Firefighters battle the Caldor wildfire in California in August.

A STUDY IN SMOKE

As wildfires get bigger and rage for more of the year, scientists are racing to understand the lingering impacts on human health. **By Max Kozlov**

On a cool September morning in San Francisco, a group of firefighters packed their gear into a bright red van. The sickly sweet odour of pine resin from a distant blaze hung in the air as the crew prepared to battle the rapidly growing Dixie fire, on its way towards becoming the largest single wildfire in California's history. Sweeping across the Sierra Nevada mountains, it would come to scorch more than 3,900 square kilometres before crews fully contained it in late October.

The firefighters had one more stop before they joined the thousands of other people working to control the blaze. In a small classroom inside the San Francisco Fire Department's training building in the Mission District, Mary Prunicki and a team of researchers collected questionnaires and blood samples from each firefighter.

Prunicki, a pollution biologist at nearby Stanford University, will use the samples as a baseline to compare with ones taken when the firefighters return. She'll be looking for signs of their bodies' reaction to the smoke, including inflammation and changes to immune and heart function.

Smoke from wildfires is responsible for tens to hundreds of thousands of premature deaths around the world each year. And Prunicki is one of hundreds of researchers trying to understand the health effects of smoke exposure. Scientists want to know what it is in wildfire smoke that makes it more harmful to humans than other forms of pollution. They are looking

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at short-term and long-term effects; who is most vulnerable to the pollutants; and how best to keep people safe and healthy in smoke plumes that can stretch for thousands of kilometres from a blaze such as the Dixie fire.

The work has taken on fresh urgency in recent years. Climate change has been exacerbating droughts and heatwaves around the world, nearly doubling the total area where the right spark could set dry vegetation ablaze and trigger an inferno. As a result, wildfires are increasing in frequency, size and intensity around the world, and smoke seasons are getting longer. Wildfires have ravaged the western United States in the past decade, but other countries have also faced their worst blazes in generations. Fires in the Siberia region of Russia this year burnt a bigger area than all the world's other blazes combined. And Australia is still reeling from its devastating 2019–20 bush-fire season — colloquially called the 'black summer' — which destroyed thousands of homes and killed at least 30 people and hundreds of millions of animals.

"If you compare the last 5 years to the 10 to 15 years before that, it's just not really comparable," says Sam Heft-Neal, an environmental economist at Stanford University who studies the health risks of wildfires. "It's like a totally different fire regime."

A toxic mix

Wildfire smoke contains dozens of different particles, such as soot, and chemicals, such as carbon monoxide, but one of the main concerns for air-quality specialists are the tiniest particles in smoke that measure 2.5 micrometres or less across (on average 1/40th the width of a human hair). The firefighters working with Prunicki will encounter copious amounts of this $PM_{2.5}$, as it is known. But according to Francesca Dominici, a biostatistician at the Harvard T. H. Chan School of Public Health in Boston, Massachusetts, there is no amount of fine particulate matter that is safe to breathe because it is known to penetrate deep into the smallest crevices of the lungs and enter the bloodstream (see 'Risky exposures').

When smoke enters the airway, the body reacts "like there's germs and infection in there", says Fay Johnston, an environmental epidemiologist at the University of Tasmania in Hobart, Australia. That comes with a whole suite of physiological changes: the hormone cortisol and blood glucose spike, which in turn makes heart rhythms less stable and blood more likely to clot. The lining of the lungs becomes inflamed, making it more difficult to breathe.

Prunicki hopes to understand these physiological changes by measuring certain biomarkers — molecules in the blood — that can give a snapshot of immune, respiratory and cardiovascular function. She has turned to firefighters, people who face high occupational exposure to smoke, to see whether she can detect any changes in their biomarkers after direct exposure — and whether the changes are long-lasting or similar to those seen in people who don't fight fires but are still subjected to smoke. Close to a fire, $PM_{2.5}$ can sometimes reach levels more than 15 times greater than the 24-hour exposure standard of 35 micrograms per cubic metre set by the US Environmental Protection Agency (EPA). But many firefighters don't wear respirators when they are battling blazes because they can be cumbersome, says Prunicki. "This level is outrageously high," says Dominici. "At that point, you're just breathing a toxic soup."

But even lower levels might pose a severe health risk, she says, because in such conditions people are less likely to take protective measures such as wearing a respirator. Prunicki has shown that, even in areas more than 100 km away from wildfires, smoke exposure is linked to a slew of changes in biomarkers that might be a sign of immune and cardiovascular dysfunction[1].

