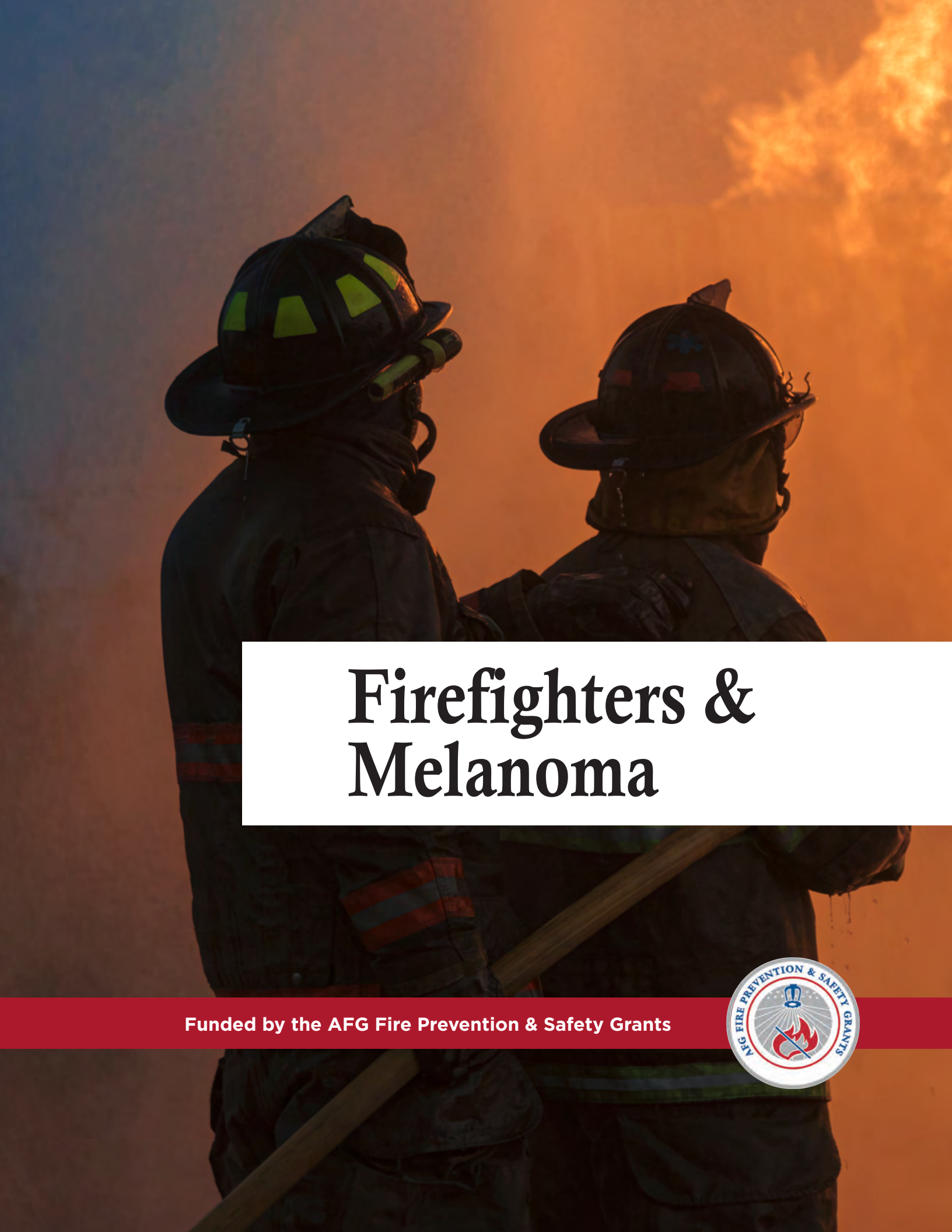

Firefighters & Melanoma

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GENERAL EPIDEMIOLOGY: MELANOMA

Skin cancer is the most common form of cancer, although melanoma accounts for only 1% of skin cancer cases, despite being responsible for the majority of skin cancer deaths[1]. In 2021, the American Cancer Society (ACS) estimated 106,110 new cases of melanoma will be diagnosed, and 7,180 individuals will die from it[1]. The lifetime risk for developing melanoma is 1 in 38 for Caucasians, 1 in 1,000 for African Americans, and 1 in 167 for Hispanics[1]. Firefighters have an elevated risk for developing melanoma, and as with many cancers, the stage at diagnosis impacts survival rates. Survival rates for melanoma vary depending on the stage at diagnosis, although the combined 5 year relative survival rate is 93%[2]. Diagnosed at Stage 1, the survival rate is 99%, and diagnosed at Stage 4, the survival rate is 27%.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC)

In June 2022, IARC convened an international meeting of scientists to re-evaluate firefighting as an exposure related to cancer. They determined the literature supports reclassifying ***firefighting to a Group 1 carcinogen (carcinogenic to humans) based on "sufficient" evidence***[3]. This is the ***highest*** classification of exposure only assigned when there is scientific certainty.

