MARCH 23, 2023—NASHVILLE, TN

Proceedings of The Future of Fire Safety: Exploring the Intersection of Wildfires and Human Health

A Symposium presented at the Society of Toxicology's 62nd Annual Meeting and ToxExpo

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Introduction

With gratitude, we acknowledge the speakers of the Symposium, "The Future of Fire Safety: Exploring the Intersection of Wildfires and Human Health" for their engaging, passionate, and professional commitment.

We also acknowledge the general participants who attended the symposium and contributed with their knowledge and interests as key stakeholders in this open and engaging dialogue.

SYMPOSIUM PRESENTERS

Marilyn Black, PhD, Chemical Insights Research Institute of UL Research Institutes

Miriam Calkins, PhD, National Institute for Occupational Safety and Health (NIOSH)

Jaclyn Goodrich, PhD, University of Michigan

Alesia Jung, PhD, Exponent

Christa Wright, PhD, Chemical Insights Research Institute of UL Research Institutes

Junfeng (Jim) Zhang, PhD, Duke University

Preface

The following proceedings provide a summary of technical information exchanged during the on-site Symposium, "The Future of Fire Safety: The Intersection of Wildfires and Human Health," as presented at the Society of Toxicology's (SOT) 62nd Annual Meeting in Nashville, Tennessee, March 23, 2023. This summary is not intended to provide a complete transcription of each speaker's presentation or participant specific comments. Speakers may be contacted directly for details of their presentations and subject expertise.

These proceedings are provided to share summaries of the presentations and technical discussions among all stakeholders. We hope this exchange of information will enable more collaborative discussions, research, innovation, informed policy advancement, and science-based initiatives around the intersection of wildfires and human health.

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Overview

SPEAKER

Christa Wright, PhD, Chemical Insights Research Institute of UL Research Institutes

Dr. Wright is the Research Director for the Center of Toxicology and Human Health. Dr. Wright's research aims to unravel particle and chemical mediated molecular mechanisms that cause cellular phenotypic changes, which may lead to disease development.

Wildfires are an emerging public health threat capable of hindering the economic and social infrastructure that we rely on daily. Climate change will sharpen this threat and therefore larger conversations among the scientific community are sorely needed to address this unprecedented global issue. Understanding the complexity of wildfires and their impact on human health is key to mitigating loss of life and quality of life as well as reducing environmental consequences including the reduction of indoor and outdoor air quality. In this session, our panelists will identify challenges in data collection and potential knowledge gaps that reduce our ability to fully quantify the human and economic costs of wildfires. Our panel of experts revealed the various fuel sources and chemical processes that occur during wildland urban interface (WUI) fires, discussed the complexity of wildfire emissions, and what is known about human exposure and adverse health outcomes. Specifically, our presenters provided new evidence on biomarkers of exposure such as brominated flame retardants and per- and polyfluoroalkyl substances and their link to epigenetic alterations found in WUI firefighters. While it is widely known that firefighters have higher cancer incidence rates than the general public, information on WUI associated reproductive health risks are sparse and new evidence linking occupational factors specific to female firefighters was shared and discussed. Lastly, a framework for evaluating the efficacy of indoor air pollution mitigation strategies such as HEPA air purification systems was discussed. The proposed strategy aims to assess how improved indoor air quality metrics can ameliorate cardiometabolic outcomes in susceptible communities was also presented. These findings may aid in the development of therapeutic and mitigation intervention strategies to protect WUI firefighters and communities during wildfire events.

SYMPOSIUM OBJECTIVES

- Recognize the impact of wildfires on the built environment, based on scientific research findings.
- Describe the health impacts from wildfires including the chemicals of concern from building construction materials and how they might impact the indoor and outdoor environments.

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Wildfires at the Wildland-Urban Interface (WUI) and Their Health Impacts on First Responders and Communities

SPEAKER

Marilyn Black, PhD, Chemical Insights Research Institute of UL Research Institutes

Dr. Marilyn Black is the Vice President and Executive Director of the Chemical Insights Research Institute, the founder of Air Quality Sciences Inc. and the GREENGUARD Environmental Institute and Certification Programs for healthy products. Dr. Black sets the stage for the challenges of assessing structure fires within the wildland urban interface (WUI) and the knowledge gaps that we face.

ABSTRACT

Wildfire activity in the U.S. is increasing as more extreme weather events occur, those that bring droughts and extreme heat. Urban development is entering wildland areas and fires at the interface between urban structures and natural vegetation are increasing. These fires are unique since they combine combustion products from both natural sources and manmade materials, or synthetics used in building construction and furnishing. Wildfire smoke contains numerous pollutants of concern including ultrafine and small particulate matter ($PM_{2.5}$ and less) and chemicals such as polyaromatic hydrocarbons, polychlorinated dibenzo-p-dioxins and dibenzofurans, flame retardants, plasticizers, volatile and semi volatile organic compounds, polychlorinated biphenyls, carbon monoxide, hydrogen cyanide, hydrogen chloride, and even heavy metals. Many of these substances are known or are probable carcinogens, irritants, respiratory sensitizers, and reproductive toxicants with linkage to cardiovascular and neurological impacts. Numerous sources of exposure occur including the outdoor contaminated air, indoor air contaminated by infiltration of the outdoor air, indoor surfaces contaminated with particle and chemical deposition, surface water contaminated with ash and aerosol deposition, contaminated surface water and drinking water. Although health studies from specific wildland urban interface fires are limited, data shows that firefighters, first responders, outdoor workers, and vulnerable communities face a higher risk of adverse health outcomes from wildfire exposures. These outcomes based on hospital visits during wildfire seasons include myocardial infarction, heart failure, pulmonary embolisms, ischemic strokes, and respiratory distress.

