



CHARLES THATCHER / GETTY IMAGES

but it is not the only one. Just 15% of smokers develop the disease. Presumably, their genetic makeup predisposes them to lung maladies. Scientists have known for decades that a mutation in the enzyme $\alpha 1$ -antitrypsin, found in 1–2% of people with COPD, puts people at greater risk — especially smokers. In the past few years, genome-wide screens have netted a slew of new gene candidates, though not all have been confirmed as risk factors.

The manner in which smoke particles damage the lungs also remains uncertain. In addition to imbalances in enzymes such as antitrypsin, another potential culprit is the immune system. Most smokers suffer from inflamed airways. But those who develop COPD endure sustained inflammation, even after they quit smoking. Some scientists see this as evidence that COPD is an autoimmune disease. Supporting the hypothesis, researchers have found that some people with COPD possess antibodies against some of their own proteins.

Another potential modulator of the immune response in COPD is vitamin D. Several studies have shown that people with COPD are more likely to have a deficiency in the vitamin, and the less vitamin D they have, the worse their lungs work. Vitamin D may squelch the negative inflammatory response while promoting beneficial immunity, but researchers have yet to confirm its effect and work out the details.

Pharmaceutical companies are pursuing new and improved versions of current COPD treatments, such as the bronchodilators that relax airway muscles and ease breathing. Both Novartis, headquartered in Basel, Switzerland, and Pearl Therapeutics, headquartered in Redwood City, California, report promising data. And a collaboration between GlaxoSmithKline (GSK), headquartered in Brentford, UK, and Theravance, a biopharmaceutical company based in South San Francisco, California, is running several trials with a dual-drug combination. But another combined therapy from GSK and Theravance, Relovair, has yielded mixed results thus far. Fortunately, drugs are not the only option. Researchers are also at work on bioartificial lungs that they hope could reduce or even eliminate the need for donor organs.

Cigarette smoke is packed with free radicals, so antioxidants — which can neutralize their damaging effects — have also been tested in clinical trials. The results have been inconsistent, perhaps because each medicine only mops up a subset of the different types of free radicals ravaging the lungs. Some scientists have now turned their attention to Nrf2, a DNA-binding protein that switches on many of the body's own antioxidants.

These treatments will be important weapons in the fight against COPD. But most are still confined to the lab rather than nearing the clinic — and scientists and health professionals must take aim at COPD now if they are to stem its rise. ■

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HEALTH IMPACT

Breathless

COPD is one of the world's biggest killers, but awareness is low, diagnosis is often missed, and in many countries the extent of the problem is not even well-documented.

BY AMBER DANCE

Worldwide, 65 million people with chronic obstructive pulmonary disease (COPD) are gasping for air — and with the World Health Organization (WHO) predicting the disease will vault from fifth to third in the leading causes of death globally by 2030, their breathless ranks are set to swell. Governments, scientists and pharmaceutical companies are taking several approaches to ease the burden of COPD, both on the patients and on healthcare systems.

COPD encompasses both emphysema and chronic asthmatic bronchitis; patients can suffer either problem or both simultaneously. Emphysema eats away at the lung's air sacs, or alveoli, so that less surface area is available for gas exchange. Bronchitis constricts the airways entering the lungs and clogs them with mucus. The winded masses face a disease that is incurable, even for those fortunate enough to receive

a proper diagnosis and treatment for symptoms.

Surveys suggest that COPD is grossly underdiagnosed in both developed and developing nations. People don't always report the relevant clinical signs, and some doctors do not use spirometry, the gold-standard method of diagnosis, because they cannot afford the machine or haven't heard of it. A patient undiagnosed means a patient untreated, which could hasten death.

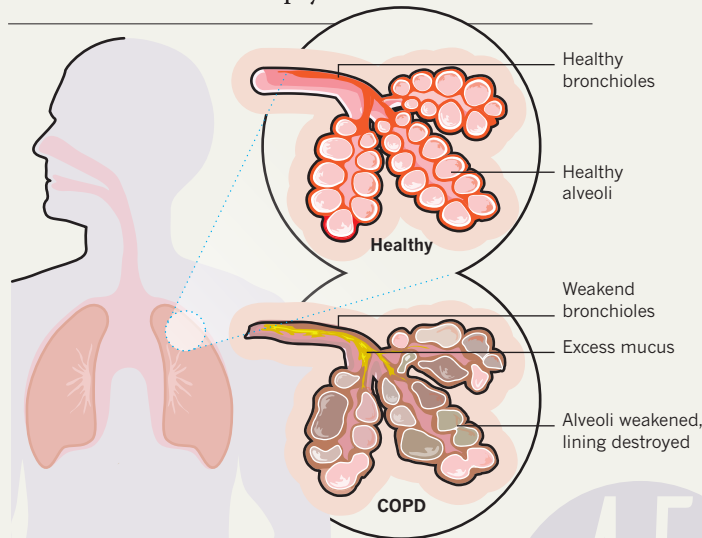
Although reliable numbers on global COPD rates are hard to come by, the WHO estimates that 90% of COPD cases occur in developing nations. COPD is likely to become an especially serious problem over the coming decades in China, the world's biggest producer and consumer of cigarettes. About a third of Chinese people smoke, among the highest rates in the world. Smoking-related diseases are the country's biggest killer, and COPD alone kills nearly two million people there each year.

