Clinical Infectious Diseases

MAJOR ARTICLE

Assessing Asymptomatic, Presymptomatic, and Symptomatic Transmission Risk of Severe Acute Respiratory Syndrome Coronavirus 2

Peng Wu,[1,2,a] Fengfeng Liu,[3,a] Zhaorui Chang,[3,a] Yun Lin,[1] Minrui Ren,[3] Canjun Zheng,[3] Yu Li,[3] Zhibin Peng,[3] Yin Qin,[3] Jianxing Yu,[3] Mengjie Geng,[3] Xiaokun Yang,[3] Hongting Zhao,[3] Zhili Li,[3] Sheng Zhou,[3] Lu Ran,[3] Benjamin J. Cowling,[1,2] Shengjie Lai,[4] Qiulan Chen,[3] Liping Wang,[3] Tim K. Tsang,[1,b] and Zhongjie Li[3,b]

[1]World Health Organization Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China; [2]Laboratory of Data Discovery for Health Limited, Hong Kong Science Park, New Territories, Hong Kong Special Administrative Region, China; [3]Division of Infectious Disease, Key Laboratory of Surveillance and Early Warning on Infectious Disease, Chinese Center for Disease Control and Prevention, Beijing, China; and [4]WorldPop, School of Geography and Environmental Science, University of Southampton, Southampton, United Kingdom

Background. The relative contributions of asymptomatic, presymptomatic, and symptomatic transmission of severe acute respiratory syndrome coronavirus 2 have not been clearly measured, although control measures may differ in response to the risk of spread posed by different types of cases.

Methods. We collected detailed information on transmission events and symptom status based on laboratory-confirmed patient data and contact tracing data from 4 provinces and 1 municipality in China. We estimated the variation in risk of transmission over time and the severity of secondary infections by symptomatic status of the infector.

Results. There were 393 symptomatic index cases with 3136 close contacts and 185 asymptomatic index cases with 1078 close contacts included in the study. The secondary attack rates among close contacts of symptomatic and asymptomatic index cases were 4.1% (128 of 3136) and 1.1% (12 of 1078), respectively, corresponding to a higher transmission risk from symptomatic cases than from asymptomatic cases (odds ratio, 3.79; 95% confidence interval, 2.06–6.95). Approximately 25% (32 of 128) and 50% (6 of 12) of the infected close contacts were asymptomatic from symptomatic and asymptomatic index cases, respectively, while more than one third (38%) of the infections in the close contacts of symptomatic cases were attributable to exposure to the index cases before symptom onset.

Conclusions. Asymptomatic and presymptomatic transmissions play an important role in spreading infection, although asymptomatic cases pose a lower risk of transmission than symptomatic cases. Early case detection and effective test-and-trace measures are important to reduce transmission.

Keywords. SARS-CoV-2; COVID-19; asymptomatic; presymptomatic; symptomatic.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused 167 million human cases of coronavirus disease 2019 (COVID-19) worldwide since the virus was first identified in December 2019. People infected with SARS-CoV-2 show a broad spectrum of clinical manifestations that range from severe pneumonia to mild acute upper respiratory symptoms; some infections remain asymptomatic [1]. With expansions in laboratory testing capacity, increasing numbers of asymptomatic infections and presymptomatic COVID-19 cases have been detected, in particular, from active monitoring of potentially exposed persons such as contacts of laboratory-confirmed cases or travelers returning from high-risk locations [2, 3]. Some individuals can be diagnosed with laboratory confirmation in the absence of symptoms or prior to the appearance of symptoms. The patterns in virus shedding observed in asymptomatic and presymptomatic cases imply the potential for these individuals to be contagious [4, 5]. In this study, we analyzed detailed contact tracing data to characterize the risk of transmission from symptomatic and asymptomatic individuals infected with SARS-CoV-2.

METHODS

Data Sources

We retrospectively collected information on laboratory-confirmed symptomatic and asymptomatic SARS-CoV-2 infections (index cases) and their close contacts from 4 provinces and 1 municipality in China, Hubei, Jiangsu, Zhejiang, Guangdong, and Chongqing, from 5 January 2020 through 7 April 2020. These data had been routinely collected since

Received 9 January 2021; editorial decision 22 March 2021; published online 27 March 2021.