PRESENTATION SUMMARY

Periodic wildfires can reduce overgrown or invasive brush, shrubs, and trees, support the new growth of native vegetation, and even restore nutrients to the soil, promoting healthy environments for wildlife. But today, wildfires are bigger, burning longer, causing more damage, and impacting public health more than ever before due to prolonged smoke exposures. Since the official tracking of wildfire data began, the number of annual acres burned has increased from roughly 2.5 million in the 1980's to 7.1 million over the last decade. Wildfires are increasing as climate change drives more frequent extreme weather events, including heat waves and droughts.

While a traditional wildfire can be a significant problem, it can quickly turn into a disaster when it meets the wildland urban interface, also known as the WUI. The WUI is defined as the zone where structures and other human development meet or intermix with undeveloped wildland or vegetation fuel. The effects of wildfires on communities in the WUI can be catastrophic, causing environmental and socioeconomic devastation. Today, close to 99 million people, or one-third of our population, now live in the WUI. More than 46 million homes, with an estimated value of $1.3 trillion, in 70,000 communities are now considered at risk from the impacts of wildfire.

Urban fuels also differ greatly from the fuels in wildland areas in their arrangement in the landscape, energy content, and elemental composition. For example, chemical elements and materials of concern, such as halogens, plastics, and metals, exist in much higher concentrations in the WUI. Compared to natural wildland fuels, physical structures are very dense

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fuel packages. While the quantities and composition of structural materials varies greatly from structure to structure, depending on size, age, function, and geographic region. An average house is about 38 tons of combustible fuel, typically including structural wood or lumber, plywood or oriented strand board for sheathing and subfloors, wood or PVC siding, asphalt shingles, insulation or spray on polyurethane foam, and electrical wires and PVC plumbing. If making a direct comparison to the woodlands, a 50-foot-tall pine tree is approximately one ton of combustible fuel. So, an average house is roughly equivalent in fuel amount to 38, 50-foot-tall pine trees.

In addition to the structure itself, there are also the contents within that contribute to its fuel load. The average residential structure may have about 8 tons of fuel, including wood or vinyl flooring, carpet, window treatments, cabinetry, furnishings, such as tables and chairs, upholstered furniture with polyurethane foam, and mattresses, and consumer products, including household chemicals such as paints, solvents and refrigerants, cleaners, and plastic items. Vehicles also contribute to urban fuel loads in WUI wildfires. The average vehicle contributes about one ton of combustible fuel, including plastic components, fluids and lubricants, and rubber.

In WUI areas, the combination of natural and urban fuels that collectively burn leads to different types of pollutants not typically found in traditional wildland fires, in the form of atmospheric emissions, residues, and effluents, or liquid waste. All wildfires produce smoke and a large mix of pollutants. Particulate matter (PM) is the most prominent. It is emitted in the highest amounts and has been directly linked to respiratory disease and premature death. In addition, wildfires emit smoke consisting of a range of different compounds, including volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs). These emissions represent a vast array of chemicals, some of which are acutely toxic, some are irritants, and some are known carcinogens. All these compounds are emitted from natural vegetation like trees, shrubs, and grasses when they burn. But when a wildfire spreads to include the urban fuels, we expect to find an entirely different mix of pollutants being released or emitted because these fuels are chemically very different from the trees and shrubs that are burning in a normal wildfire. The composition of WUI fire pollutant mixtures is relatively unknown because there is limited research on WUI fire emissions.

Once the emissions are put into the atmosphere near the fire, they immediately cool and change through a process called atmospheric transformation. The entire plume will evolve over time and change its chemical nature. Initially, gas-based compounds will start to condense onto particles. More reactive compounds will start to react with other atmospheric compounds and turn into new compounds. Moving ten to hundreds of miles down wind, there are slower processes that continue to occur. Large particles will start to fall out of that plume in the form of ash that is often seen falling out of the sky. Atmospheric chemistry will also continue as the plume emissions mix with other pollutants that may be emitted from cars and trucks and industrial processes. The sunlight will also drive chemical reactions within the plume, causing photochemical reactions.

There are also many emissions in the soil that are left behind after a WUI fire. WUI fires often produce metals or organic pollutants that are not normally seen in wildland fires and many of those pollutants are left behind in the form of ashes or in residues. In the aftermath of a WUI fire, metals like arsenic, lead, antimony, copper, zinc, and chromium have been found at elevated levels and in the soil. If there is a rainfall event after the fire, many of these residues can then be washed away into the surface waters. When contaminated water makes its way into a treatment plant, higher levels of dissolved organic matter can have a big impact on disinfection byproducts, causing them to be transmitted into the water treatment systems and can ultimately cause contamination of household water.

Something that has also been observed and is unique to WUI fires is high levels of VOCs, such as benzene, in water distribution systems, which have also led to household water contamination. While the mechanism for such pollutants is not fully understood, these WUI fires do have some very strong impacts on the environment as well as human health.

The health effects from the different components of the plume are relatively unknown. While we do have some understanding of immediate or near-field exposure to fresh emissions, we are at the infancy of our understanding of regional and continental exposure to the transformed WUI plume. WUI fires may lead to higher human exposures than wildland fires because of their proximity to communities. Some areas in the U.S. can be impacted by multiple fires at the same time causing exposure to smoke from fires for days, weeks, or even months at a time.