Their statement indicated:

There was also "strong" mechanistic evidence that occupational exposure as a firefighter shows the following key characteristics of carcinogens in exposed humans: "is genotoxic", "induces epigenetic alterations", "induces oxidative stress", "induces chronic inflammation", and "modulates receptor-mediated effects".

Specific to melanoma, IARC ***noted "limited" evidence in humans for melanoma as related to firefighting***. While typical use of the word "limited" implies a lack of evidence or support, IARC's classification with the word limited "means that ***a positive association has been observed*** between exposure to the agent and cancer but that other explanations for the observations (technically termed "chance", "bias", or "confounding") could not be ruled out with reasonable confidence." ***It should be noted that IARC criteria and classifications are focused on scientific levels of certainty which are more stringent than those focused on the "weight of the evidence"[4] which is often used in cases of workers compensation.***

GENERAL RISK FACTORS FOR MELANOMA

There are a number of risk factors associated with developing melanoma:

- **Gender:** Before the age of 50, the risk is higher for women, however, after the age of 50, the risk is higher for men[5].
- **Age:** While melanoma is one of the more common cancers among younger people, the average age of diagnosis remains approximately 65 years[1].
- **Race:** Melanoma is more than 20 times more common in Caucasians than in African Americans[1]. This may be related to the risk of melanoma being higher for individuals with red or blonde hair, blue or green eyes, or fair skin[5].
- **Personal health history:** Having a weakened immune system increases the risk of melanoma, as does having a history of melanoma or other skin cancers[5], including a family history. Having a first-degree relative (parents, siblings, or children) who has had melanoma increases the likelihood of developing it.
- **Ultraviolet light exposure*:*** Exposure to UV light is a major risk of melanoma. Examples of exposure include tanning beds, sun lamps, or direct sun exposure[5].

RISK FACTORS RELEVANT TO FIREFIGHTERS

Firefighters are exposed to a broad range of chemicals, both in the firehouse and during emergency response. Recent research conducted with live burns has begun to identify and quantify the presence of carcinogens that are typically present on the fire ground. Most alarming are findings that, even when the air appears "clear" there are often ultra-fine respirable particles and gaseous chemicals of several known carcinogens present. Unfortunately, this time period when there is no visible smoke is typically when firefighters remove their personal protective equipment and self-contained breathing apparatus. Particularly noted in the research is the presence of carcinogens such as polybrominated diphenyl ethers (PBDEs), perfluorooctanoic and perfluorooctanesulfonic acids (PFOA and PFOS), phthalates, dioxins, benzene, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), vinyl chloride, and heavy metals[6–14]. Firefighters face several routes of exposure including inhalation, dermal absorption, secondary exposure through contaminated dust from particulates post incident, and potentially the semi-volatile off-gassing of gear. PCBs specifically have been identified by the International Agency for Research on Cancer (IARC) as having *sufficient evidence* of causing malignant melanoma in humans[15]. While still being evaluated by the IARC process, many of the other known carcinogens found on the fire ground also have been implicated in the development of melanoma[16,17].

Polychlorinated biphenyls (PCBs). PCBs are man-made organic chemicals commonly used as coolants, lubricants in transformers, capacitors, and other electrical equipment. While the chemicals have been banned since the late 1970s due to evidence that they are a probable human carcinogen, they remain in products manufactured prior to the ban and have been found in the fire environment as a product of combustion and are identified as a major contributor to melanoma in the general population[18] and among firefighters[19].

Other known fireground exposures with a growing literature relating them to malignant melanoma include:

Polybrominated Diphenyl Ethers (PBDEs). PBDEs are a complex grouping of chemicals present in polyurethane foam in furniture, electronics, plastics, and flame retardants. Clearly, these common household products are present in many house fires and result exposures on the fireground. These chemicals exert effects on hormonal systems and the thyroid systems, linking them to the development of cancer[20,21] in general and malignant melanoma in particular[15].