[a]P. W., F. L., and Z. C. contributed equally to this work.

[b]T.K.T., and Z.L. contributed equally to this work.

Correspondence: Zhongjie Li, Division of Infectious disease, Key Laboratory of Surveillance and Early Warning on Infectious Disease, Chinese Center for Disease Control and Prevention, No. 155 Changbai Road, Changping District, Beijing, China 102206 (lizj@chinacdc.cn).

Clinical Infectious Diseases® 2021;73(6):e1314–20

DOI: 10.1093/cid/ciab271

COVID-19 was classified as a notifiable disease in China starting in early 2020. For each index case, we extracted information from the National Reporting System of Notifiable Infectious Diseases on age, sex, date of symptom onset (for symptomatic cases only), date of confirmation, number of close contacts, type of contact, and severity status (asymptomatic, mild, normal, severe, and critical). For all close contacts, we collected data on age, sex, start date and end date of contact with the index case, start date and end date of quarantine, presence or absence of symptoms during quarantine, onset date of symptoms (if any), date of specimen collection, laboratory test result for SARS-CoV-2, date of confirmation, and severity status. Severity status was determined by the patient's attending physician in the hospital following the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia published by the National Health Commission (1st–7th versions; Supplementary Materials).

Case Definitions

Symptomatic COVID-19 cases were laboratory-confirmed SARS-CoV-2 cases who developed symptoms at confirmation, following the definitions provided in the Guidelines in Diagnosis and Treatment of COVID-19 published by the National Health Commission, with 7 updated versions since mid-January 2020 [6]. Asymptomatic SARS-CoV-2 cases were patients who tested positive for SARS-CoV-2 without presenting any symptoms potentially related to COVID-19, such as fever, chills, dry cough, nasal congestion, loss of taste or smell, runny nose, sore throat, headache, tiredness, muscle pain, joint pain, shortness of breath, difficulty breathing, conjunctivitis, nausea, vomiting, diarrhea, or abdominal pain, and without lung infections indicated by a chest X ray throughout the course of infection. Following the guidelines for contact tracing, close contacts of symptomatic cases were individuals who had been exposed to a patient with confirmed SARS-CoV-2 infection without wearing proper personal protective equipment (including practicing optimal hand hygiene or wearing gloves and wearing surgical face masks and gowns) and/or stayed with the case in close proximity (<1 m) in a close/semiclose environment, such as a household, office, or elevator, which should have occurred within 2 days before the onset of the symptomatic case until when the symptomatic index case was isolated. Close contacts of asymptomatic SARS-CoV-2 cases were individuals who had a close contact (same definition as above) with the confirmed asymptomatic index case within 2 days before the asymptomatic case provided specimens to test for SARS-CoV-2 to the time when the index case was isolated (Supplementary Materials). The index case had a laboratory-confirmed infection with SARS-CoV-2 and was the first identified infection.

Inclusion and Exclusion Criteria

In our analysis, we included only index cases (both symptomatic and asymptomatic) and their close contacts based on inclusion and exclusion criteria.

Inclusion Criteria

The inclusion criteria were symptomatic index cases that were confirmed with reverse transcription polymerase chain reaction (RT-PCR) and reported on the date of symptom onset and the date of confirmation. Asymptomatic index cases were confirmed with RT-PCR and reported with the date of confirmation. A close contact had a solely possible source of infection being the index case identified. An identified close contact received RT-PCR tests for SARS-CoV-2 with oropharyngeal swabs provided during quarantine. The mode and time of the contact between the index case and the close contact can be clearly identified.

Exclusion Criteria

The exclusion criteria were close contacts that were potentially exposed to multiple confirmed cases (either symptomatic or asymptomatic). Close contacts had the last exposure to the index case 7 days earlier than the onset of the symptomatic index/confirmation of the asymptomatic index, as the potential risk of transmission from the index case to the close contact through the exposure was assumed to be extremely low.