Certain members of the population, children, and pregnant women for example, may be more vulnerable than others. Since WUI fires cannot be left to naturally burn out, the individuals who work near them, such as fire fighters, emergency response teams and clean-up recovery crews, are increasingly being exposed to WUI-type fires. Additionally, outdoor workers in surrounding areas, such as farmers and landscapers, may be at greater risk. Depending on proximity to the fire, individuals may be exposed to emissions in different ways — through inhalation, through ingestion, and through dermal absorption. Our direct knowledge of WUI emissions is based on extrapolations and inferences from what is known of wildfires and urban fires since data on fires at the WUI are limited. There are opportunities and challenges associated with measurements of fires and their emissions at the WUI. The latest research is in a new report from the National Academy of Sciences: "The Chemistry of Fires at the Wildland-Urban Interface". The bottom line is that while we are still learning about the impact of emissions from WUI fires, we know they are creating significant air quality issues for large amounts of the population.

Evaluation of Biomarkers of Exposure in Southern California Firefighters Responding to WUI Fire Incidents

SPEAKER

Miriam Calkins, PhD, National Institute for Occupational Safety and Health (NIOSH)

Dr. Miriam Calkins is a Research Industrial Hygienist at the National Institute for Occupational Safety & Health within the Division of Field Studies and Engineering – located at the Centers for Disease Control and Prevention. Dr. Calkin's presentation focuses on the dangers that first responders face within WUI fires and relevant biomarkers of exposure found in California firefighters who participated in the Fire Fighter Cancer Cohort Study.

ABSTRACT

Firefighters suppressing wildland fires work long hours performing physically demanding tasks and can be exposed to wildfire smoke. They work in the wildland urban interface (WUI), where wildland vegetation and urban areas meet. Exposure to smoke can be from burning vegetation or homes, other structures, or vehicles. WUI firefighters may experience structural firefighting exposures without wearing the PPE routinely used by municipal firefighters during a structural response (e.g., self-contained breathing apparatus [SCBA], turnout gear) and without the ability to follow recommended decontamination practices for structural fire response. To understand exposures and health effects, we enrolled WUI firefighters from southern California in the Fire Fighter Cancer Cohort Study (FFCCS), a national collaborative research study with NIOSH and the Universities of Arizona and Miami. Upon enrollment, participants provided urine and blood samples (September 2019) and completed a survey about demographic, work history, health, and behavioral risk factors. Post-fire exposure urine samples (n=125) were collected in the fall of 2019 from 89 WUI firefighters approximately one hour after completing fire suppression duties for the day. Urine was analyzed for polycyclic aromatic hydrocarbon metabolites, organophosphate flame retardants, metals, and volatile organic compounds. A follow-up blood sample was collected approximately one year later from 64 of the firefighters who provided post-fire urine samples and 20 firefighters who did not respond to a WUI event that season. Blood was analyzed for brominated flame retardants and per- and polyfluoroalkyl substances, and epigenetic markers (DNA methylation and microRNA). This presentation focused on the results of the biomarkers of exposure from this population, including comparisons to the general U.S. population, pre- and post-fire response, and characteristics of the fire incidents.

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PRESENTATION SUMMARY

Wildland urban interface (WUI) fires contain a mixture of fuels from where wildland vegetation and urban areas meet. Smoke may include combustion by-products and other hazards from burning vegetation or homes, other structures, and vehicles. However, the approach to suppressing large WUI fires often involves wildland fire response methods as urban resources may be unavailable. Firefighters in these settings may perform wildland firefighting tasks and work long hours performing physically demanding tasks under challenging conditions such as extreme temperatures and rugged terrain. As a result, firefighters responding to WUI events may be exposed to smoke that is similar to structural fires, but without access to personal protective equipment or other exposure-reducing measures routinely used by municipal firefighters during a structural response, such as SCBA and turnout gear. They additionally may not have the ability to follow recommended decontamination practices for a structural fire response.

All wildfires produce smoke and a large mix of pollutants. Particulate matter (PM) is the most prevalent component. In addition, wildfires emit smoke consisting of a complex mixture of different compounds, including volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), nitrogen oxides, carbon monoxide, and carbon dioxide. For WUI fires, the emissions are expected to be even more complex since WUI fuels include not only wildland fuel but also fuels from structures, building contents, and even vehicles.

The objective of this research was to evaluate exposure to chemical hazards for firefighters responding to WUI events in southern California by using biomarkers of exposure and information on fire response activities. The working hypothesis was that biomarkers of exposure would be higher after fire response when compared to baseline data collected upon enrollment in the study. This study was part of a larger collaborative research study with NIOSH and the Universities of Arizona and Miami. This multicenter study, called the Fire Fighter Cancer Cohort Study (FFCCS), is looking at carcinogenic exposures, effects, and cancer prevention in firefighters. Assessing WUI exposures can be difficult for a number of reasons including limited access to firefighters working in remote, hazardous, or restricted areas, highly variable conditions, and irregular exposure windows. Also, WUI firefighters are often a diverse population that includes career, municipal firefighters as well as seasonal wildland crews.

Participants from two southern California fire departments were enrolled in the study in fall of 2019. At that time, participants provided baseline urine and blood samples and completed a survey including demographics, work history, current job characteristics, health, and behavioral risk factors. Post-fire data collection occurred between October and November 2019 over the course of 5 fire events. Post-fire exposure urine samples (n=125) were collected from 89 WUI firefighters approximately one hour after completing fire suppression duties for the day. Urine was analyzed for polycyclic aromatic hydrocarbon (PAHs) metabolites, organophosphate flame retardants, metals, and volatile organic compounds. A follow-up blood sample was collected approximately one year later from 64 of the firefighters who provided post-fire urine samples and 20 firefighters who did not respond to a WUI event that season. Blood was analyzed for brominated flame retardants and per- and polyfluoroalkyl substances (PFAS), as well as epigenetic markers (DNA methylation and microRNA).