Wildfires don't happen in a bubble, either, says Dominici. Smoke can predispose people to infectious diseases or exacerbate the symptoms of other respiratory conditions, including COVID-19 and influenza. Dominici and her colleagues estimate that increased $PM_{2.5}$ levels during the 2020 fire season in Washington, California and Oregon correlated with about an extra 19,700 COVID-19 cases and 750 deaths[2].

The leading hypothesis for the cause of the excess cases is that $PM_{2.5}$ compromises the immune system and causes inflammation, which could make people more susceptible to infection or exacerbate the effects of disease, leading to a rise in positive diagnoses. A more controversial take, says Dominici, is that some respiratory viruses might hitch a ride on fine particulate matter when entering lung tissue.

Underlying health conditions pose another problem, says Johnston, especially if smoke is affecting millions of people at once, as it did during Australia's black summer. Her team reported that those fires led to an excess of thousands of hospitalizations and hundreds of deaths from heart and respiratory problems stemming from the smoke, which blanketed nearly 80% of the country's population[3].

On high-smoke days, hospital-admissions data show an increase in the number of people being admitted with cardiovascular and respiratory problems and diabetes, particularly children and older people. Pregnant people might also be at higher risk of having gestational diabetes, high blood pressure or giving birth to low-weight babies: Heft-Neal's research estimates that nearly 7,000 excess premature births in California between 2007 and 2012 can be attributed to wildfire smoke exposure during pregnancy[4].

Socio-economic status, too, cannot be overlooked, says Dominici. People in under-resourced communities are more likely to have outdoor occupations, such as farming or landscaping, higher rates of accompanying diseases and conditions and less access to adequate health care and air purifiers — all of which make wildfires an even greater burden for communities of colour and low-income communities, she says.

Long-term effects

Studying the long-term health effects of smoke on humans has proved difficult. Longitudinal studies to track people's health after exposure would need to span decades and distinguish between the effects of many different environmental exposures.

In 2008, Lisa Miller, a respiratory immunologist at the University of California, Davis, had a useful, if unfortunate, opportunity to observe long-term effects in a controlled population. She had been working with a troop of rhesus macaques (*Macaca mulatta*) to study allergies and asthma when a bad fire season hit northern California. Twenty-five newborn macaques, housed outside, were exposed to ten days of ambient $PM_{2.5}$ levels above federal guidelines.

Miller has been monitoring their health — and that of their offspring — ever since.

Compared with macaques born the following year, the 2008 group had a reduced immune response and decreased lung capacity. In a study that is not yet published, Miller and her colleagues scanned the lungs of these monkeys and found that the tissue had stiffened in a way that might change how the animals move around and breathe to compensate for the reduced respiratory function.

Miller says these data offer some tantalizing hints about the long-term toxicity of wildfire smoke on respiratory and immunological function in humans: "We know it's bad," she says.

Still, the work has caveats, Miller says. The experiment is controlled because the researchers know the whereabouts of the animals at all times, but most people do not experience round-the-clock outdoor exposure, and humans might react to smoke differently from macaques.

Indoors or outdoors

Scientists are still trying to pin down the extent of people's wildfire smoke exposure in different settings. Only in the past few years have researchers applied machine-learning techniques to meteorological models and high-quality satellite data to try to predict how smoke moves through the atmosphere. And household air-quality sensors offer researchers a deluge of real-time data with which to track $PM_{2.5}$ levels more precisely.

But scientists are running out of comparator groups, says Miller. Because poor air quality is so ubiquitous today — more than 90% of children around the world breathe air laden with $PM_{2.5}$ levels above World Health Organization guidelines — the number of unexposed humans or other primates in long-term studies is dwindling, making research all the more pressing, she says.

The next key area of research, Miller says, will be to understand exactly which chemicals in wildfire smoke make it more dangerous to respiratory health than other types of pollution, and how those interact with and harm human cells. "We've been burning wood in our fireplaces since the dawn of time," she says. "It's not just the combustion of biomass, it's the combustion of man-made materials with that biomass."