Statistical Analyses

We described and compared the characteristics of symptomatic and asymptomatic index cases of SARS-CoV-2 infection. Secondary infections identified from close contacts of these index cases and the secondary attack rates were examined separately by type of index. Secondary infections were classified by place where the contact between the index case and the secondary cases would have occurred in order to investigate the potential transmission risk by setting of social mixing. We also examined the number of infections identified among all close contacts of symptomatic index cases and estimated the cumulative proportion of infected contacts against the date of symptom onset of the index to illustrate the risk of transmission of a symptomatic case over time. Factors possibly affecting the risk of infection among close contacts of the index cases were explored, including age, sex, type of contacts between the index case and the contact, the index case being symptomatic or not, and the geographic locations of the cases identified.

The data on the time of contact, time of laboratory confirmation, and time of symptom onset allowed us to explore the proportion of secondary cases generated from the close contacts of the symptomatic index case and to infer the possible risk of transmission over time considering the onset time of symptoms for symptomatic index cases. Information on transmission pairs with available onset dates was collated and used to infer the infectiousness profile of symptomatic SARS-CoV-2 infections following a similar method as published by He et al [7]. The observed serial interval distribution was used as a convolution between the infectiousness profile and the known incubation period distribution.

A gamma distribution was fitted to estimate the time-varying risk of infection, $\beta(t)$, allowing for an early occurrence of infectiousness being c days prior to symptom onset of the index case (presymptomatic transmission). Parameters of this gamma distribution were estimated using the maximum likelihood. With the estimated infectiousness profile and the information on transmission pairs associated with symptomatic index cases, we further examined the temporal probability of infection and the cumulative probability of infection per day during the exposure window in relation to the symptom onset of the index case using the proportional hazards model. The probability of presymptomatic transmission was therefore estimated as the cumulative probability of transmission from the symptomatic index case to their close contacts before index case onset, as ascertained by exposure and symptom onset dates. Sensitivity analyses were conducted to explore the impact of assumptions about the distribution of hazards before, on, and after onset applied in the model on the estimation of the infectiousness profile (Supplementary Materials).

We also examined the seriousness of infected close contacts of the symptomatic and asymptomatic index cases by classifying these secondary cases into the following categories: asymptomatic, mild, normal, severe, critical, and fatal based on the presentation during the clinical course and the final outcome of the infection episode. Definitions for asymptomatic, mild, normal, severe, and critical cases are provided in the Supplementary Materials. Severe secondary cases were defined as secondary cases with the clinical status being severe or critical. All statistical analyses were conducted in R, version 3.6.3 (R Development Core Team, 2020).

RESULTS

In this study, we obtained data on 578 index cases of COVID-19 and 4214 close contacts of these index cases to examine the occurrence of infections given their exposure to the index patient (Supplementary Figure 1). In total, 393 symptomatic index cases with 3136 close contacts and 185 asymptomatic index cases with 1078 close contacts were included in the analysis. The median age of the symptomatic index cases was similar to that of asymptomatic index patients (43 years vs 41 years), while there were more child and slightly fewer adult cases (45 years and older) in the asymptomatic index group than in the symptomatic index group (Supplementary Table 1).

The median age was 39 years and 37 years for the close contacts of symptomatic and asymptomatic index cases, respectively. A variety of types of contacts were reported, including living in the same household, sharing meals, having conversations, having healthcare contacts, and sharing transportation. More than one third of the contacts reported a household exposure in both the symptomatic and asymptomatic index groups, and contacts of asymptomatic index cases more frequently reported an exposure to an index case through conversation (25% vs 16%; Supplementary Table 2).

Overall, there were 140 infections identified from the 4214 contacts of both symptomatic and asymptomatic index cases. The proportion of infection was higher among the contacts exposed to symptomatic index cases (128 of 3136, 4.1%) compared with those exposed to asymptomatic index cases (12 of 1078, 1.1%; Table 1). Among the infections identified in the contacts, 75% (96 of 128) were symptomatic in the contacts who were exposed to a symptomatic index case compared with 50% (6 of 12) identified in the contacts of asymptomatic index cases. The proportions of infection among contacts were generally similar across the age and sex groups and geographical locations by type of index.

