

Household Transmission of SARS-CoV-2, Zhuhai, China, 2020

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Summary

We found that the overall second infection rate of SARS-COV-2 was 32.4% within household. The estimated median incubation period and serial interval were 4.3 days and 5.1 days, respectively. Early isolation of patients and contact investigation should be initiated urgently.

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Abstract

Background: To illustrate the extent of transmission, identify affecting risk factors and estimate epidemiological modeling parameters of SARS-CoV-2 in household setting.

Methods: We enrolled 35 confirmed index cases and their 148 household contacts, January 2020–February 2020, in Zhuhai, China. All participants were interviewed and asked to complete questionnaires. Household contacts were then prospectively followed active symptom monitoring through the 21-day period and nasopharyngeal and/or oropharyngeal swabs were collected at 3-7 days intervals. Epidemiological, demographic and clinical data (when available) were collected.

Results: Assuming that all these secondary cases were infected by their index cases, the second infection rate (SIR) in household context is 32.4% (95% confidence interval [CI] 22.4%–44.4%), with 10.4% of secondary cases being asymptomatic. Multivariate analysis showed that household contacts with underlying medical conditions, a history of direct exposure to Wuhan and its surrounding areas, and shared vehicle with an index patient were associated with higher susceptibility. Household members without protective measures after illness onset of the index patient seem to increase the risk for SARS-CoV-2 infection. The median incubation period and serial interval within household were estimated to be 4.3 days (95% CI; 3.4 to 5.3 days) and 5.1 days (95% CI; 4.3 to 6.2 days), respectively.

Conclusion: Early isolation of patients with COVID-19 and prioritizing rapid contact investigation, followed by active symptom monitoring and periodic laboratory evaluation, should be initiated immediately after confirming patients to address the underlying determinants driving the continuing pandemic.

Key words: SARS-CoV-2; Household transmission; Second infection rate (SIR); Incubation period; Serial interval

Introduction

On 11 March 2020, the World Health Organization (WHO) in Geneva, Switzerland, declared that the outbreak of coronavirus disease 2019 (COVID-19), caused by the virus SARS-CoV-2 (SARS-CoV-2), constituted a pandemic, and more than 143 0 000 confirmed cases, including 85 522 deaths, had been reported worldwide as of 9 April 2020[1, 2]. The control of this pandemic disease relies on interrupting chains of person-to-person transmission through implemented mitigation policies, including expeditious diagnosis and isolation of patients, monitoring of all close contacts and using special protective measures[3-5]. However, previous investigation showed that many secondary cases were household members of confirmed patients[4]. Household transmission are thought to play a significant role in the outbreak of SARS-CoV-2[4]. Despite this, the epidemiologic features and the risk factors for transmission of this emerging virus remain poorly characterized.

To determine pivotal transmission dynamics and to identify the risk factors for transmission of the virus in the household setting, we conducted a prospective study of household transmission of SARS-CoV-2 in Zhuhai, China in February and March 2020. We assessed the extent of transmission by estimating the secondary infection rate (SIR) for household contacts and factors influencing secondary transmission of SARS-CoV-2, which is important to guide preventive procedures, characterized secondary cases including the range of features, along with the fraction of silent or subclinical secondary infections, and estimated the incubation period and serial interval in a household context, which could be useful for informing recommendations with respect to the quarantine time and for appraisal the effect of delays in measures on transmission.

METHODS

Since the outbreak of COVID-19 in December 2019[6], surveillance project under local health authorities in Zhuhai, China, was initiated to survey travelers from high risk areas, individuals detected by fever screening in communities and patients at clinics or hospitals. All individuals with suspected, probable or confirmed SARS-CoV-2 infection in Zhuhai, based on the WHO interim guidance[7] and National Health Commission definition[8], were compulsorily referred to the Fifth Affiliated Hospital, Sun Yat-sen University, the only hospital designated to treat patients with COVID-19 pneumonia in this city. This prospective observational household transmission investigation was performed during the first wave of the outbreak of COVID-19 from February 1, 2020 to March 1, 2020, when the majority of the public were aware of COVID-19.

Definitions

A confirmed case was defined by a positive result of SARS-CoV-2-specific reverse-transcriptase polymerase chain reaction (RT-PCR) [9]. The illness severity of COVID-19 was typed according to the " Guidelines for the Diagnosis and Treatment of 2019 New Coronavirus Pneumonia " (Sixth trial version)[8]. A household was defined as two or more people living together in the same indoor living space. A household index was the first person to introduce SARS-CoV-2 into the household.