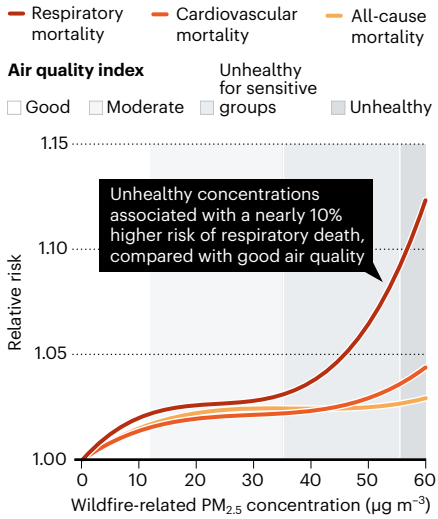
Other important questions involve how well smoke infiltrates indoor spaces, says Heft-Neal. Public-health officials generally recommend that high-risk groups stay indoors and shut all doors and windows during days with poor air quality. But these recommendations are "very generic and not nuanced", says Johnston, who adds that the advice isn't especially helpful in Australia, where housing doesn't tend to be very well insulated.

Preliminary research in California households with indoor air monitors shows that, although indoor air contained less than half the concentration of fine particulates found outdoors, indoor $PM_{2.5}$ levels nearly triple during wildfire events, often surpassing the EPA's 24-hour $PM_{2.5}$ exposure standard[5]. Still, infiltration rates are likely to differ from house to house, and Heft-Neal says it will be crucial to understand the types of housing structure best suited to protecting against air pollution.

Colleen Reid, a health geographer at the University of Colorado Boulder, is investigating air quality in schools. These are crucial sites, given that children generally seem to be more vulnerable to wildfire smoke than adults. She and her colleagues plan to study the air quality inside and outside school buildings in Colorado and compare it with that at pupils' homes.

RISKY EXPOSURES

An analysis of more than 65 million deaths in 43 countries found an increased risk of death from all causes soon after exposure to particulates ($PM_{2.5}$) from wildfire smoke.



SOURCE: G. CHEN *ET AL. LANCET PLANET. HEALTH* **5**, E579–E587 (2021).

> **"Just like X-ray technicians wear badges to see how much exposure they've had, why can't we do that with smoke?"**

The current public-health guidance in the United States leaves it up to individual school districts to determine whether to stay open during air-pollution events, depending on whether the air quality is better in the schools or at home, Reid says. "But nobody actually has any of that data," she adds.

She says this research could help local authorities to determine whether to establish 'clean air shelters', where people could access purified air. Schools could provide clean air to pupils during the day and to the community when classes aren't in session, Reid says.

More indoor and community-level air-quality sensors will help with these public-health recommendations. So, too, will personal monitoring, Prunicki says, particularly for those who, like her firefighter volunteers, are being heavily exposed. Using her research on cardiovascular and immunological biomarkers, Prunicki envisages a day when firefighters and other vulnerable populations could take a simple blood test to see whether they've reached a dangerous level of lifetime smoke exposure, and should take extra precautions to avoid continued contact. "Just like X-ray technicians wear the X-ray badges to see how much cumulative exposure they've had, why can't we do that with smoke?" she says.

But, Johnston says, however essential it is to understand the intricacies of how smoke harms the human body and people's risk levels, that research doesn't address the root of the problem — climate change.

"We could have all the research in the world that tells you to take an anti-inflammatory or use a subsidized HEPA filter, but we're gonna be going backwards until we actually address the fundamental underlying problem," she says of climate change. "We're on a terrible trajectory right now."

Climate modellers predict that the kinds of fire that charred California and Russia this year are just the beginning. The area burnt in California each year, for example, will increase by 77% by the end of the century if greenhouse-gas emissions continue to rise, according to the state's 2018 climate-change assessment. Researchers and policymakers alike are scrambling to avert these nightmare scenarios.

Current predictions show that rising emissions would be linked to an enormous health-care burden, with potentially millions of people having reduced respiratory, cardiovascular and immunological function — especially in high-risk communities. The health cost associated with premature death and hospital admission from Australia's black summer, for example, is estimated at Aus$2 billion (US$1.47 billion) — about 10 times higher than that of previous years, says Johnston.

In the meantime, scientists are continuing to piece together the risks of exposure. Front-line workers are willing to take part in the research, but they worry about learning the answers. As the firefighters pack into the van bound for the Dixie fire, the driver, lieutenant Ken Smith, is opening his door and starting to climb inside when he stops.

"We don't think about what's in the smoke," he says. "If we knew what we breathe in while we work, we couldn't do it."

Max Kozlov writes for *Nature* from Washington DC.

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