Among the symptomatic secondary cases in the contacts, all the symptomatic contacts of an asymptomatic index case (6 of 6) were classified as normal without cases being severe or fatal, while 12 of 96 infected symptomatic contacts of a symptomatic index case were fatal or severe (Supplementary Figure 2). In the regression model, we found that the risk of infection was substantially higher among contacts who were exposed to a symptomatic index case than those with exposure to an asymptomatic index case (odds ratio, 3.79; 95% confidence interval [CI], 2.06–6.95; Figure 1). In addition, it was shown that the contact's type of household or having a shared meal were also associated with a higher risk of infection from close contacts.

With the data on infections identified among the close contacts of symptomatic index cases, we found that no infections were identified among contacts with the latest date of exposure to the index case being 2 days before index case onset or earlier. Approximately 12% (15 of 128) of the infected contacts were exposed 1 day before symptom onset of the index case or earlier (Supplementary Table 3). Approximately 76% of the infected contacts had the last exposure to the index case within 7 days after index case onset or before the index's symptom onset, while 97% reported the last exposure being within 14 days after onset of the symptomatic index case.

Using the information on these 96 pairs of symptomatic index cases and their infected symptomatic contacts, we estimated the infectiousness profile (Supplementary Figure 3). As our estimate allowed for an early occurrence of infectiousness before onset, it was inferred that infectiousness started to increase from 7 days before the index case onset, while infectiousness peaked around the date of onset. Based on the estimated hazard of infection, the cumulative proportion of transmission by a certain day and the probability of infection on a certain day are shown in Figure 2. Approximately 38% (95% CI, 28%–49%) of the infections occurred before symptom onset of the index case, and the probability of transmission peaked at around the time of index case onset and dropped rapidly within 5–7 days after onset to a very low level.

Table 1. Characteristics of Infected Close Contacts of Symptomatic and Symptomatic Index Cases of Severe Acute Respiratory Syndrome Coronavirus 2 Identified in Hubei, Guangdong, Jiangsu, Zhejiang, and Chongqing in China

Characteristic	All Contacts (N = 4214)	*P* Value[a]	Contacts of Symptomatic Index Cases (N = 3136)	*P* Value[a]	Contacts of Asymptomatic Index Cases (N = 1078)	*P* Value[a]	*P* Value (Symptomatic vs Asymptomatic)
Infected close contacts	140/4214 (3.3 %)		128/3136 (4.1%)		12/1078 (1.1%)		<.01
Symptomatic[b]	102/140 (72.9%)		96/128 (75%)		6/12 (50%)		.09
Age, y		.21		.49		.15	
0–14	13/476 (2.7%)		13/348 (3.7%)		0/128 (0%)		.02
15–44	59/2059 (2.9%)		56/1510 (3.7%)		4/549 (0.7%)		<.01
45–64	49/1293 (3.8%)		42/970 (4.3%)		7/323 (2.2%)		.09
65+	19/415 (4.6%)		18/331 (5.4%)		1/84 (1.2%)		.14
Sex		.01		.06		.01	
Male	60/2274 (2.6%)		58/1682 (3.4%)		2/592 (0.3%)		<.01
Female	80/1940 (4.1%)		70/1454 (4.8%)		10/486 (2.1%)		.01
Symptoms[b]		<.01		<.01		<.01	
Present	102/169 (60.4%)		97/152 (63.8%)		5/17 (29.4%)		.01
Absent	38/4045 (0.9%)		31/2984 (1.0%)		7/1061 (0.7%)		.35
Region		.23		.04		.03	
Hubei	32/989 (3.2%)		30/585 (5.1%)		2/404 (0.5%)		<.01
Guangdong	34/1273 (2.7%)		32/946 (3.4%)		2/327 (0.6%)		<.01
Jiangsu	36/973 (3.7%)		33/861 (3.8%)		3/112 (2.7%)		.79
Zhejiang	16/304 (5.3%)		15/189 (7.9%)		1/115 (0.9%)		.01
Chongqing	22/675 (3.3%)		18/555 (3.2%)		4/120 (3.3%)		1
Type of contact		<.01		<.01		.04	
Household	104/1516 (6.9%)		96/1105 (8.7%)		8/411 (1.9%)		<.01
Shared meal	14/444 (3.2%)		11/395 (2.8%)		3/49 (6.1%)		.19
Medical reasons	1/209 (0.5%)		1/192 (0.5%)		0/17 (0%)		1
Shared transportation	1/397 (0.3%)		1/309 (0.3%)		0/88 (0%)		1
Conversation	7/769 (0.9%)		7/504 (1.4%)		0/265 (0%)		.1
No direct contact[c]	2/283 (0.7%)		2/240 (0.8%)		0/43 (0%)		1
Multiple contacts	4/134 (3%)		4/96 (4.2%)		0/38 (0%)		.58
Others[d]	7/462 (1.5%)		6/295 (2%)		1/167 (0.6%)		.43

