Think you might have COVID? Wait two days to test

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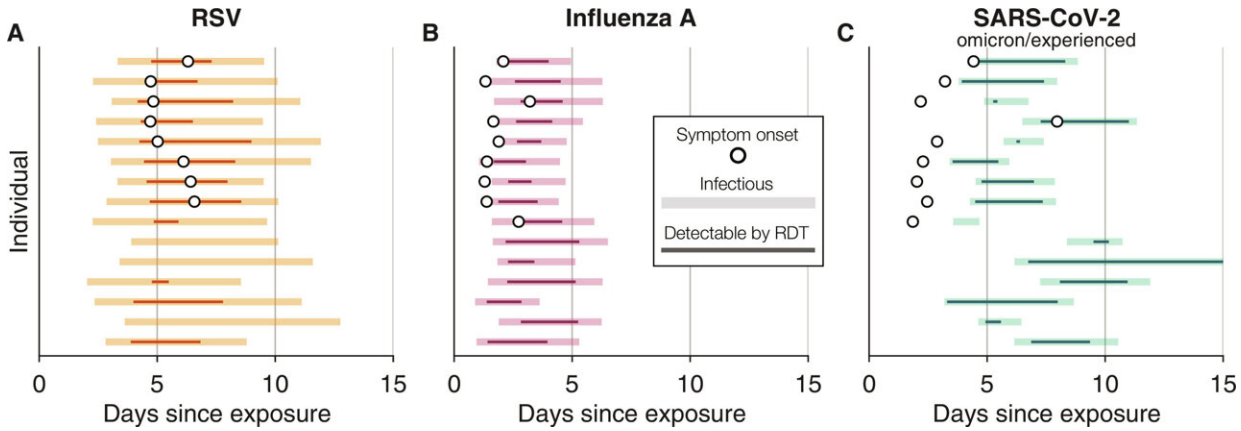

Relative timing of symptom onset, infectiousness, and detectability vary by pathogen and individual. Symptom onset time (open circles), infectious period (shaded rectangles), and window of detectability by an RDT (colored lines) are shown for 15 stochastic realizations of RSV [(A) orange], influenza A [(B) pink], and SARS-CoV-2 omicron/experienced [(C) green] infections. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.adk5108

Peek in medicine cabinets across the U.S. and you'll find stacks of leftover COVID tests.

When symptoms arise, so do questions: When should I test? How accurate is it really? And what should I do if I test positive?

In a paper published June 14 in the journal *Science Advances*, University of Colorado Boulder researchers unveil a new mathematical model to quickly answer such questions, not only for COVID but also for emerging rapid tests for Respiratory Syncytial Virus (RSV), the flu and other infectious diseases.

One key takeaway: Advice can differ widely depending on the bug.

"For COVID, we found that if you only have one test, it's best to wait two days after symptoms arise to use it, because the virus is unlikely to be detectable until then," said first author Casey Middleton, a Ph.D. student in the department of Computer Science and the IQ Bio program. "For flu and RSV, you're best off to take that rapid test when you first feel symptoms."

A new era of DIY testing

Middleton and senior author Daniel Larremore, a professor of computer science at the BioFrontiers Institute, developed the model to address several challenges that have emerged with the post-pandemic proliferation of rapid tests.

In recent years, companies have rolled out "all-in-one" tests that check for SARS-CoV-2 (the virus that causes COVID-19), influenza A and B, and RSV simultaneously, and some doctor's offices and pharmacies offer a combo, while-you-wait option.

Meanwhile, at-home COVID testing has become the norm, with people routinely self-collecting nasal swabs to protect friends and family.

"If you're trying to make a decision about whether to go to book club or go to Bingo night with the grandparents, testing is a really good idea," said Larremore, whose lab combines computer science, math,

epidemiology and biology to address public health challenges. "But COVID has changed, each variant behaves differently and that means the way that they interact with tests may be different."

When he and Middleton plugged information about omicron variants, patient behavior and other factors into their new computational model, it revealed that if a person with COVID tests immediately with a rapid test when symptoms emerge, they receive a false negative as much as 92% of the time.

Waiting two days after symptoms brings that rate down to 70%. For those who can afford to take a second test on day 3, the false negative rate dips lower, with the tests catching about a third of infections.

That's because, with most people already previously exposed, their immune systems are primed to react upon seeing COVID again, and that immune response itself causes symptoms. In addition, new variants in folks with some immunity grow slightly more slowly than the original strain.

"Our symptoms are happening sooner, but it takes longer to reach enough virus in your body for it to be detectable," said Middleton.

With RSV and flu, on the other hand, the virus multiplies so quickly that once symptoms set in, there's already plenty to make a test show up positive.

"This is the conundrum," said Larremore. "If you go in right away and test for all three, you can learn a lot from the flu and RSV tests, but you may have swung too early for COVID. If you wait a few days, the timing might be right to catch COVID but you are too late for flu and RSV."

While a 66% false negative rate may seem high for a COVID test,

Larremore notes that the tests are designed to identify folks who have a high viral load and are, thus, most likely to infect others.

"Diagnosing only one third of infections can still cut transmission substantially if we've diagnosed the most infectious third," he said.

Rethinking isolation policies

Assuming that enough at-home tests are available, their study also suggests that a "test to exit" strategy—in which people test again before determining whether to return to work and socialize—can prevent more COVID infections with less inconvenience than the five-day isolation policy that was standard Centers for Disease Control advice until March.

"The five-day isolation policy made people isolate for too long in most cases," said Middleton. "Test-to-exit does a good job releasing people early who aren't going to transmit but holding those who still have high amounts of virus."

Larremore's previous research was instrumental in informing how COVID-19 vaccines were distributed early in the pandemic and for helping to convince policymakers to prioritize rapid testing.

He and Middleton hope that their new model can help companies develop better tests, help clinicians give better advice and, should another pandemic arise, enable policy-makers to offer swift, data-driven guidance on testing.

"If done correctly, the next generation of rapid tests have the potential to be really impactful," Larremore said.

More information: Casey Middleton et al, Modeling the transmission mitigation impact of testing for infectious diseases, *Science Advances*

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