Urine samples were analyzed for a mixture of 20 VOCs, 4 prevalent PAHs, 20 metals, and 10 organophosphate flame retardants (OFRs). Blood samples were analyzed for 8 different species of PFAS and a wide variety of brominated flame retardants (BFRs), polychlorinated biphenyls (PCBs) and persistent pollutants (PPs). The table below provides a summary of the parent compounds analyzed in post-fire urine and blood analysis. While analyses are ongoing, initial quantitative analyses suggest total VOCs, PAHs, and OFRs were higher in the post-fire samples as compared to enrollment samples. Changes in concentrations of metals were minimal and concentrations of blood serum analytes were similar in enrollment and one-year follow up samples.

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VOCs	PAHs	Metals	OFRs
1,3-Butadiene 1-Bromopropane Acrolein Acrylamide Acrylonitrile Acrylonitrile Vinyl chloride Ethylene oxide Benzene Carbon disulfide Crotonaldehyde Cyanide N, N-Dimethylformamide Methyl isocyanate Isoprene Propylene oxide Styrene, Ethylbenzene Toluene Benzyl alcohol Xylene	Naphthalene (NAP) Fluorene (FLU) Phenanthrene (PHE) Pyrene (PYR)	Antimony (Sb) Arsenic (As) Barium (Ba) Beryllium (Be) Cadmium (Cd) Cesium (Cs) Chromium (Cr) Cobalt (Co) Iodine (I) Manganese (Mn) Mercury (Hg) Molybdenum (Mo) Lead (Pb) Nickel (Ni) Platinum (Pt) Strontium (Sr) Thallium (Tl) Tin (Sn) Tungsten (W) Uranium (U)	Tris(2-chloroethyl) phosphate (TCEP) Tris(1-chloro-2-propyl) phosphate (TCP P) Tris(1,3-dichloro-2-propyl) phosphate (TDCPP) Tributyl phosphate (TBP) Tribenzyl phosphate (TBzP) Tricresyl phosphates (TCP) Triphenyl phosphate, Isopropylphenyl diphenyl phosphate, t-butylphenyl diphenyl phosphate and 2-ethylhexyldiphenyl phosphate (TPP or TPhP) Isopropylphenyl diphenyl phosphate Tertbutylphenyl diphenyl phosphate (BPDP) Non-Polybrominated Diphenyl Ether: 2-Ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB)
PFAS	**BFRs**	**PCBs**	**PPs**
Perfluorooctanoic acid (PFOA) (linear and branched) Perfluorooctane sulfonic acid (PFOS) (linear and branched) Perfluorohexane sulfonic acid (PFHxS) Perfluoromethylhyptane sulfonic acid (PFHpS) Perfluorodecanoic acid (PFDeA) Perfluorononanoic acid (PFNA) Perfluoroundecanoic acid (PFUA) 2-(N-Methyl-perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH)	BDEs 17, 28, 47, 85, 99, 100, 153, 154, 183 BB 153	PCBs 28, 66, 74, 99, 105, 114, 118, 138-158, 146, 153, 156, 157, 167, 170, 178, 180, 183, 187, 189, 194, 196-203, 199, 206, and 209	Hexachlorobenzene B-Hexachlorocyclohexane Oxychlordane Tans-Nonmacho 2,2-Bis(4-chloropheyl)-1,1-dichloroethane (DDE) 2-(4-chlorophynyl)-2-(2-chlorophenyl)- 1,1,1-trichloroethan (DDT) 2,2-Bis(4-chlorophynyl-1,1,1-trichloroethan) (DDT) Mirex

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Epigenetic Biomarkers of Toxicity in California Firefighters Working in the WUI

SPEAKER

Jaclyn Goodrich, PhD, University of Michigan

Dr. Jackie Goodrich is a Research Associate Professor in the Department of Environmental Health Sciences at the University of Michigan School of Public Health. Dr. Goodrich's research and presentation focuses on the epigenetic consequences of WUI fire exposures in California firefighters also within the Fire Fighter Cancer Cohort Study.

ABSTRACT

Epigenetic modifications including DNA methylation and microRNA (miRNA) expression are responsive to toxicant exposures, including those that firefighters in the wildland-urban interface (WUI) may encounter. Widespread changes to DNA methylation and miRNA expression are part of the development of cancers and other diseases. Thus, epigenetics may serve as an early indicator of the effects from exposures. This study, which is part of the Fire Fighter Cancer Cohort Study, examines whether DNA methylation and miRNA expression change in blood samples collected from WUI firefighters at baseline and after one fire season. WUI firefighters (n=100) from southern California were enrolled who provided blood samples at baseline and approximately one year later after the fire season. We quantified blood leukocyte DNA methylation at ~750,000 loci throughout the genome via the Infinium EPIC array. We quantified relative abundance of 800 miRNAs in baseline and post-season blood samples using the nCounter Human v3 miRNA expression panel. We used linear mixed models to compare DNA methylation at each loci and expression of each miRNA across time, adjusting for potential confounders and the matched sample design. We assessed associations in all WUI participants and in those who attended at least one WUI event during the follow-up time. In this presentation, we will report on differential methylation and miRNA expression between baseline and follow-up, and its potential relationship to firefighter health.