[a]The *P* values indicate the statistical significance for comparison of the proportions of infected close contacts between subgroups under each variable listed in the table.

[b]Symptoms include fever, chills, dry cough, nasal congestion, loss of taste or smell, runny nose, sore throat, headache, tiredness, muscle pain, joint pain, shortness of breath, difficulty breathing, conjunctivitis, nausea, vomit, diarrhea, and abdominal pain.

[c]No direct contact refers to close contacts exposed to the environment contaminated by cases infected with severe acute respiratory syndrome coronavirus 2, whereas without direct contact with the infected case (Supplementary Materials).

[d]Others refer to other individuals assessed by onsite investigators who met criteria for close contact (eg, individuals who have had close contact in an office, factory, workshop, elevator, canteen).

Results from the sensitivity analyses indicated that the model assumptions would not substantially affect the estimates of the infectiousness profile, with the proportion of presymptomatic transmission ranging from 29.6% to 40.7%; probabilities of transmission all peaked at onset under these 4 conditions (Supplementary Table 4, Supplementary Figures 4 and 5).

DISCUSSION

In this study, we collated detailed information on laboratory-confirmed COVID-19 index cases and their close contacts. The characterized transmission pairs allowed us to compare and infer the risk of transmission from symptomatic and asymptomatic index cases to their contacts and to explore risk factors for the transmission and for the observed severity of the infected close contacts. In addition to demonstrating that asymptomatic transmission did occur, as shown in previous studies [5, 8], with this large sample of contact/transmission pairs, we showed that symptomatic index cases posed a higher risk of transmission to their close contacts than asymptomatic index cases after considering the difference in exposure settings. More importantly, our study illustrated that the clinical presentations of infected contacts varied by the type of index cases exposure, that is, secondary cases were more likely to be symptomatic if exposed to symptomatic index cases or to be asymptomatic if exposed to asymptomatic index cases.

With improved case detection and test-and-trace measures, more COVID-19 cases were identified as asymptomatic at confirmation [2]. The majority of these early detected cases often came from quarantine as close contacts of a confirmed case, while only a small fraction remained free of symptoms