Smoking is the major risk factor for COPD,

COPD IN THE UNITED STATES

INSIDE THE LUNGS

It is not a single disease but a constellation of symptoms. And comes in two forms: emphysema and chronic bronchitis.



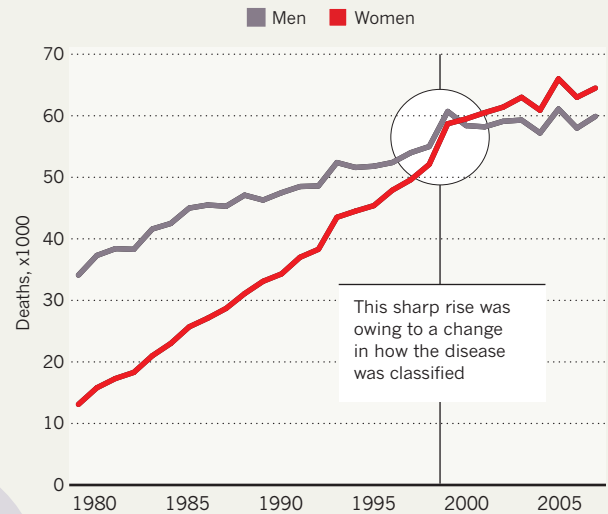
Patients with COPD suffer primarily because their alveoli, or air sacs, lose their elastic quality or are destroyed. The airways may also become thick and stiff, inflamed, or clogged with mucus, so that patients can take only shallow breaths.

4.5

A person dies of COPD-related illness every four to five minutes in the United States.

A DISEASE ON THE RISE

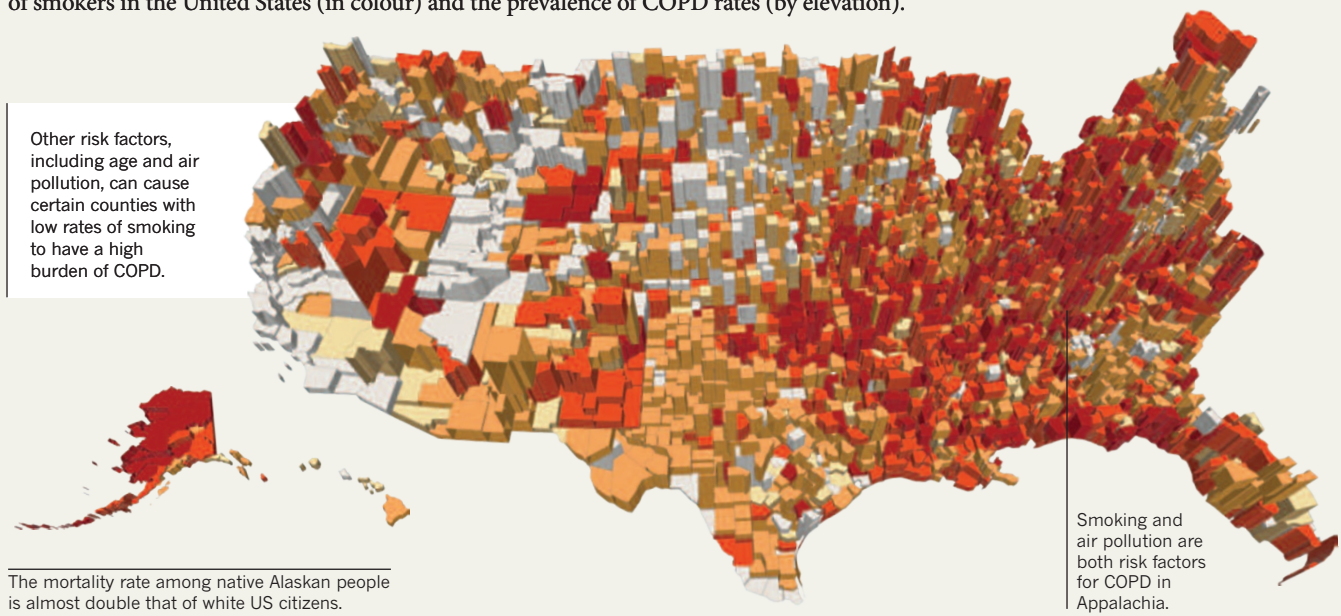
Of the ten most common causes of death in the United States, COPD is the only one with an increasing death rate.



The rise was fuelled partly by a sharp increase of COPD among women, who in 2000 became more likely than men to die of the disease owing to several trends including more women smoking at a younger age and doctors' increasing awareness of the syndrome.

SMOKE SCREEN

Tobacco smoking is the primary risk factor for COPD in industrialized countries. This map shows the prevalence of smokers in the United States (in colour) and the prevalence of COPD rates (by elevation).



The mortality rate among native Alaskan people is almost double that of white US citizens.

Smoking rates



COPD rates

Counties are elevated by COPD prevalence

Data for 'A disease on the rise' came from the American Lung Association. Data for the map came from the American Lung Association and the CDC's Behavioural Risk Factor Surveillance System. Map illustrated by Chris Wilson.