Household contacts were defined as person who spent at least one night in the house after the symptom onset of the index patient. We assumed that all household secondary cases were generated by their corresponding index cases and ignored infections acquired from outside the household (community infections) or the possibility of tertiary or higher infection. We defined the second infection rate (SIR) within household as the number of confirmed secondary cases of SARS-CoV-2 in the household within 21 days after index case isolation divided by the total number of contacts in that household. We calculated the incubation period of SARS-CoV-2 as the number of days between the earliest and latest dates of exposure after index patient onset and the date of the secondary case onset. The serial interval was estimated by identifying the number of days between the reported onset date in the household contact and the reported onset date for that household's index case patient.

Study Design

All consecutive patients with probable or confirmed COVID-19 admitted to the Fifth Affiliated Hospital of Sun Yat-sen University from January 17 to February 29, 2020, were enrolled. All included patients and their household members were interviewed and asked to complete internet-based questionnaires to obtain information on epidemiological and sociodemographic characteristics, underlying diseases, clinical presentation, exposure time, and so forth. Epidemiological, sociodemographic and clinical data (when available) for all included cases were collected and reviewed by two physicians. Our study partially followed the Household Transmission Investigation Protocol for 2019–Novel Coronavirus (2019-nCoV) Infection[10]. The Ethics Committee of The Fifth Affiliated Hospital, Sun Yat-sen University approved the study (2020L00931), with oral informed consent being authorized from all participant. For details on follow-up, please see Supplemental Methods.

Statistical Analyses

Continuous variables were expressed as median (interquartile ranges), and categorical variables as percentages (%). Group comparison was performed by the t-test, the Wilcoxon rank sum test, Pearson's χ^2 test or the Fisher's exact test, as appropriate. For univariate analyses of case and household factors, we calculated individual SIR to examine transmission risk. To account for household clustering for individual SIR analyses, generalized estimating equations were used to obtain the SIR and corresponding 95% confidence interval. We also performed sensitivity analysis to account for the varying probability of infection apart from the index case. An analyst-driven backward selection was used to develop multivariable model. The Quasi-likelihood information criterion and z statistic were employed to determine the most parsimonious model in the general estimating equation. The incubation period and serial interval were estimated using a previously described parametric regression techniques which assumed that these data follows a log-normal distribution[11]. Data analyses were conducted using the R statistical package (<http://www.r-project.org/>) and the SAS software (version 9.4).

RESULTS

Characteristics of index case patients, contacts and households.

There were 104 probable or confirmed COVID-19 cases, resided in 46 households, in Zhuhai, China during the period between January 17 to February 29, 2020 (Figure 1). Of the 104 patients from 46 households by the initial survey, 21 (pertaining to 11 households) were excluded because of the index lived alone, refusal to participate, having more than one index case or not a confirmed case; the remaining confirmed 83 cases, resided in 35 households, were considered eligible for inclusion in this study. Ultimately, the baseline characteristics of the 35 index cases (1 index case treated in Macao) and 148 household contacts (5 noncases from 2 households refused to complete questionnaires) enrolled were summarized in Table 1 and Supplemental Table 1.

Household Second Infection Rate and Risk Factors of Household Transmission

A secondary case of COVID-19 occurred in 22 (62.9%) of 35 households with contacts. Among these, 8 households had 1 secondary case, 7 had 2 cases, 4 had 3 cases, 2 had 4 cases and 1 had 6 cases. Generally, the 35 index cases gave rise to 48 secondary cases among 148 exposed household contacts, giving an SIR of 32.4 (95% confidence interval [CI] 22.4%-44.4%) (Table 2 and Supplemental Table 2). Sensitivity analyses of low probability of infection apart from the index case (10%) resulted in an SIR of 29.2% and high probability of infection apart from the index case (80%) resulted in an SIR of 6.5%. Full results of the varying probability of infection apart from the index case were given in the Supplemental Table 3. Five noncases who declined to participate in this survey were subsequently excluded from further analyses owing to missing data.