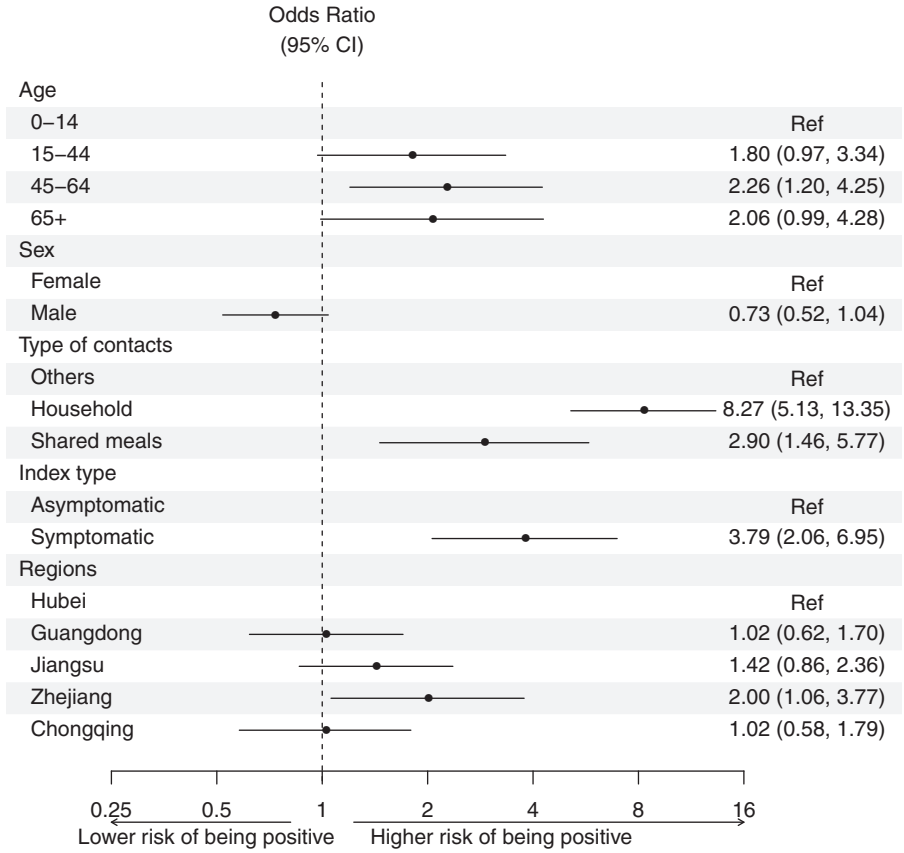

Figure 1. Risk factors potentially associated with the transmission risk of severe acute respiratory syndrome coronavirus 2 shown with the estimated odds ratio and 95% confidence intervals from a multivariable regression analysis adjusting for age, sex, and region. Abbreviations: CI, confidence interval; Ref, reference.

throughout the course of infection as asymptomatic cases [9, 10]. It was challenging to accurately record and report the numbers of asymptomatic infections because it often required comprehensive testing and follow-up on individuals that involved multiple departments for case identification and management, especially when capacity was limited as COVID-19 cases surged [11]. Considerable uncertainty remains over the role that asymptomatic cases play in transmission of SARS-CoV-2 [11]. In our study, we collected transmission pairs identified through contact tracing and verified information on the cases being truly asymptomatic or not. We found that asymptomatic index cases with SARS-CoV-2 infection were contagious but posed a lower risk to transmit infections compared with their symptomatic counterparts [8, 12].

The secondary attack rates in close contacts exposed to symptomatic index cases (4.1%) or asymptomatic index cases (1.1%) estimated in our study were generally lower than reported in other studies [13–15]. The difference in the observed secondary attack rates might be due to the varied investigation settings across the studies, and some studies specifically reported outbreaks in places where closer and more frequent contacts might have occurred [13, 16], while similar estimates were reported in another study [17]. In addition, intense public health measures were implemented in China during the study period, including active case finding and isolation, effective contact tracing, and widely adopted social distancing measures. These might have greatly reduced the numbers of close contacts and contact frequency and durations of exposure to an infected case and, therefore, led to a relatively low secondary attack rate in the close contacts.

Symptomatic and asymptomatic COVID-19 cases differed in many ways. For instance, symptomatic cases might generate more virus-laden particles because of the presented symptoms compared with asymptomatic cases, leading to a higher risk of transmission to their contacts [17]. On the other hand, symptomatic and asymptomatic cases might behave differently, including symptom-initiated self-isolation, delay in healthcare-seeking, and therefore delayed detection and isolation in asymptomatic infections [10, 18]. It is still uncertain whether SARS-CoV-2 viral shedding profiles vary in asymptomatic and symptomatic cases, although viral shedding seemed to decrease more slowly among symptomatic cases [4].

