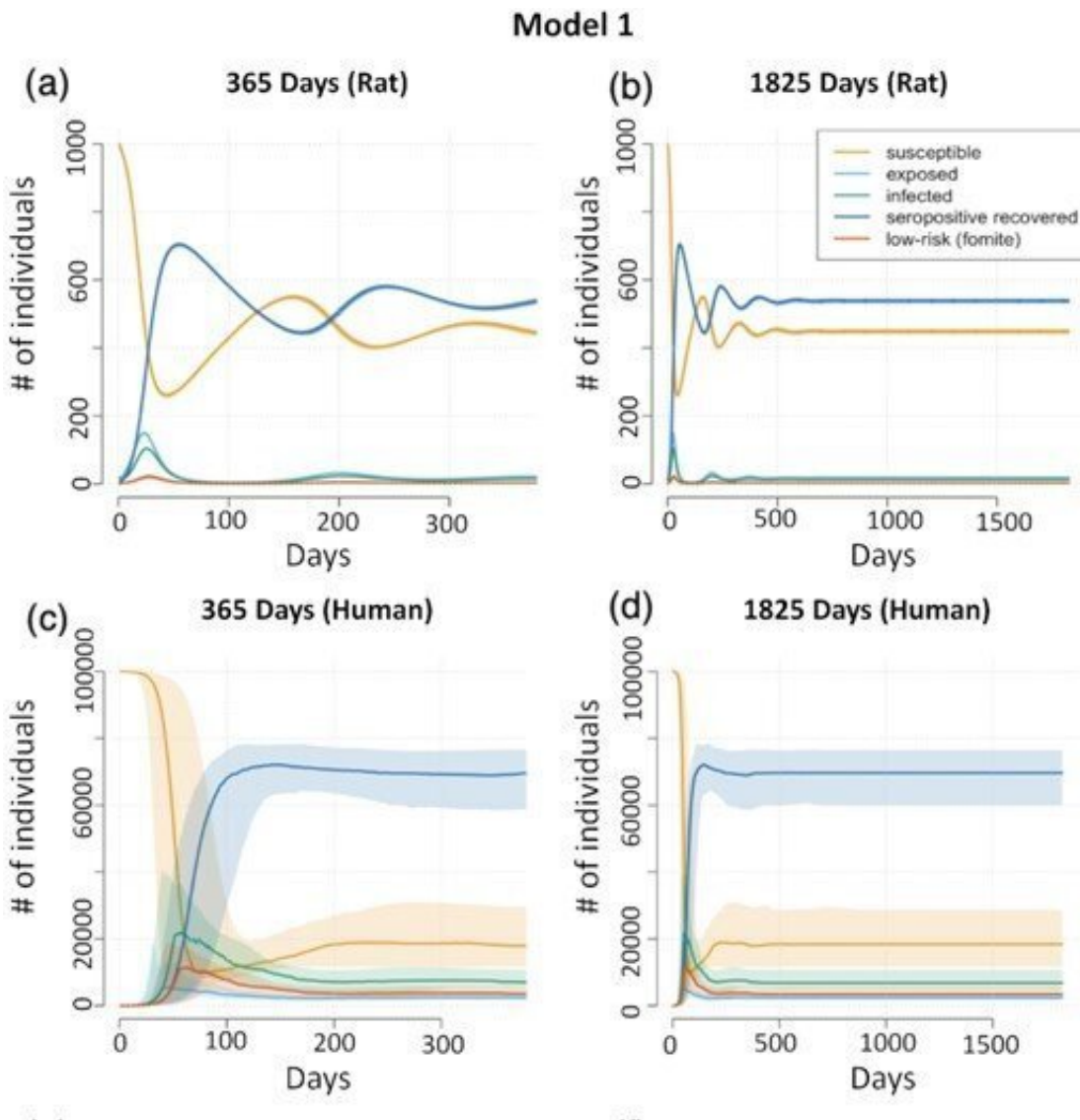


For COVID-19, endemic stage could be two years away

July 5 2022, By Mallory Locklear



SARS-CoV-2 Disease Compartment Curves for Model 1 with predominantly in vivo rat study estimates (a) and (b) and human-adapted estimates (c) and (d) accounting for the effects of successive variants and varying immunity (e) and

(f). (a) and (b): using predominantly rat data, iterated for 365 days (a) and for 1,825 days (b). The model stabilizes after approximately 724 days at an endemic state with approximately 41% of the population susceptible to reinfection. (c) and (d): using translational human estimates, iterated for 365 days (c) and for 1,825 days (d). Curves are the median at time t (25th and 75th percentile) to show the sensitivity of the curves to our set of chosen parameters. When an analysis of endemic stability across all parameter choices is performed, endemic stability is reached at a median of 1,119 days (IQR = 1017.75). (e) and (f): assessing an introduction of variants into our SARS-CoV-2 Disease Compartment Curves with human estimates and introducing increasingly transmissible variants at 180-day intervals. In (e), we model decreasing length of natural immune protection from reinfection, whereas in (f), immune protection is held constant. The compartments and associated curves are denoted in the legend and are defined as follows: susceptible (yellow; S), exposed (light blue; E), infected (green; I), seropositive recovered (dark blue; R^+), and low-risk/fomite (orange; L). Population size (closed with no births or deaths) is given as # of individuals on the Y-axis. Credit: *PNAS Nexus* (2022). DOI: 10.1093/pnasnexus/pgac096

Illnesses like the common cold and the flu have become endemic in human populations; everyone gets them every now and then, but for most people, they aren't especially harmful. COVID-19 will eventually transition to endemic status at some point—but when?