Benzene. Benzene is present as a product of combustion from several standard household materials (e.g. PVC pipe, PVC siding, Christmas trees)[6], from exposure to diesel exhaust, and has been found to off-gas from firefighters' PPE[10] and is widely recognized as a fireground risk. Benzene is not only present on the fire ground as a product of combustion, but also at high rates in many fire stations as trucks and ambulances are housed in the bay areas. While efforts are being made to increase the use of exhaust mitigation devices in the firehouse, their introduction and use is relatively new to the fire service. Exposure to benzene has been found to increase malignant melanoma risk[16].

Shift Work. In 2019, the International Agency for Research on Cancer classified alternative shift work (including evening, night, rotating, and other unspecified schedules) as a probable human

carcinogen[22]. The relationship between shift work and cancer development occurs through several mechanisms, including circadian rhythm disruptions, impacted melatonin secretion and production, and affecting lifestyle choices[23]. Given the nature of the job and emergency calls, it is not surprising that firefighters – who are faced with a career of 24–48-hour shifts and emergency calls during the night – struggle with the negative health implications of shift work. Long-term shift work, especially night shifts, has been linked to an increased risk of cancer[24–27], including melanoma[28].

RISK OF MELANOMA AMONG FIREFIGHTERS

A number of methodologically sound studies have studied the relationship between melanoma and firefighting and have found increased risks.

For instance, Tsai et al.[29] conducted a case-control study of cancer risk among firefighters in California from 1988-2007 using the California Cancer Registry (CCR). The study included 3,996 male firefighters with cancer and 48,725 non-firefighter controls. **The authors found that firefighters were at a 56% greater risk for melanoma cancer** (OR = 1.56, 95% CI = 1.44-2.13) even after adjusting for age of diagnosis, race, and year of diagnosis.

Lee et al.[30] retrospectively examined over 100,000 career Florida firefighters over a 34-year period, identifying 3,760 male and 168 female primary cancer incidences using the Florida State Fire Marshall's Office and Florida Cancer Data System. After adjusting for age and year of cancer diagnosis, the authors found **male firefighters had 56% higher risk of developing melanoma** (aOR = 1.56, 95% CI = 1.39 – 1.76). While female firefighters had an even higher elevated risk, the relationship was not significant likely due to small sample size (aOR = 1.68, 95% CI = 0.97 – 2.90).

Additional international work has found similar patterns. Pukkala and colleagues[31] examined data from five Nordic countries and found **firefighters had a 25% increased risk** of developing skin cancer compared to the general population (SIR =1.25, 95% CI =1.03 – 1.51). Canadian[32] research found **firefighters were at a 67% greater risk** of developing melanoma (HR=1.67, 95% CI=1.17-2.37), while a cohort study from Australia[33] found **firefighters were 25% more likely to develop melanoma** (SIR=1.25, 95% CI=1.28-1.62). Danish firefighters[34] were found to be **24% more likely** than the general population to develop melanoma (SIR=1.24, 95% CI=0.98-1.57). In a study based on a Canadian cohort of more than a million men, **firefighters were 67% more likely to develop melanoma** (HR=1.67, 95% CI=1.17-2.37) than non-firefighting peers[32]. A comparison of firefighters in Scotland **found a rate 121% higher for melanoma compared to non-firefighters** (13.5 vs. 7.1, 95% CI=3.0-8.8, p<.001)[35].

Meta-Analytic Findings. While individual studies provide a strong foundation for the likely relationship between melanoma and firefighting, even more convincing are the meta-analytic findings. It is difficult to make decisions about whether firefighting increases the risk of any type of cancer based on a single report because results often vary from study to study and studies vary with respect to a number of important design factors including sample size which is a primary determinant of the power to detect group differences. Meta-analysis is a widely-accepted procedure for statistically combining data from multiple studies. *By combining all relevant studies, a meta-analysis provides the maximum possible sample size (at the time the review is conducted) and thus provides the smallest possible confidence interval around an estimate*. This is why meta-analysis is a particular important tool for identifying risks for rare

diseases. Meta-analytic findings for the relationship between melanoma and firefighting provide strong evidence for the relationship

The meta-analysis of LeMasters and colleagues[36] published in 2006 found **more than a doubling of mortality for firefighters from malignant melanoma** (PMR=2.25, 95% CI=1.03-4.27) which led the authors to classify malignant melanoma as probably related to firefighting (*the highest category*).

More recently, a meta-analysis conducted by Jalilian and colleagues[37] found **a 21% elevated risk of developing malignant melanoma** in firefighters (SIREs=1.21, 95% CI=1.02-1.45).

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