## Over Half of COVID Transmission May Occur via Asymptomatic People

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As COVID-19 cases surge and vaccinations lag, health authorities continue to seek additional ways to mitigate the spread of the novel coronavirus.

Now, a modeling study estimates that more than half of transmissions come from pre-, never-, and asymptomatic individuals, indicating that symptom-based screening will have little effect on spread.

The US Centers for Disease Control and Prevention (CDC) study, published online today in *JAMA Network Open*, concludes that for optimal control, protective measures such as masking and social distancing should be supplemented with strategic testing of potentially exposed but asymptomatic individuals.

"In the absence of effective and widespread use of therapeutics or vaccines that can shorten or eliminate infectivity, successful control of SARS-CoV-2 cannot rely solely on identifying and isolating symptomatic cases; even if implemented effectively, this strategy would be insufficient," CDC biologist Michael J. Johansson, PhD, and colleagues warn. "Multiple measures that effectively address transmission risk in the absence of symptoms are imperative to control SARS-CoV-2."

According to the authors, the effectiveness of some current transmission prevention efforts has been disputed and subject to mixed messaging. Therefore, they decided to model the proportion of COVID-19 infections that are likely the result of individuals who show no symptoms and may be unknowingly infecting others.



Dr. Jay Butler

"Unfortunately, there continues to be some skepticism about the value of community-wide mitigation efforts for preventing transmission such as masking, distancing, and hand hygiene, particularly for people without symptoms," corresponding author Jay C. Butler, MD, told *Medscape Medical News*. "So we wanted to have a base assumption about how much transmission occurs from asymptomatic people to underscore the importance of mitigation measures and of creating immunity through vaccine delivery."

Such a yardstick is especially germane in the context of the new, more transmissible variant. "It really puts [things] in a bigger box and underscores, boldfaces, and italicizes the need to change people's behaviors and the importance of mitigation," Butler said. It also highlights the advisability of targeted strategic testing in congregate settings, schools, and universities, which is already underway.

## The Analysis

Based on data from several COVID-19 studies from last year, the CDC's analytical model assumes at baseline that infectiousness peaks at the median point of symptom onset, and that 30% of infected individuals never develop symptoms but are nevertheless 75% as infectious as those who develop overt symptoms.

The investigators then model multiple scenarios of transmission based pre- and never-symptomatic individuals, assuming different incubation and infectious periods, and varying numbers of days from point of infection to symptom onset.

When combined, the models predicts that 59% of all transmission would come from asymptomatic transmission - 35% from presymptomatic individuals and 24% from never-symptomatic individuals.

The findings complement those of an earlier CDC analysis, according to the authors.

The overall proportion of transmission from presymptomatic and never-symptomatic individuals is key to identifying mitigation measures that may be able to control SARS-CoV-2, the authors state.

For example, they explain, if the infection reproduction number (R) in a particular setting is 2.0, a reduction in transmission of at least 50% is needed in order to reduce R to below 1.0. "Given that in some settings R is likely much greater than 2 and more than half of transmissions may come from individuals who are asymptomatic at the time of transmission, effective control must mitigate transmission risk from people without symptoms," they write.

The authors acknowledge that the study applies a simplistic model to a complex and evolving phenomenon, and that the exact proportions of presymptomatic and never-symptomatic transmission and the incubation periods are not known. They also note symptoms and transmissions appear to vary across different population groups, with older individuals more likely than younger persons to experience symptoms, according to previous studies.

## "Assume That Everyone Is Potentially Infected"

Other experts agree that expanded testing of asymptomatic individuals is important. "Screening for fever and isolation of symptomatic individuals is a common-sense approach to help prevent spread, but these measures are by no means adequate since it's been clearly documented that individuals who are either asymptomatic or pre-symptomatic can still spread the virus," said Brett Williams, MD, an infectious disease specialist and assistant professor of medicine at Rush University in Chicago, Illinois.

"As we saw with the White House Rose Garden superspreader outbreak, testing does not reliably exclude infection either because the tested individual has not yet become positive or the test is falsely negative," Williams, who was not involved in the CDC study, told *Medscape Medical News*. He further noted that when prevalence is as high as it currently is in the United States, the rate of false negatives will be high because a large proportion of those screened will be unknowingly infected.

At his center, all visitors and staff are screened with a temperature probe on entry, and since the earliest days of the pandemic, universal masking has been required. "Nationally there have been many instances of hospital breakroom outbreaks because of staff eating lunch together, and these outbreaks also demonstrate the incompleteness of symptomatic isolation," Williams said.



Dr. Frank Esper

For his part, virologist Frank Esper, MD, a pediatric infectious disease specialist at the Cleveland Clinic in Cleveland, Ohio, said that while it's been understood for some time that many infected people will not exhibit symptoms, "the question that remains is just how infectious are they?"

Esper's takeaway from the modeling study is not so much that we need more screening of possibly exposed but asymptomatic people, but rather testing symptomatic people and tracing their contacts is not enough.

"We need to continue to assume that everyone is potentially infected whether they know it or not. And even though we have ramped up our testing to a much greater capacity than in the first wave, we need to continue to wear masks and socially distance because just identifying people who are sick and isolating or quarantining them is not going to be enough to contain the pandemic."

And although assumption-based modeling is helpful, it cannot tell us "how many asymptomatic people are actually infected," said Esper, who was not involved in the CDC study.

Esper also points out that the study estimates are based on data from early Chinese studies, but the virus has since changed. The new, more transmissible strain in the United States and elsewhere may involve not only more infections but also a longer

presymptomatic stage. "So the CDC study may actually undershoot asymptomatic infections," he said.

He also agreed with the authors that when it comes to infection, not all humans are equal. "Older people tend to be more symptomatic and become symptomatic more quickly so the asymptomatic rate is not the same across board from young people age 20 to older people."

The bottom line, said David. A. Hirschwerk, MD, an infectious disease specialist at Northwell Health in Manhasset, New York, is that these data support the maintenance of protective measures we've been taking over the past months. "They support the concept that asymptomatic people are a significant source of transmission and that we need to adhere to mask wearing and social distancing, particularly indoors," Hirschwerk, who was not involved in the analysis, told *Medscape Medical News*. "More testing would be better but it has to be fast and it has to be efficient, and there are a lot of challenges to overcome."

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