Previous studies characterized the risk of presymptomatic transmission with viral shedding data [7, 19], similar to the unimodal trend of infectiousness illustrated in our study that peaked at around symptom onset among symptomatic cases. Presymptomatic transmission accounted for 38% of all transmission events that occurred

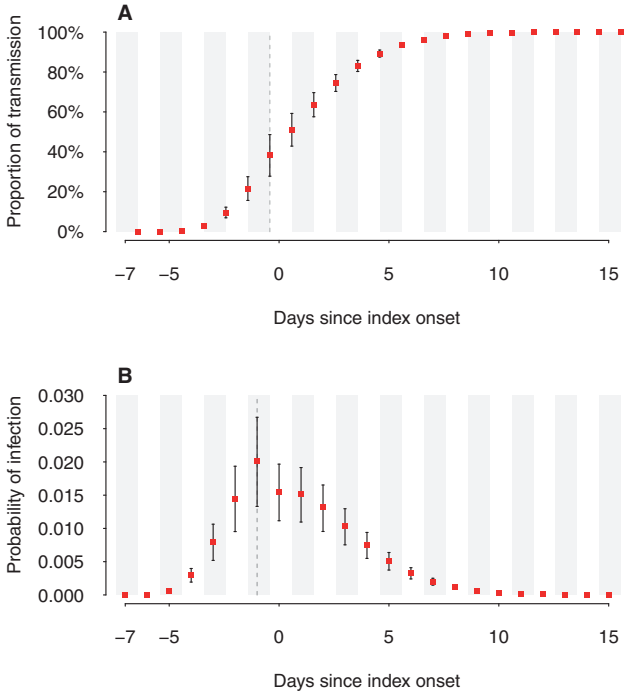

Figure 2. Temporal risk of transmission from symptomatic index case to their close contacts in relation to the time of index onset. *A,* Cumulative proportions of infection in relation to the clinical presentation of symptomatic index cases. *B,* Probability of infection in exposed close contacts in relation to the clinical presentation of symptomatic index cases. The dots refer to the point estimates, and the error bars correspond to the estimated 95% confidence intervals.

in our study, which was likely to be the upper limit of contribution to the overall infections since further transmission might have been interrupted by isolation of confirmed cases depending on the efficiency in case finding. Nonetheless, within our data, less than 1% of the close contacts were exposed to their index cases 5 days or later after the index case onset, and the onset-to-admission delay was reported to be 8–14 days in China [4], indicating that our estimate suffered little from such interruption.

Our study also suggested that the close contacts that occurred in households and through shared dining were associated with a higher risk of transmission from the index case to their close contacts than contacts that happened in other settings. The increased risk of infection in these situations might be due to longer durations of exposure, social interactions at a closer distance, and perhaps not being able to wear face masks properly [20]. Studies on superspreading of COVID-19 indicate that a small proportion of cases were responsible for the majority of the transmissions that occurred, and clusters of cases were often identified in places where unprotected contacts (not wearing a face mask) happened for a longer duration [21].

Our study has several limitations. First, we constructed transmission pairs based on the relationship between the identified index cases and their close contacts. However, we could not rule out the possibility that an index case might have been misclassified as a primary case if the case only presented symptoms earlier but was infected later by the true primary case. Second, we did not collect data on virus testing, which was not ideal in exploring the risk of transmission from asymptomatic and symptomatic index cases, although our findings were largely consistent with the viral shedding patterns described elsewhere [4, 7]. Last, we could not estimate the temporal risk of transmission from asymptomatic index cases due to the lack of information on the time of infection of the asymptomatic index case and the relatively small number of infected close contacts exposed to asymptomatic cases.

Our study illustrates that the risk of transmission varied according to the symptom profile of COVID-19 cases. Asymptomatic cases infected their close contacts at a lower risk than those who presented with symptoms. Presymptomatic transmissions accounted for more than one third of the infections that occurred from exposure to symptomatic cases. Risk of transmission was relatively higher within households and through shared dining than in other social settings. Active case finding with increased testing capacity could help to reduce transmission from symptomatic and asymptomatic COVID-19 cases. Social distancing measures and wearing a face mask might not be sufficient to prevent infection from spreading in settings where these measures cannot be maintained.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. The study was conceived by Z. C. and Z. L. Data collection and cleaning were conducted by F. L., M. R., C. Z., Y. L., Z. P., Y. Q., J. Y., M. G., X. Y., H. Z., Z. L., S. Z., L. R., Q. C., and L.W. Data analyses were performed by F. L., Y. L., and T. K. T. P. W. wrote the first draft of the manuscript. All authors provided critical review and revision of the text and approved the final version.

