The Problem With Stories About Dangerous Coronavirus Mutations

Ed Yong

There's no clear evidence that the pandemic virus has evolved into significantly different forms—and there probably won't be for months.

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Editor's Note: *The Atlantic* is making vital coverage of the coronavirus available to all readers. Find the collection here.

As if the pandemic weren't bad enough, on April 30, a team led by scientists at Los Alamos National Laboratory released a paper that purportedly described "the emergence of a more transmissible form" of the new coronavirus, SARS-CoV-2. This new form, the team wrote, "began spreading in Europe in early February." Whenever it appeared in a new place, including the U.S., it rapidly rose to dominance. Its success, the team suggested, is likely due to a single mutation, which is now "of urgent concern."

The paper has not yet been formally published or reviewed by other scientists. But on May 5, the *Los Angeles Times* wrote about it, claiming that "a now-dominant strain of the coronavirus could be more contagious than [the] original." That story quickly went … well … viral.

But "the conclusions are overblown," says Lisa Gralinski of the University of North Carolina, who is one of the few scientists in the world who specializes in coronaviruses. "To say that you've revealed the emergence of a more transmissible form of SARS-CoV-2 without ever actually testing it isn't the type of thing that makes me feel comfortable as a scientist." She and other virologists I've spoken with who were not involved in the Los Alamos research agree that the paper's claims are plausible, but not justified by the evidence it presents. More important, they're not convinced different strains of the coronavirus exist at all.

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"We have evidence for one strain," says Brian Wasik at Cornell University.

"I would say there's just one," says Nathan Grubaugh at Yale School of Medicine.

“I think the majority of people studying [coronavirus genetics] wouldn’t recognize more than one strain right now,” says Charlotte Houldcroft at the University of Cambridge.

Everyone else might be reasonably puzzled, given that news stories have repeatedly claimed there are two, or three, or even eight strains. This is yet another case of confusion in a crisis that seems riddled with them. Here’s how to make sense of it.

Whenever a virus infects a host, it makes new copies of itself, and it starts by duplicating its genes. But this process is sloppy, and the duplicates end up with errors. These are called mutations—they’re the genetic equivalent of typos. In comic books and other science fiction, mutations are always dramatic and consequential. In the real world, they’re a normal and usually mundane part of virology. Viruses naturally and gradually accumulate mutations as they spread.

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As an epidemic progresses, the virus family tree grows new branches and twigs—new lineages that are characterized by differing sets of mutations. But a new lineage doesn’t automatically count as a new strain. That term is usually reserved for a lineage that differs from its fellow viruses in significant ways. It might vary in how easily it spreads (transmissibility), its ability to cause disease (virulence), whether it is recognized by the immune system in the same way (antigenicity), or how vulnerable it is to medications (resistance). Some mutations affect these properties. Most do not, and are either silent or cosmetic. “Not every mutation creates a different strain,” says Grubaugh. (Think about dog breeds as equivalents of strains: A corgi is clearly different from a Great Dane, but a black-haired corgi is functionally the same as a brown-haired one, and wouldn’t count as a separate breed.)

There’s no clear, fixed threshold for when a lineage suddenly counts as a strain. But the term has the same connotation in virology as it does colloquially—it implies importance. Viruses change all the time; strains arise when they change in meaningful ways.

New strains of influenza arise every year. These viruses quickly acquire mutations that change the shape of the proteins on their surface, making them invisible to the same immune cells that would have recognized and attacked their ancestors. These are clearly meaningful changes—and they're partly why the flu vaccine must be updated every year.

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But influenza is notable for mutating quickly. Coronaviruses—which, to be clear, belong to a completely separate family from influenza viruses—change at a tenth of the speed. The new one, SARS-CoV-2, is no exception. “There’s nothing out of the ordinary here,” says Grubaugh. Yes, the virus has picked up several mutations since it first jumped into humans in late 2019, but no more than scientists would have predicted. Yes, its family tree has branched into different lineages, but none seems materially different from the others. “This is still such a young epidemic that, given the slow mutation rate, it would be a surprise if we saw anything this soon,” Houldcroft says.

What of the Los Alamos study, then? The team, led by Bette Korber, looked at mutations that affect the virus’s “spike”—the protein on its surface that it uses to recognize host cells. One particular mutation, known as D614G, caught their attention. It changes just one of the many

molecules that make up the spike, subtly altering the protein's shape. The viruses without this mutation—the D lineage—include the one that first emerged in Wuhan, China. The viruses with the mutation—the G lineage—appeared sometime in February. Worldwide, the G's were relatively uncommon in early March, but by April, they had become dominant in much of Europe, North America, and Australia.