Contact-level risk factors significantly associated with SIRs in univariate analysis included having underlying medical conditions, a history of direct exposure to Wuhan and its surrounding areas, physical contact, shared living room and vehicle with an index patient. Additionally, contacts with more than 72 hours of exposure (SIR, 41.7%; [95%CI; 26.8%-58.3%]) had a higher SIR compared with those without (SIR, 23.2%; [95%CI; 11.4%-41.5%]). One household-level factor was

significantly associated with SIR: household members without protective measures after illness onset of the index patient (odds ratio (OR), 4.43; [95%CI; 1.37-14.34]). Among the index case factors, patient having coughing, lower lymphocyte counts of less than $1.5 \times 10^9/L$ and higher BNP level of more than 125 pg/ml on admission were associated with larger proportions of secondary cases (42.9%, 41.3% and 62.5%, respectively), but these associations were of borderline significance.

To further assess risk factors for SARS-COV-2 transmission, factors of three different levels with a significance level of less than 0.2 in univariate analysis were separately analyzed by three multivariable models, variables with a P value ≤ 0.1 being kept. A composite model was then constructed based on variables included in the above three models and variables with P value ≤ 0.05 were kept. After adjustment for the other variables included in the multivariate analysis, having underlying medical conditions (OR, 5.99; [95%CI; 1.81-19.83]), history of direct exposure to Wuhan and its surrounding areas (OR, 4.14; [95%CI; 1.25-13.68]), shared vehicle with an index patient (OR, 4.37; [95%CI; 1.8-10.58]) and household members without protective measures (OR, 4.95; [95%CI; 1.59-15.39]) remained significantly associated with increased risk for COVID-19 (Table 3).

Serial interval and incubation period

Finally, 48 secondary cases provided information for calculation of the serial interval and incubation period. Fitting the log-normal model to all household secondary cases, we estimated that the median incubation period of COVID-19 was 4.3 days (95%CI; 3.4-5.3 days) (Figure 2A) and the serial interval was 5.1 days (95%CI; 4.3 to 6.2 days) (Figure 2B).

DISCUSSION

Household transmission research is an essential step in understanding this pandemic emerging virus, providing valuable insights on the dynamics of its transmission, including characterizing the risk factors of transmission and estimating its transmissibility, and epidemiological modeling parameters - incubation period and serial interval[10]. To address this, we conducted a prospective observational

study during the period of February-March 2020 in Zhuhai, China, to portray the transmission of SARS-CoV-2 within household.

Assuming that all these secondary cases were infected by their index cases, a realistic assumption given a time lag of symptom onset between them, we observed an SIR of 32.4% for RT-PCR-confirmed SARS-CoV-2 with 62.9% of households having one or more secondary cases. This SIR we observed is comparable to secondary attack rates from Wang et al (30%)[12] and Liu et al (35%) [13], but it is substantially higher than data published by WHO (3-10%)[4] or those reported in Shenzhen, China (15%)[14], or in the United States (10.5%)[15]. Several differences between our study and those published may have contributed to our higher SIR, including approaches of identifying or defining secondary cases, features of the cases investigated, environment and behavioral differences, and interventions for mitigating virus spread. Moreover, we systematically screened all household contacts (symptomatic or not) by laboratory testing and active follow-up, with respiratory specimens being collected at 3-7 days intervals. Another possible reason leading to overestimation of the SIR is that some of the infections in household contacts were acquired from outside the household or from second or higher cases. Any inferences about SIR must be made with caution owing to the fact that SIR within household changes with the varying probability of infection outside the household in our study. However, high SIR could be associated with the lack of preexisting immunity against this emerging virus. While the actual SIR is likely lower than that observed in our study, the still high household infection prevalence underscores the need for effective control approaches for SARS-CoV-2, including active surveillance and containment measures[4].

Our estimates of the incubation period of COVID-19 were somewhat shorter than that proposed by Lauer et al (median, 4.3 days vs. 5.1 days) [16] and were similar to that published by Guan (median, 4.3 days vs. 4 days) [17]. The estimated mean incubation period of COVID-19 was 5.8 days, comparable to 5.2 days reported by Li et al [18]. Similarly, our estimates of the serial interval were a little bit longer than that summarized by Nishiura et al (median, 5.1 days vs. 4 days)[19], with 5% of cases developing within 1.8 days and 95% within 14.8 days after the index onset. The estimated mean serial interval was 6.3 days, slightly shorter than that pictured by Li et al (mean, 7.5 days)[18],

perhaps owing to early infection and repeat exposure in household setting. Most secondary cases (31/48) had already occurred at the time of contact survey, with a median interval of 8 days between the secondary case's onset and the date of the contact survey. The rapid transmission and high infection rate implied that most secondary cases were likely infected around the time of symptom onset of the primary cases and that measures for mitigating household transmission of SARS-COV-2 should be initiated promptly to be effective. Therefore, household routine infection control procedures (such as hand washing, cough etiquette, wearing masks)[3-5] should be implemented quickly because it is sometimes challenging for local health authorities to intervene immediately after symptom onset of the primary cases. Furthermore, contact investigation should be performed instantly after confirming index patients, a practical measure for detecting new cases and interrupting transmission[4].