PRESENTATION SUMMARY

Structural firefighters encounter multiple hazards in the effort to mitigate fires, protect lives, and save homes. During these events, firefighters are exposed to a number of stressors associated with structural fires such as heat and chemicals including flame retardants, polycyclic aromatic hydrocarbons, metals, and particulates, all of which contribute to the exposure burden of firefighters and ultimately mediate health outcomes. However, firefighters who work within the wildland urban interface or WUI, face a separate and unique exposure paradigm that may enhance stressor interactions and potentially the severity of adverse health effects.

Within the WUI, firefighters endure longer response times to fires that inevitably places them in harm's way for greater intervals than structural firefighters. Additionally, WUI firefighters do not have the typical personal protective equipment or PPE that structural firefighters rely on daily. This lack of PPE exposes them to greater inhalation, dermal, and potentially ingestion exposure risks than their structural firefighter peers. Likewise, the decontamination procedures that are normal practice in structural firefighter daily activities are not always possible within the WUI due to logistical issues such as distance of fire from fire station and other factors that would prevent WUI firefighters' access to decontamination resources. According to the International Agency for Research on Cancer (IARC), these factors alone provide evidence that occupational exposure to the hazards experienced as a firefighter are carcinogenic. Further, IARC has determined that there is high level of certainty and sufficient evidence that firefighters have higher cancer incidence rates for mesothelioma and bladder cancer than any other occupation. Although the unique risks to wildland and WUI fires are not well understood, preventive measures such as screening tools to identify early indicators of carcinogenicity such as epigenetic alterations could be developed to reduce incidence rates and improve outcomes in all firefighters.

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One such effort to mitigate adverse outcomes in firefighters is the Fire Fighter Cancer Cohort Study (FFCCS). The FFCCS has established a prospective multicenter study focused on carcinogenic exposures and health effects. To date, over 3000 firefighters have been enrolled in this study from across 26 states, of which 19% are female, 23% new recruits, and 19% are volunteers. The FFCCS aims to institute preventive measures by focusing on three pillars of public health – harm reduction, identification of potential therapeutic treatments, and early detection. Within the identification of potential therapeutic treatments, DNA methylation, a known catalyst of carcinogenicity, has become a major priority and study focus.

Epigenetic modifications are defined as heritable changes in gene function that occur without a change in the sequence of nuclear genetic material, which may be reversible. There are three main forms of epigenetic modifications including DNA methylation, histone modifications, and non-coding RNA. Evaluating epigenetic changes are considered biomarkers of effect and may provide critical insight into cancer pathways and potential factors that may increase cancer susceptibility in firefighters. More importantly, by characterizing epigenetic modifications that are potential early indicators of carcinogenesis in response to firefighter stressors may aid in therapeutic intervention development.

Within the FFCCS firefighter study, epigenetic modifications in structural firefighters were characterized including changes in microRNA (miRNA), which are molecules that help cells control the kinds and amounts of proteins they make, along with DNA methylation. The results of these assessments were compared to epigenetic modifications observed in new WUI recruits before they started working (baseline) and after two years of working (post) to aid in determining what, if any, unique epigenetic patterns could arise from fighting fires within the WUI. Previous longitudinal miRNA analyses on structural firefighters revealed 9 potential biomarkers of effect that play major roles in either promoting or suppressing cancer development. Of these potential biomarkers of effect, three (miR-422a, miR-92a-3p, and let-7f-5p) were associated with colorectal cancer. Two microRNA (miR-494-3p and miR-549a-3p) were positively associated with prostate cancer, while miR-26a and miR-525-3p were affiliated with hepatocellular cancers. Similarly, longitudinal DNA methylation analyses on structural firefighters showed significant epigenetic modifications in genes linked to cancer, non-coding RNAs, immune and neurological function.

However, when the same analyses for WUI firefighters was performed, distinct differences and patterns emerged highlighting what additional risks working within the WUI presents. For example, while 9 microRNAs associated with cancer were found due to structural firefighter exposure, a total of 50 miRNAs were altered from baseline to post in firefighters who responded to WUI incidents. Importantly, a strong association between WUI firefighter responses and a decrease in let-7i-5p expression, which has a known role in colon cancer suppression, was found. However, longitudinal DNA methylation analysis of WUI firefighters revealed very limited genetic alterations over time. Epigenetic data reported here could aid in WUI fire risk assessments, understanding mechanism of toxicity, and the creation of prevention/intervention strategies including the identification of early indicators of disease and biomarkers of previous exposure.

Assessment of Adverse Pregnancy Outcomes Among U.S. Female Firefighters

SPEAKER

Alesia Jung, PhD, Exponent

Dr. Alesia Jung is an Epidemiologist and Scientific Consultant at Exponent. Prior to joining Exponent, Dr. Jung completed her doctorate in Epidemiology on occupational risk factors that influence firefighter reproductive health outcomes at the University of Arizona's Mel and Enid Zuckerman College of Public Health in Tucson, Arizona. Dr. Jung's presentation highlights her dissertation work centered around occupational risk factors and associated outcomes specific to female firefighters.