Acknowledgments. The authors thank the Hubei, Jiangsu, Zhejiang, Guangdong, and Chongqing provincial Centers for Disease Control and Prevention for assistance in coordinating the data collection.

Financial support. This work was supported by the National Key R&D Program (2020YFC0846900) and the National Natural Science Foundation (82041029) of the Ministry of Science and Technology of China and the Theme-based Research Scheme (T11-712/19-N) of the Research Grants Council of the Hong Kong SAR Government.

Potential conflicts of interest. B. J. C. consults for Roche and Sanofi Pasteur. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann Intern Med **2020**; 173:362–7.
2. Cao S, Gan Y, Wang C, et al. Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China. Nat Commun **2020**; 11:5917.
3. Bae SH, Shin H, Koo HY, Lee SW, Yang JM, Yon DK. Asymptomatic transmission of SARS-CoV-2 on evacuation flight. Emerg Infect Dis **2020**; 26:2705–8.

4. Lee S, Kim T, Lee E, et al. Clinical course and molecular viral shedding among asymptomatic and symptomatic patients with SARS-CoV-2 infection in a community treatment center in the Republic of Korea. JAMA Intern Med **2020**; 180:1447–52.
5. Furukawa NW, Brooks JT, Sobel J. Evidence supporting transmission of severe acute respiratory syndrome coronavirus 2 while presymptomatic or asymptomatic. Emerg Infect Dis **2020**; 26:e201595.
6. Tsang TK, Wu P, Lin Y, Lau EHY, Leung GM, Cowling BJ. Effect of changing case definitions for COVID-19 on the epidemic curve and transmission parameters in mainland China: a modelling study. Lancet Public Health **2020**; 5:e289–96.
7. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med **2020**; 26:672–5.
8. Shi Q, Hu Y, Peng B, et al. Effective control of SARS-CoV-2 transmission in Wanzhou, China. Nat Med **2021**; 27:86–93.
9. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill **2020**; 25:2000180.
10. Kimball A, Hatfield KM, Arons M, et al; Public Health–Seattle and King County; CDC COVID-19 Investigation Team. Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility—King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:377–81.
11. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: a living systematic review and meta-analysis. PLoS Med **2020**; 17:e1003346.
12. Hung IF, Cheng VC, Li X, et al. SARS-CoV-2 shedding and seroconversion among passengers quarantined after disembarking a cruise ship: a case series. Lancet Infect Dis **2020**; 20:1051–60.
13. Chen Y, Wang AH, Yi B, et al. [Epidemiological characteristics of infection in COVID-19 close contacts in Ningbo city]. Zhonghua Liu Xing Bing Xue Za Zhi **2020**; 41:667–71.
14. Jing QL, Liu MJ, Zhang ZB, et al. Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study. Lancet Infect Dis **2020**; 20:1141–50.
15. Expert Taskforce for the COVID-19 Cruise Ship Outbreak. Epidemiology of COVID-19 outbreak on cruise ship quarantined at Yokohama, Japan, February 2020. Emerg Infect Dis **2020**; 26:2591–7.
16. Shen Y, Li C, Dong H, et al. Community outbreak investigation of SARS-CoV-2 transmission among bus riders in eastern China. JAMA Intern Med **2020**; 180:1665–71.
17. Luo L, Liu D, Liao X, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. Ann Intern Med **2020**; 173:879–87.
18. Vermund SH, Pitzer VE. Asymptomatic transmission and the infection fatality risk for COVID-19: implications for school reopening. Clin Infect Dis **2021**; 72:1493–6.
19. Wölfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. Nature **2020**; 581:465–9.
20. Sun K, Wang W, Gao L, et al. Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2. Science **2021**; 371:eabe2424.
21. Adam DC, Wu P, Wong JY, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. Nat Med **2020**; 26:1714–9.