Several factors had been examined to evaluate their associations with susceptibility. We found that underlying medical conditions and history of direct exposure to Wuhan and its surrounding areas were strong risk factors for household transmission in our study, with a 6-fold and 4-fold increased risk for COVID-19 respectively. Many reasons can account for the association between underlying medical conditions and household transmission. Correlation of underlying medical conditions among household members is one of them. Additionally, some diseases could impair the function of immune system, which could inhibit the body's response to the coronavirus. Moreover, underlying medical comorbidities are also risk factors for severe illness and mortality[20-23]. Preliminary homology analyses of the virus sequences confirmed that infections in household members in the short interval after onset of the index case would have been infected within households rather than from outside the household [24], confirming the feasibility of this study assumption to assess household transmission. However, most of the contacts reported direct exposure to Wuhan or the surrounding area, implying that some of the household contacts might infect this emerging virus outside of household. These high-risk groups identified above could potentially be targeted by SARS-COV-2 vaccination strategies[25] aiming to decrease susceptibility and to further reduce overall SIR.

Moreover, greater hours of exposure (>72 hours) to an index patient, and greater closeness of exposure by physic contact or by sharing a living room or vehicle, reflecting both closer contact resulting in increased risk of sharing infectious aerosols, and greater duration of contact contributed to an increased exposure-viral load, were all associated with increased COVID-19 risk. Although the factor of shared vehicle was independent predictors of household transmission, an association for exposure duration was not statistically included in multivariate analysis. A probably explanation was that household contacts who had greater exposure proximity to the index patient by shared a living room or vehicle were many of the same persons with higher exposure duration. Thus, the likely collinearity of the different exposure approaches educed the only factor of shared vehicle identified as independent predictors of COVID-19. These finding implies that behavioral changes aiming to decrease intensity of exposure can be effective in reducing the risk of household transmission[3-5]. This emphasizes the importance of prioritizing rapid contact investigation, screening, diagnosis and early isolation of patients with COVID-19 for this high-risk group[4].

Household members without protective measures was the only household level factor independently related to increased transmission risk. The result also demonstrated that the person-to-person transmission hazard of SARS-COV-2 in the household fluctuated with the size of the household, household with 4 members having the highest SIR of 66.7%. Separate dining, indoor isolation, ventilation and disinfection, index patient living alone, and wearing masks after index case symptom onset were not associated with COVID-19 prevalence, implying presymptomatic transmission[26]. These findings indicated that preventing household infection requires early precautions to be taken and joint efforts of all family members[3-5].

With respect to factors related to infectivity, index patient age, sex, smoking, and fever were not significantly associated with COVID-19 household transmission after adjustment for clustering of secondary infections within households. However, having coughing was associated with borderline significance with increased infectivity. These findings have practical meanings for defining settings where there is a high risk of SARS-COV-2 transmission based on index patient clinical features. Contact, droplet and aerosol precautions should be implemented for hospital personnel[7].

The limited sample size of this investigation was its principal shortcoming. This did not allow us to detect mild to moderate effects of risk factors and to adjust potential confounders. Furthermore, our study design assumed that each household was a single homogenous source which was an oversimplification because the index cases we identified may not have been the initial case in the household, let alone infections acquired from outside the household or a chain of household transmission. The lack of sero-epidemiological data was another limitation in this investigation. A SARS-COV-2 specific RT-PCR method may not be perfectly sensitive to detect low viral loads[27]. We may have missed some RT-PCR–positive infections if viral shedding occurred over a short period of time. Nevertheless, repeat testing in our study may improve diagnostic accuracy. Also, the evolution of SARS-CoV-2[28], the narrow spatial and temporal distribution, and relatively small sample size in this cohort limited the representativeness and generalizability of our findings. Still, the fact that households with more cases may be more likely to seek medical evaluation may be subject to selection bias, a factor that would overestimate the SIR. Further study in which a cohort of households is prospectively enrolled before infection begin in their household and is followed through the whole of the course of the pandemic is needed to address these limitations.