ABSTRACT

Previous evidence suggests that women firefighters have a greater risk of experiencing adverse reproductive outcomes. Mechanisms associated with this potential increased risk in firefighters are hypothesized to be related to some occupational exposures, which have been associated with reproductive outcomes in other populations. We used cross-sectional survey data from a national study of women firefighters to investigate the burden and occupational factors associated with reported miscarriage, preterm birth, and infertility. Additionally, we collected dried blood spot samples to compare levels of anti-Müllerian hormone (AMH), a marker of ovarian reserve, among a subset of firefighters to non-firefighter controls. We observed that firefighters were 2.33 times more likely to report a miscarriage (95% confidence interval [CI] 1.96-2.75) and 1.41 times more likely to report a pre-term birth (95% CI 1.18-1.68) compared to non-firefighting populations. Volunteers had an increased risk of both miscarriage and preterm birth compared to career firefighters. This association varied by wildland firefighter status, with the greatest risk observed among wildland and WUI firefighters versus structural firefighters. An estimated 30% of women firefighters reported ever experiencing infertility and years of employment was potentially associated with increased risk of infertility. Finally, firefighters were found to have 33% lower AMH levels compared to non-firefighters (95% CI: -54.97, -1.43). Our findings suggest that women firefighters may benefit from increased occupational protections, though further evidence is needed to inform policy development and personal decision-making.

PRESENTATION SUMMARY

According to the National Fire Protection Association (NFPA), 9% of the one million firefighters working within the U.S. in 2020 are women. There are notable career differences among the nearly 90,000 female firefighters, where 12% are wildland firefighters, 5% career firefighters, and 11% are volunteers. These differences in career paths may subject female firefighters to unforetold exposure risks and unknown health outcomes. While the hazardous nature of fighting fires as an occupation is well known, female firefighter-associated reproductive health risks are understudied as it relates to specific factors involved with fire events that occur within the wildland urban interface or WUI.

Although reproductive health outcomes can be negatively impacted by a number of factors, environmental exposures are known to play a key role in both males and females. Factors such as ambient temperatures, stress, air pollution, and shift work have all been associated with preterm birth, low birth weight, stillbirths, infertility, low sperm quality, menstrual disruption, and miscarriages. To understand how various work environment, health, and perceived experiences contribute to adverse reproductive outcomes in female firefighters, a study called the Health and Wellness of Women Firefighters (HWWF) was developed in the U.S. Between 2017-2019, over 3,100 women firefighters were recruited and enrolled in the HWWF study and information including demographics, occupational history, pregnancy history, reproductive health and infertility were recorded. The majority of the women firefighter cohort identified as non-Hispanic White with a median age of 38 years old who generally lead healthy lifestyles.

Using data from the HWWF, the two main goals were: 1) to determine if rates of miscarriages, pre-term birth, and infertility are more prevalent among firefighters compared to other groups of women such as nurses or the general population; and 2) determine what firefighter related occupational factors are associated with risk of miscarriage. The analysis found that the prevalence of miscarriage in firefighters was 2.33 times higher than nurses. Career path or status also played a role in the outcomes observed in the HWWF study where volunteers displayed greater risk of miscarriage than career firefighters. Additionally, if the volunteers had wildland firefighting responsibilities, the risk for miscarriage became more pronounced. Results revealed volunteers working in the wildland also contributed to increased pre-term birth in comparison to structural firefighters. Importantly, the HWWF study found that the prevalence of preterm birth among firefighters is almost 1.5 times greater than nurses and female non-firefighters. No associations were found between occupational factors such as shift schedule, working fire/rescue calls at pregnancy start, work restrictions during pregnancy, number of fire incidents responded to during pregnancy and reproductive health outcomes measured. However, a modest association was found between timing of work restriction and the risk of preterm birth, where if work restrictions occurred by the second trimester, the risk of preterm birth was lowered.

One of the final metrics of reproductive health outcomes measured during the HWWF study in female firefighters was infertility, which is defined as the inability to become pregnant after 12 months of regular intercourse without use of contraceptives. Among 562 women who provided infertility data via HWWF surveys, 30% (n=168) reported previously experiencing infertility. In comparison, an estimated 12.5% of U.S. women have similarly reported experiencing infertility. The length of time working as a firefighter was associated with modest, non-significant increased risk of infertility if length of time exceeded 15 years in comparison to working less than five years. An important clinical biomarker of ovarian reserve and female fertility, anti-Mullerian hormone (AMH), was assessed in the blood of 106 firefighters and 58 non-firefighters to determine the influence of occupational stressors on this key indicator of reproductive health. Levels of AMH were found to be 33% lower in firefighters in comparison to non-firefighters after adjusting for age and BMI. Key conclusions of HWWF study suggest that infertility among women firefighters may be greater than U.S. women and the length of career could increase risk of infertility. In sum, the HWWF study evaluated the largest cohort of U.S. women firefighters to date and provided occupational risk factors associated with adverse reproductive outcomes, which may be used to create intervention strategies and guidance to help alleviate the occupational burden of firefighting on women's health.

Modulation of $PM_{2.5}$ Mediated Cardiometabolic Indicators in Wildfire Exposed Communities Through Air Filtration Intervention Strategies

SPEAKER

Junfeng (Jim) Zhang, PhD, Duke University

Dr. Jim Zhang is a Professor within the Global Health Institute at Duke University. Dr. Zhang joined the Duke Faculty in fall 2013 from the University of Southern California. His prior positions include professor, department chair, and associate dean at the Rutgers School of Public Health. Dr. Zhang's research interests include developing novel biomarkers of human exposure and health effects, assessing health and climate co-benefits of air pollution interventions, and examining biological mechanisms by which environmental exposures exert adverse health effects.