Possibly within two years, according to a new Yale study published July 5 in the journal *PNAS Nexus*.

To develop a better understanding of when and how COVID-19 might become endemic, Yale researchers turned to rats, which, like us, are also susceptible to coronaviruses. By collecting data on coronaviral reinfection rates among rats, they were able to model the potential trajectory of COVID-19.

There are many different types of coronaviruses, including SARS-CoV-2—the virus behind COVID-19—and several that cause the common cold. Animals like pigs and chickens live with endemic coronaviruses, too, and a key factor identified in the spread of animal and human coronaviruses alike is their tendency to evoke what's known as non-sterilizing immunity.

"It means that initially there is fairly good immunity, but relatively quickly that wanes," said Caroline Zeiss, a professor of comparative medicine at Yale School of Medicine and senior author of the study. "And so even if an animal or a person has been vaccinated or infected, they will likely become susceptible again."

Over the past two years, scientists have come to see that SARS-CoV-2 yields non-sterilizing immunity; people who have been infected or vaccinated are still at risk of reinfection. So experts expect that the virus won't go away any time soon.

To better understand what SARS-CoV-2 might do over time, scientists have used mathematical models. And given the strong similarities between animal and human coronaviruses, collecting [relevant data](#) from animals presents an opportunity to better understand SARS-CoV-2, says Zeiss.

"There are many lessons to be learned from animal coronaviruses," she said.

In this study, Zeiss and her colleagues observed how a coronavirus similar to one that causes the common cold in humans was transmitted through rat populations. The team modeled the exposure scenario to resemble human exposures in the United States, where a portion of the population is vaccinated against COVID-19 and where people continue to face natural exposure to SARS-CoV-2. They also reproduced the

different types of exposure experienced by people in the U.S., with some animals exposed through close contact with an infected rat (high risk of infection) and others exposed by being placed in a cage once inhabited by an infected rat (low risk of infection).

Infected animals contracted an upper respiratory tract infection and then recovered. After three to four months, the rats were then reorganized and re-exposed to the virus. The rates of reinfection showed that natural exposure yielded a mix of immunity levels, with those exposed to more virus through close contact having stronger immunity, and those placed in a contaminated cage (and therefore exposed to lower amounts of the virus) having higher rates of reinfection.

The takeaway, Zeiss says, is that with natural infection, some individuals will develop better immunity than others. People also need vaccination, which is offered through a set dose and generates predictable immunity. But with both vaccination and natural exposure, the population accumulates broad immunity that pushes the virus toward endemic stability, the study showed.

She and her team then used this data to inform mathematical models, finding that the median time it could take for SARS-CoV-2 to become endemic in the United States is 1,437 days, or just under four years from the start of the pandemic in March 2020.

In this scenario, according to the model, 15.4% of the population would be susceptible to infection at any given time after it reaches endemic phase.

"The virus is constantly going to be circulating," said Zeiss. So it will be important to keep more vulnerable groups in mind. "We can't assume that once we reach the endemic state that everybody is safe."

Four years is the median time predicted by the model, she said, so it could take even longer to reach the endemic stage. And this doesn't take into account mutations that could make SARS-CoV-2 more harmful.

"Coronaviruses are very unpredictable, so there could be a mutation that makes it more pathogenic," said Zeiss. "The more likely scenario, though, is that we see an increase in transmissibility and probable decrease in pathogenicity." That means the virus would be easily transmitted between people but less likely to cause severe illness, much like the common cold.

There is precedent for this trajectory. In the late 1800s, what was known as the "Russian flu" killed approximately one million people around the world. Researchers now think the virus behind that pandemic was a coronavirus that originated in cattle and eventually evolved into one of the common cold viruses still in circulation. Reduced pathogenicity associated with the transition from epidemic to endemic status has also been observed in pig coronaviruses. And almost all commercial chicken flocks across the globe are vaccinated for an endemic respiratory coronavirus that has been present since the 1930s.

Longstanding experience with coronaviral infections in other animals can help us navigate a pathway to living with SARS-CoV-2.

However, endemic stability in the United States also depends on what happens to the [virus](#) elsewhere.

"We are one global community," Zeiss said. "We don't know where else these mutations are going to arise. Until we reach endemic stability around the entire globe, we are vulnerable here to having our U.S. endemic stability disrupted by introduction of a new variant.

"But I think overall the picture's hopeful. I think we will be in endemic

stability within the next year or two."

More information: Sarah Mullin et al, Modeling pandemic to endemic patterns of SARS-CoV-2 transmission using parameters estimated from animal model data, *PNAS Nexus* (2022). [DOI: 10.1093/pnasnexus/pgac096](https://doi.org/10.1093/pnasnexus/pgac096)

Provided by Yale University

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