Why Are Smokers Being Hospitalized Less Often From Coronavirus?

A Greek cardiologist and French neuroscientist are trying to find out.

By **Alex Norcia**

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The Chinese smoke. Well over half the nation's men are smokers, and the World Health Organization (WHO) estimates that one third of the planet's cigarettes are smoked in China. But earlier this year, Konstantinos Farsalinos noticed something odd: Very few of those hospitalized for the coronavirus in the country appeared to be smokers.

Farsalinos, a cardiologist and tobacco harm-reduction specialist in Greece, has since been wondering if nicotine, the chemical substance found in tobacco, could be preventing people from getting COVID-19, or stopping the symptoms from becoming worse.

While no conclusions can yet be drawn, Farsalinos' prevailing hypothesis is essentially that nicotine has certain anti-inflammatory effects. The most severe COVID-19 symptoms seem to come from an overreaction of the body's immune system known as a "cytokine storm." During that storm, the immune system targets an infection, say in the lungs, and they can become inflamed, leading to difficulty breathing. Nicotine, Farsalinos reasons, might be able to at least lessen that intensity.

Scientists Say Another Panic-Fueling Vaping Study Needs to Be Retracted

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On the surface, it's an odd theory. Smoking is still the leading cause of preventable death in the world; certainly nobody is advocating picking up the habit as some kind of preventive measure. And nicotine is only one of many unusual solutions that are also in the early stages of scientific consideration. Scientists, seemingly in throw-everything-at-the-wall mode, are dosing infected men with estrogen, considering over-the-counter

heartburn medication, and testing immune-system-modulating drugs meant for treating cancer, all in hopes of finding a way to control the virus or the body's reaction to it. (None are considering having anybody drink bleach.)

Farsalinos' observations, available in preprint and soon to be published in the journal *Internal and Emergency Medicine*, have caught the attention of scientists, policymakers, and tobacco control experts across the globe, some of whom believe this counterintuitive information is important enough to pursue: It's still too early to tell, but the role nicotine plays might have to be carefully rethought, especially given the unfamiliar circumstances.

"We all know that smoking is obviously bad for you," said Raymond Niaura, the interim chair of the Department of Epidemiology at New York University and an expert in tobacco dependence and treatment. "It follows logically that smokers would be way worse off. I would think that too. But I've been surprised: That's not the story we're necessarily seeing."

Niaura is a co-author with Farsalinos, as well as with the Greek public-health scholar Anastasia Barbouni, on the *Internal and Emergency Medicine* paper. It's expected to be released imminently, and will be the first peer-reviewed paper on the subject. (Farsalinos told VICE that another of his papers, with similar and more thorough conclusions, will also shortly be available in a different journal, *Toxicology Reports*.)

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The theory is not totally out of left field. Nicotine, a stimulant found in tobacco (as well as other plants like tomatoes, albeit in much smaller quantities), has already been studied for its neuro-protective qualities, which is of interest to scientists who study Parkinson's and Alzheimer's diseases. It's the chemicals from burning tobacco, Niaura noted, that are what cause heart attacks, cancer, and lung disease.

FDA Admits There's Actually No Evidence Vaping Makes COVID-19 Worse

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"As a policymaker, you should be asking what the consequences are in acting that this is right if you end up in fact being wrong," said Clive Bates, a former public-health official in the United Kingdom and a prominent expert in tobacco control. "The downsides appear negligible to trying to figure it out. There is a way forward."

A group of French researchers led by neuroscientist Jean-Pierre Changeux is doing just that—hoping to test out nicotine patches on healthcare workers and patients who tested positive for coronavirus. A team, based at the prestigious Pitié-Salpêtrière in Paris, observed similar data in the French population that Farsalinos did with the Chinese: Of 343 hospitalized patients, only 4.4 percent were recorded as smokers; of 139 outpatients, only 5.3 percent were recorded as smokers. This is compared to the larger French population, more than a quarter of which smokes cigarettes.

The news caused such a stir in France last week that the government suspended the online sale of nicotine patches and other smoking cessation tools, apparently fearing citizens would buy them in bulk to treat themselves.

Unlike Farsalinos' study, the French one has not yet been through the peer-review process. Those researchers also have a different hypothesis, though still follow a similar logic—nicotine might be preventing the coronavirus from entering through cells in the body, and could also be calming those cytokine storms. (Farsalinos' hypothesis in the *Internal and Emergency Medicine* paper centers on what's called the angiotensin-converting enzyme 2, or ACE2, the receptor that the coronavirus is commonly believed to latch

onto to enter human cells; the French, on the other hand, think that the virus could be getting into the body through nicotinic acetylcholine receptors, or nAChRs—different receptors in the lungs or olfactory system.)

Preliminary data out of New York and elsewhere in the United States appears to be suggesting that hospitalization of smokers is low as well, leading to more and more calls for clinical trials like the French want to pursue.

Still, every scientist and tobacco control expert VICE spoke to repeatedly emphasized that these were just hypotheses, and that they don't have the luxury to collect perfect data at such a rapid pace; everybody is working double-time trying to help before a vaccine is eventually created. There could very well be other explanations for why so few smokers with the coronavirus seem to be entering and leaving the hospital in such small numbers—one that does not have to do with nicotine.

"Is there some kind of reporting problem?" said Derek Yach, the president of the Foundation for a Smoke-Free World and the former executive director for noncommunicable diseases and mental health at the WHO. "Are they dying before they get to the hospital? Are they not classifying smoking status correctly? I want to be as skeptical as possible."

The UK Government Says What the US Won't: Vaping Is Safer Than Cigarettes

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There are abundant reasons to be, as Yach acknowledged. The healthcare system could be so overwhelmed that medical history is simply not recorded correctly. There is also the possibility that some other chemical in tobacco—not nicotine—could be producing a protective effect. And the

proposed French trial could be flawed from the outset, since nicotine enters the blood differently via a cigarette and a nicotine patch.

When smoking, nicotine gets into the body in "peaks," whereas a nicotine patch maintains a much more sustained level, explained Jed Rose, a professor in psychiatry and behavioral sciences at Duke University and the co-inventor of the nicotine skin patch.

Michael Siegel, a professor of community health sciences at Boston University, had a specific concern for the French study too, and remained wary overall.

"Smokers who have developed chronic disease have likely quit because of their disease," Siegel said. "Many of the smokers who are continuing to smoke are doing so because they don't have disease yet. So this would be expected to skew the sample of hospitalized patients toward people who do not smoke."

But the irony, should it turn out that nicotine has a protective effect on the coronavirus, is that public-health agencies across the world have been advising people to quit it entirely since the pandemic took off—urging, for example, both smokers of combustible cigarettes *and* vapers to stop. The distinction between nicotine and tobacco—which are often lumped together and demonized—is one emphasized by tobacco control experts focused on harm reduction. Getting a nicotine fix from anything safer than a traditional cigarette has been crucial in cessation methods and is a foundation in tobacco harm-reduction research.

Now, it has potentially gained new urgency.

"If you make the wrong calls on things," Bates said, "you can kill people."