But this pattern is hard to interpret. The D614G mutation might make the coronavirus more transmissible, and G-viruses might have become more common because they outcompeted the D-viruses. But it's also possible that the mutation might do nothing, and G-viruses have become more common because of dumb luck.

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If those viruses happened to be in the right people—those who traveled from China to Italy before the latter went into lockdown—they could easily have spread explosively across Europe, and eventually into the U.S. Indeed, that's the pattern we see: The D614G mutation first appeared just before the coronavirus moved into Europe, and almost all the G-viruses around today are descendants of that initial continent-hopping pioneer. China's intense social restrictions likely stamped out many other coronavirus lineages within its borders, and stopped them from spreading further. "The only lineages you'll see are those that got out, which include the ones with this mutation," says Bill Hanage of Harvard, who studies pathogen evolution.

Such events are especially important in the early stages of a pandemic. Some virus lineages will do really well and others will disappear for reasons that have nothing to do with the viruses themselves and everything to do with the movements of their human hosts, whom those hosts interact with, and the policies enacted by the countries those hosts live in.

This isn't to say that the Los Alamos study is bad or wrong—it comes from a respected team and presents interesting data. But the evidence it provides cannot distinguish between two equally plausible explanations—that the G-viruses were more transmissible, or that the G-viruses were just lucky. (Korber didn't respond to a request for an interview.)

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More definitive evidence could take two forms. First, scientists could compare the spread of the epidemic among groups of people who were infected by the D- and G-viruses. But "that's a very difficult study to design," Houldcroft says. You'd need to ensure that the two groups were closely matched, so that any differences between them were actually due to the virus. You'd need both reliable clinical data and viral sequences from each person. And you'd need to look at a lot of people—and viruses—to be confident the results weren't statistical flukes. "I wouldn't put much weight on studies that had fewer than thousands of viral genomes, or tens of thousands," Houldcroft says. "And we won't have those kinds of samples collected and analyzed for several months yet."

Second, scientists could compare the two types of viruses in experiments with lab-grown cells or lab-reared animals. Do the G-viruses stick to cells more readily, or grow more quickly, or spread more easily? Such studies aren't easy, and results would likely take months to arrive. Even then, Grubaugh cautions, several labs would need to find the same results before virologists at large could be confident about them. Past epidemics illustrate why it pays to be careful. In 2016, two independent teams of scientists showed that during the West African

Ebola outbreak, that virus picked up a mutation called A82V, which made it better at infecting lab-grown human cells. Those teams had a stronger case than the Los Alamos team now does for SARS-CoV-2—but they still clarified that they didn't know whether the mutation influenced the course of the historic outbreak. Sure enough, later work revealed that the A82V mutation doesn't affect Ebola's ability to infect actual animals.

The bottom line: It will take time to know whether different strains of the new coronavirus even exist, let alone whether any are more or less dangerous than the others. Any claims of that kind should be taken with a grain of salt for the next several months, if not longer. "In the short term, it's highly unlikely that we'd be able to define new strains," Wasik says.

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The same goes for the studies from Singapore and Arizona showing that certain coronavirus lineages are missing sections of their genes that might (or might not) make them less dangerous. It goes for the much-discussed S and L groups. It goes for the so-called A, B, and C groups, two of which supposedly pummeled New York from opposite directions. (The study behind that claim was heavily criticized by experts for its methods and for using a backdoor route to publication.) "None of these has convinced me that they have a smoking gun for why one particular sequence of SARS-CoV-2 is more successful than any other," Houldcroft says.

Finding a smoking gun is not a priority right now, according to the experts I spoke with. Gralinski, for example, is focused on testing vaccines and drugs. She wouldn't start checking whether different mutations affect the virus's behavior until next year, "when the urgency has waned," she says. Grubaugh agrees: Studies of viral evolution are the backbone of his career, but he says they "wouldn't change the public-health picture." To control the coronavirus, countries need to test widely, isolate infected people, trace their contacts, and use social-distancing measures when other options fail. "Identifying a mutation that does something different doesn't really change our response," Grubaugh says. "It just creates a diversion from what we need to be focusing on."

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Last month, in an article about why the pandemic is so confusing, I wrote that "individual pieces of research are extremely unlikely to single-handedly upend what we know about COVID-19." But between our insatiable need for information to assuage our anxiety and uncertainty, the media's tendency to report uncritically on incremental studies, and social channels that amplify extreme voices over careful ones, it's no wonder that confusion reigns.

The misconceptions about dangerous strains are also seductive in their own right. If we believe that the virus has changed into some especially challenging form, we can more easily explain why certain people and places have been hit worse than others—a mystery whose answer more likely (but less satisfyingly) lies in political inaction, existing inequalities, and chance. Powerful antagonists make for easy narratives. Ineptitude, bias, and randomness make for difficult ones.

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