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alveolar macrophages. Notably, these virions were not detected in the endothelial cells in this study, conflicting with the aforementioned mechanism of SARS-CoV-2 dissemination via infected pulmonary epithelium and endothelium. Also noteworthy is that co-infection with secondary microorganisms was uncommon in this series, possibly because of the rapidity with which death can occur in cases of COVID-19.

Despite the limitations inherent to retrospective descriptive studies, Carsana and colleagues¹⁰ provide valuable information, corroborating clinical observations of coagulopathy, which could have implications on viable treatment strategies. Carsana and colleagues' work to provide these valuable findings amid the ongoing crisis should be lauded.

We declare no competing interests.

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Household studies provide key insights on the transmission of, and susceptibility to, SARS-CoV-2



Studies of household members and close contacts of individuals infected with a communicable disease such as COVID-19 are a key source of information for infectious disease epidemiologists. Exposure to an infectious individual is the most important risk factor for communicable diseases. In household studies, only individuals who have been exposed are included, allowing for careful examination of other individual-level risk factors and quantification of transmission probabilities. The study by Qin-Long Jing and colleagues¹ published in *The Lancet Infectious Diseases* provides important insights into factors affecting transmission from COVID-19 primary cases and susceptibility of their close contacts.

The considerable contact tracing effort undertaken in Guangzhou, China, by the Guangzhou Center for Disease Control and Prevention, enabled the comprehensive analysis by Jing and colleagues. Surveillance has shown that older individuals (aged ≥ 60 years) are disproportionately represented among diagnosed

COVID-19 cases.² However, this observation might reflect the fact that older individuals are more likely to be infected or that they have greater severity of symptoms than younger individuals, making these individuals more likely to be diagnosed. In this retrospective cohort study, the close contacts of primary cases (all ages) were identified and quarantined, with nasal swabs collected on days 1 and 14 for RT-PCR testing.¹ Thus, typical biases associated with which individuals are exposed and which are tested were minimised. Compared with the oldest age group (≥ 60 years), the risk of household infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was lower among younger age groups (odds ratio [OR] 0.23 [95% CI 0.11–0.46] among individuals aged younger than 20 years; OR 0.64 [0.43–0.97] among individuals aged 20–59 years) and only 5% of contacts aged younger than 20 years were infected, which suggests that older age is associated with increased risk of infection conditional on exposure.¹



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Although household studies provide a unique opportunity to study transmission in a clearly identified cohort of close contacts, it is still possible that transmission events might have been missed. For example, individuals with an asymptomatic infection that resolved during the 2 weeks between follow-up tests would remain undetected. The proportion of identified infections among contacts that were asymptomatic was lower in this study (5%)¹ than estimates from other studies of SARS-CoV-2 (13–18%).^{3,4} Unidentified asymptomatic infections might affect the interpretation of the estimated secondary attack rate and could lead to underestimation of the secondary attack rate.

The secondary attack rate for SARS-CoV-2 has been estimated to be approximately twice as high as that of SARS-CoV,^{5,6} and comparable to that of influenza,⁷ although the estimated daily probability of transmission was similar to SARS-CoV. 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,^{1,8} whereas little to no transmission occurred before symptom onset for SARS-CoV.⁶ Thus, SARS-CoV was much easier to control through case isolation and quarantine of contacts.⁹ Jing and colleagues estimate that prompt case isolation only prevented 20–50% of secondary cases of COVID-19 in Guangzhou.¹

Stringent control measures were implemented in Guangzhou on Jan 23, 2020, soon after the epidemic was found to have spread from Wuhan. To determine how control measures affected the transmission of SARS-CoV-2 at the population level, Jing and colleagues estimated the effective reproductive number (R_t) as the mean number of contacts per case multiplied by the probability of transmission to those contacts on each day of the epidemic.¹ This approach differs from statistical methods typically used to estimate R_t from population-level data.¹⁰ The approach used by Jing and coauthors might underestimate R_t , even for the most permissive scenario (represented by the upper bounds of R_t), since they assume that all contacts have been identified and reported, and that all asymptomatic infections have been identified. These assumption seem unlikely to have been fully met, considering that more than 50% of all identified cases in Guangzhou were considered primary infections (ie, with no known

source of exposure, or were assumed to have been infected outside of Guangzhou) and the low proportion of asymptomatic infections.¹ Furthermore, this approach does not account for local primary cases (ie, primary cases who had not recently travelled to or resided in Hubei province), which have no identified source of exposure and accounted for 16% of all identified cases in Guangzhou.¹ Thus, these estimates might underestimate R_t and overstate the effectiveness of control measures imposed in Guangzhou.

Understanding of the factors that affect SARS-CoV-2 transmission has been rapidly evolving over the past few months. This study demonstrates the value of carefully collected contact tracing data to understand risk factors for transmission and susceptibility. The findings also confirm the relative importance of presymptomatic transmission, and the association between older age and susceptibility, key insights which should inform the design of intervention strategies.

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