Study from Chinese city of Guangzhou provides key insights on how COVID-19 spreads in households

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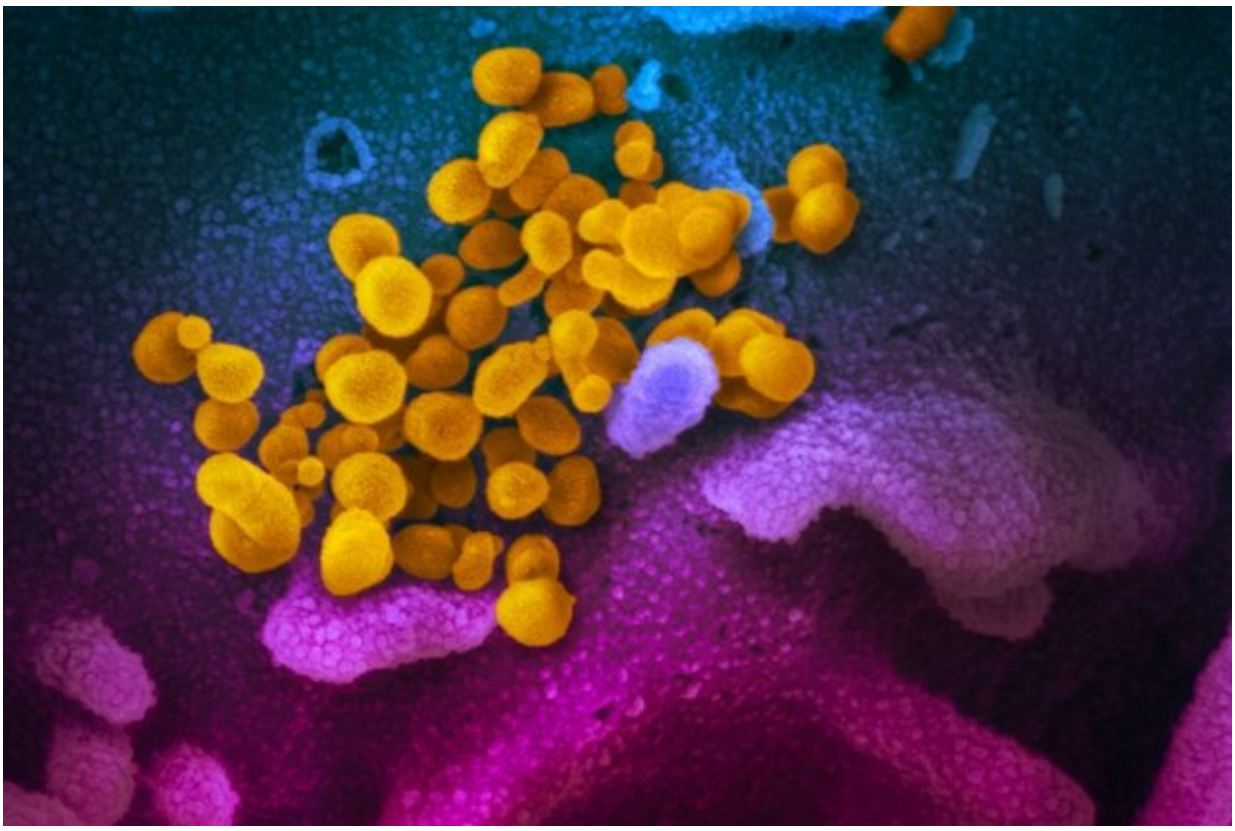

This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient, emerging from the surface of cells (blue/pink) cultured in the lab. Credit: NIAID-RML

New modelling research, published in *The Lancet Infectious Diseases* journal, suggests the coronavirus (SARS-CoV-2) that causes COVID-19 may spread more easily among people living together and family members than severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS). The estimates are the first of their kind to quantify symptomless transmission.

The analysis, based on contact tracing data from 349 people with COVID-19 and 1,964 of their close contacts in Guangzhou (the most populated city in southern China), found people with COVID-19 were at least as infectious before they developed symptoms as during their actual illness, and that older people (aged 60 years or more) were most susceptible to household infection with SARS-CoV-2.

The study of people living together and family members (not living at the same address), and non-household contacts (eg, friends, co-workers, passengers) suggests that breaking the chain of transmission within households through timely tracing and quarantine of close contacts, in addition to case finding and isolation, could have a huge impact on reducing the number of COVID-19 cases.

While the model has been updated to reflect the current knowledge about the transmission dynamics of COVID-19, the authors caution that it is based on a series of assumptions, for example about the length of incubation and how long symptomatic cases are infectious, that are yet to be confirmed, and might affect the accuracy of the estimates.

"Our analyses suggest that the infectiousness of individuals with COVID-19 before they have symptoms is high and could substantially increase the difficulty of curbing the ongoing pandemic", says Dr. Yang Yang from the University of Florida in the USA who co-led the research. "Active case finding and isolation in conjunction with comprehensive contact tracing and quarantine will be key to preventing

infected contacts from spreading the virus during their incubation periods, which will be crucial when easing lockdown restrictions on movement and mixing."