ABSTRACT

Cardiometabolic and cardiovascular diseases are the leading cause of death in the U.S. for both men and women of all ages. It is now well established that exposure to air pollutants, especially fine particulate matter ($PM_{2.5}$), increases the risk of adverse cardiovascular events and cardiometabolic disorders. Considering widespread $PM_{2.5}$ pollution worldwide and the increasing frequency and intensity of wildfires in California and elsewhere, interventions to reduce personal exposure to $PM_{2.5}$ may offer a practical preventive measure especially in older individuals with conditions such as obesity. Several short-term (days to weeks) air pollution intervention studies, including our own study in China, consistently found that reduction in $PM_{2.5}$ exposure can improve acute indicators for cardiorespiratory outcomes. However, no studies have evaluated a longer-term intervention in reducing the risk for chronic cardiometabolic disorder. Our new study is assessing the effectiveness of a six-month residential-based $PM_{2.5}$ exposure reduction strategy in a cohort of ethnically diverse and at-risk individuals (overweight or obese adults) residing in the Los Angeles area where air pollution levels are among the highest in the U.S. The intervention period will naturally cover wildfire episodes, allowing us to evaluate the acute health impact of indoor filtration during wildfires. Using a block-randomized crossover study design, homes of participants undergo a true HEPA filtration session and a sham filtration session (HEPA filter removed), separated by a washout period. Each participant dwelling is being measured before, during, and at the end of each session for indoor and outdoor air pollutant concentrations. This presentation will describe the design and protocol of a new study to examine the impact of a 6-month residential HEPA filtration intervention on cardiometabolic outcomes during the presence or absence of wildfire events.

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PRESENTATION SUMMARY

Proper air filtration is an important factor in maintaining and improving indoor air quality especially during catastrophic events such as wildfires. Portable air filters containing HEPA filters and/or activated carbon filters are useful tools to improve indoor air quality in both residential and commercial settings. However, the efficacy of using portable air filters during wildfires to lower or remove hazardous particulate matter and other pollutants has yet to be tested and validated. As the prevalence and severity of wildfires continue to grow, the development of air filtration strategies to improve health outcomes among vulnerable populations is critical to alleviating the exposure burden experienced during wildfire events.

Previous studies have demonstrated the utility of portable air filters in reducing $PM_{2.5}$ exposure in homes located in China, which has severe indoor and outdoor air pollution levels year-round. It is well known that indoor and outdoor air pollution can exacerbate respiratory conditions such as asthma. A seminal study was conducted to evaluate whether using air purifiers in the bedrooms can alleviate indoor air pollutants and improve the lung function of asthmatic children living in Shanghai. The results revealed that air filtration can significantly reduce $PM_{2.5}$ levels in bedrooms of asthmatic children. This reduction in particles and enhanced indoor air quality over a two-week period was associated with 25% improvement in airway inflammation, 5% increase in lung function along with a 25-75% increase in multiple airway resistance and reactance endpoints. The findings from this study and other previous studies provide empirical evidence that air filtration can be a potent intervention that can reduce indoor $PM_{2.5}$ levels by 40-90% and using HEPA air purifiers for even a short period can improve acute cardiovascular and respiratory health outcomes, which may be useful in the effort to mitigate wildfire exposure associated health risks. However, to date, no published studies have evaluated the potential benefits of longer-term indoor filtration interventions in improving cardio-metabolic profiles in at-risk adults who live within areas that face wildland urban interface (WUI) fire events.

To address these knowledge gaps, a framework to assess the efficacy of HEPA air purifier intervention was developed with the following four aims: 1) assess intervention effectiveness across 6 months in 52 adults who were at risk for Type 2 diabetes ; 2) examine dose-response relationship between indoor $PM_{2.5}$ levels and changes in metabolic outcomes; 3) explore pathophysiologic biomarker changes related to cardiometabolic profile to identify potential molecular mechanisms; 4) explore the impact of wildfires on HEPA intervention effectiveness and determine impact of HEPA intervention of wildfire related particle exposure. The study design includes a cross-over method and prioritization of census tract-level with historical $PM_{2.5}$ exposure levels. The study design flowchart is illustrated in **Figure 1** as shown below.