Household transmission of COVID-19 is suspected to have contributed substantially to the rise in cases in China following the introduction of lockdown measures. But little research has assessed the spread of disease at the household level. Previous estimates of household infections are specific to the setting where the data were obtained, and represent the proportion of infections among all traced contacts, which does not fully account for the difference in individual exposure history, or the fact that infections may not necessarily be secondary, and could be tertiary—ie, the possibility of transmission among contacts themselves, or infection risks from objects such as clothes, utensils, and furniture.

In the study, researchers developed a transmission model that accounted for individual-level exposure, tertiary transmission, potential exposure to untraced infection sources, and asymptomatic infections. Using data gathered by the Guangzhou Center for Disease Control and Prevention (CDC) on 215 primary COVID-19 cases (ie, with no known source of exposure, or assumed to have been infected outside Guangzhou), 134 secondary/tertiary cases, and 1,964 of their close contacts between January 7 and February 18, 2020, the study estimated the secondary attack rate (the probability that an infected person transmits the disease to a susceptible individual) among people living together and family members, and non-household contacts. Close contacts—unprotected individuals who had been within a metre of a person with COVID-19 less than 2 days before their symptoms developed—were traced, quarantined, and tested for SARS-CoV-2 on days 1 and 14.

The study also modelled the effects of age and sex on the infectivity of COVID-19 cases and susceptibility of their close contacts. For the primary results, researchers assumed an average incubation period of 5

days and a maximum infectious period of 13 days (including up to 5 days before illness onset). Among the 349 laboratory-confirmed primary and secondary COVID-19 cases, 19 (5%) reported no symptoms during the follow-up period.

The analyses estimated that the likelihood of secondary transmission—spread from an infected person to non-household contacts—was 2.4%. The likelihood of passing on the virus was higher among people living together and family members, with an attack rate of 17.1% (or around 1 in 6) among people living at the same address, and 12.4% (about 1 in 8) among family members.

"Family members such as parents and older children may not be living at the same address, which might explain why they appear at less risk of secondary infections than those living in the same household as the COVID-19 case", says co-author Dr. Natalie Dean from the University of Florida, USA. "While the likelihood of transmitting COVID-19 in households may seem quite low, it is around twice what has been estimated for SARS (4.6-8%) and three times higher than for MERS (4-5%), although these data are only based on a small number of studies."

The model also suggests that the likelihood of household infection is highest among older adults aged 60 or more (attack rate of 28% or around 1 in 4 of those living together, 18.4% or about 1 in 5 family members), and lowest in those aged 20 years or younger (attack rate 6.4% or around 1 in 15 of those living together, 5.2% or about 1 in 20 family members).

The estimates also suggest substantial infectivity during the incubation period, comparable to, and potentially higher than, during the illness period. After one day of exposure (daily infection probability), family members were 39% less likely (OR 0.61) to become infected after

symptoms emerged than during the incubation period, while those living together had 41% lower odds (OR 0.59)—although the difference was not statistically significant (table 3). There was no difference in the risk of infection between the sexes.

The researchers also calculated that the local reproductive number (the average number of infections a COVID-19 case can generate during the entire infectious period via both people living together and family members, and non-household contacts) was 0.5. However, had isolation of cases or quarantine of their contacts not been implemented the estimated local reproductive number would have been 20-50% higher, increasing to 0.6-0.76. If the reproductive number remains less than one, infection is not able to spread effectively.

"The relatively low reproductive number in the absence of case isolation reflects the small average number of contacts per person per day, which is probably partly due to the stringent control measures in Guangzhou during the study", explains co-author Dr. Qin-Long Jing from Guangzhou CDC, China. "Although the effect of case isolation seems moderate, the high infectivity of the virus during the incubation period suggests quarantine of asymptomatic contacts could have prevented more onward transmissions."

The authors note some important limitations, including that they were unable to reliably quantify the infectivity of asymptomatic infections, since only two of 15 asymptomatic cases included in the analyses were considered primary cases, and some asymptomatic infections may have been missed as close contacts were only tested twice, and the tests were done 14 days apart. Furthermore, the model assumed that asymptomatic infections have the same infectivity as symptomatic cases during their incubation period, which might not be accurate. The authors also note that some imported primary cases might have been infected locally, and that some asymptomatic infections or cases might have been missed by

contact tracing or by false negative tests, which could underestimate the secondary attack rate. Finally, the rapid isolation of cases and quarantine of their close contacts might have limited the number of transmissions when the cases were ill and affected the accuracy of the estimates.

Writing in a linked Comment, Dr. Virginia Pitzer (who was not involved in the study) from Yale School of Public Health, says, "The key difference between SARS-CoV-2 and SARS-CoV is that the probability of transmission is substantially higher during the presymptomatic incubation period for SARS-CoV-2, whereas little to no transmission occurred prior to the onset of symptoms for SARS-CoV. This made SARS-CoV much easier to control through case isolation and quarantine of contacts. Notably, the authors estimate that prompt case isolation was only able to prevent 20-50% of secondary cases of COVID-19 in Guangzhou."

She concludes, "This study demonstrates the value of carefully collected contact tracing data to understand risk factors for transmission and susceptibility. The findings confirm the relative importance of pre-symptomatic transmission and the relationship between older age and susceptibility, key insights which should inform design of intervention strategies."

More information: Qin-Long Jing et al, Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study, *The Lancet Infectious Diseases* (2020). DOI: 10.1016/S1473-3099(20)30471-0

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