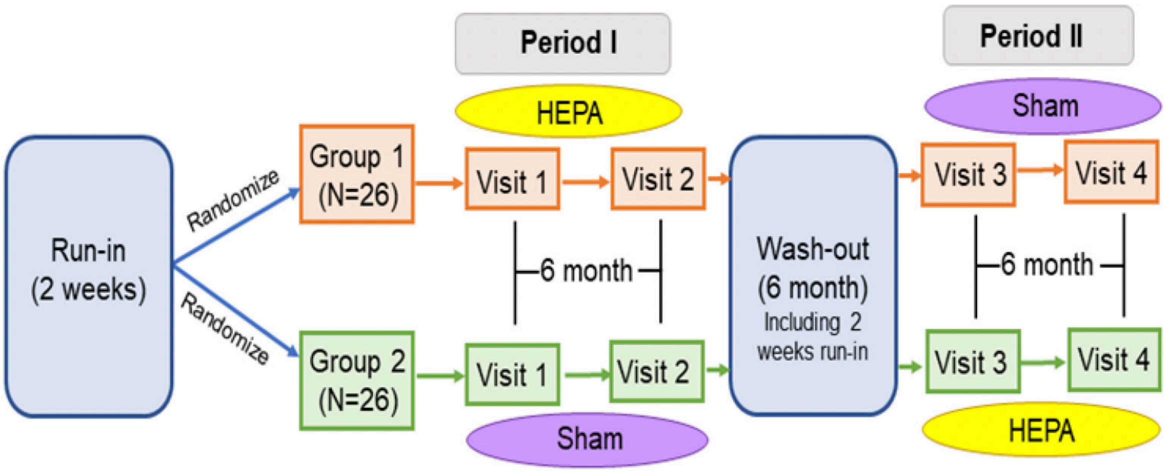

Figure 1. UL2 Study Design Flowchart

The study design will be implemented in southern California near residential locations in close proximity to wildfires. The participants are older adults who are either overweight or obese, characteristics of elevated risk for Type 2 diabetes. Both male and female (1:1 ratio) participants will be measured for cardiometabolic outcomes such as continuous glucose and blood pressure monitoring through home visits every 6 months. Blood and urine samples will also be evaluated using targeted and untargeted omics approaches to uncover molecular mechanisms centered around pathophysiological pathways of cardiometabolic dysfunction. Specifically, metabolites of combustion products such as polycyclic aromatic hydrocarbons (PAHs) will be evaluated including amino-PAHs and PAH-tetrol in blood and hydroxy-, amino-, carboxy-PAHs will be assessed in urine. Covariates such as health related lifestyles, behaviors that mediate exposure, and dietary recall will be considered and accounted for. Measuring the alteration and potential reduction of these biomarkers of exposure will be used to augment wildfire exposure health assessments and help establish the efficacy of low-cost $PM_{2.5}$ sensor monitoring and air filtration strategies in participants' homes. Air quality monitoring will be employed by utilizing paired indoor and outdoor low-cost pollutant monitors, real-time data assessments, and daily basis monitoring to check for potential abnormal data output to enable corrective actions if necessary. Outdoor air quality monitors will consist of BlueSky $PM_{2.5}$ and PM_{10} sensors and indoors sensors will enable the detection of $PM_{2.5}$, PM_{10}, and gases such as carbon monoxide, carbon dioxide, sulfur dioxide, ozone, and nitrogen dioxide along with total volatile organic compound (VOCs) analysis. Each external and internal sensor will endure regular calibration and alignment with air quality management district (AQMD) reference monitors.

Initial preliminary data using the study design mentioned above revealed that low-cost $PM_{2.5}$ sensors employed in San Francisco Bay and Los Angeles County areas are effective in detecting outdoor and indoor disturbances to fire events that occurred across June through November in 2020. A separate study to identify biomarkers of campfire exposure in eight healthy volunteers revealed an increase in urinary biomarker, 1-pyrene carboxylic acid (1-PYRCA) twelve hours post-exposure. Interestingly, 1-PYRCA may potentially be a unique metabolite of campfire and potentially wildfire exposure as this biomarker was not found in relation to traffic related air pollution nor coal combustion exposures as indicated in other studies. The framework and preliminary data described herein illustrate that the proposed study design is feasible and may help identify novel biomarkers of exposure and effect in vulnerable populations who face wildland urban interface (WUI) or wildland fires.

Panel Discussion

During the panel discussion, several insightful questions were raised by audience members and the ensuing discussions revealed major knowledge gaps in our effort to protect firefighters and communities during WUI fires. Additionally, the symposium chair and panel discussion moderator, Dr. Christa Wright, asked the following questions to the panelists in relation to each of their presentations:

- Are firefighter participants aware of the hazards and health issues presented?
- What interventions are being developed to help mitigate WUI related hazards or issues?
- What are future steps to increase awareness?

In response to the first question, an audience member who identified as a veteran WUI firefighter described the numerous hazards incurred while working in the field that were previously unknown. One such issue highlighted how firefighters commonly manipulate fire hosing, where the hose is draped over the firefighters' shoulder for better control. This common form of controlling the hose position inadvertently allowed for dermal exposure of the neck area to highly contaminated surfaces of the fire hose. Due to limited decontamination strategies available to WUI firefighters as described earlier, the veteran firefighter recommended that guidance or mitigation strategies be developed to reduce this high exposure risk scenario alongside the numerous other challenges WUI firefighters endure.

Regarding how the findings from the Fire Fighter Cancer Cohort Study (FFCCS) are shared with first responders to improve awareness, Dr. Miriam Calkins and Dr. Jackie Goodrich described the dissemination strategy in which firefighters are informed about the hazards within the WUI. A newsletter and a report of individual and group health outcomes are shared with all FFCCS participants at the end of each phase of the study. While every effort is made to enhance awareness, it was noted that guidance on exposure protection measures for volunteer firefighters should be improved within the WUI. Current evidence suggests volunteer firefighters may unintentionally create a secondary exposure risk by transporting their gear to and from fire events in the personal vehicles. Guidance on how to decontaminate gear prior to travel and/or gear containment storage options using simple easy-to-deploy methods are sorely needed.

Of the many mitigation strategies that were discussed, simple steps to reduce WUI related exposures were proposed by the panelists. One measure to reduce dermal exposure consisted of dermal wipes that could be easily deployed in the field. Additionally, redesigned and WUI appropriate turnout gear was proposed and discussed as highly needed advancement that would increase WUI firefighter health outcomes. Lastly, Dr. Jim Zhang recommended increasing the consumption of antioxidant rich foods as a nutritional intervention for WUI firefighters, which may enhance innate defenses and/or potentially reduce combustion by-product exposure effects on a cellular level.

At the end of the panel discussion, steps to increase awareness of the health disparities that may arise from working in the WUI were presented. One agreed upon measure would be to establish new or enhance existing collaborations between academia, nongovernmental organizations, and regulatory agencies to provide standard guidance for WUI firefighters and communities facing these unprecedented events to minimize public health impacts.

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