In conclusion, our study raises important insights on secondary infection rates, risk factors and epidemiological modeling parameters associated with COVID-19 diagnosis in household contacts with recent exposure to patients with SARS-COV-2. The rapid transmission and high infection rate emphasize the importance of rapid contact investigation, rigorous screening and active monitoring of asymptomatic contacts and hospital isolation of symptomatic contacts, thus mitigating virus spread and interrupting the transmission chain of this pandemic. Further studies from different settings to confirm or refute our estimates and to investigate the duration of viral shedding are warranted to inform public health prevention and elimination efforts.

Contributors

Conception and design: JW, YH, JL, XZ. Development of methodology: JW, JL, XZ. Acquisition of data (interview, collection, acquired and managed data, and provided facilities, etc.): JW, YH, CT, CB, ZC, MC, CT, LL, MH, ZW, KW, YL. Analysis and interpretation of data (e.g., statistical, biostatistics and computational analysis): LZ, JW, YH, MC, CT, JL, XZ, JH, LL, MH. Writing, review, and/or revision of the manuscript: JW, JL, XZ, JH, LL, MH. Study supervision: JL, XZ. All authors reviewed and approved the final manuscript.

Acknowledgments

We thank Dr. Lizhi Zhou, a senior statistician, for his insightful and helpful suggestions on statistical analyses.

Funding

This work was financially supported by grants from Natural Science Foundation of Guangdong Province of China (Grant No. 2020A1515011147 to Jing Liu). Fundamental Research Funds for the Central Universities (Grant No. 19ykpy51 to Xiaobin Zheng).

Declaration of interests

All authors declare no competing interests.

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Tables

Table 1. Characteristics of Index Cases, Secondary Cases and Noncases.

Characteristic	Index cases (n=35)	Secondary cases (n=48)	Noncases (n=95)	P value
Demographics and clinical characteristics				
Gender				0.44 ^a
Male	19(54.3)	19(39.6)	44(46.3)	
Female	16(45.7)	29(60.4)	51(53.7)	
Age, years	49(34.5-62)	43.5(35.8-62.3)	37(14.5-58)	0.09 ^a
BMI, Kg/M ²	24(21.9-25.5)	23.3(20.6-25.1)	22(19.5-24.7)	0.25 ^a
Education level ^b				0.54 ^a
Elementary and below	3(8.6)	9(18.8)	25(26.9)	
Secondary education	16(45.7)	20(41.7)	33(35.5)	
Higher education	16(45.7)	19(39.6)	35(37.6)	
Direct exposure to Wuhan and its surrounding areas	31(88.6)	36(75)	34(35.8)	<0.01^a
Smoking	9(25.7)	7(14.6)	18(18.9)	0.52 ^a
Underlying medical conditions	18(51.4)	25(52.1)	18(18.9)	<0.01^a
Hypertension	9(25.7)	8(16.7)	9(9.5)	
Diabetes	4(11.4)	1(2.1)	3(3.2)	
Cardiovascular disease	3(8.6)	2(4.2)	6(6.3)	
Carcinoma	3(8.6)	1(2.1)	1(1.1)	
Chronic kidney disease	1(2.9)	1(2.1)	0(0)	
Hepatitis or cirrhosis	4(11.4)	2(4.2)	1(1.1)	
Cerebrovascular	2(5.7)	1(2.1)	1(1.1)	
Pulmonary Disease	3(8.6)	1(2.1)	0(0)	
Endocrine	3(8.6)	6(12.5)	2(2.1)	
Other	4(11.4)	12(25)	2(2.1)	
Asymptomatic	3(8.6)	5(10.4)	87(91.6)	
Initial symptoms				
Fever	15(44.1)	23(47.9)	4(4.2)	
Coughing	13(38.2)	10(20.8)	3(3.2)	
Shortness of breath	1(2.9)	1(2.1)	0(0)	
Sore throat	1(2.9)	5(10.4)	0(0)	
Headache	2(5.9)	2(4.2)	0(0)	
Muscle aches or fatigue	1(2.9)	3(6.3)	1(1.1)	
Clinical symptoms				
Fever	28(82.4)	28(58.3)	6(6.3)	
Coughing	23(67.6)	31(64.6)	3(3.2)	
Shortness of breath	6(17.6)	5(10.4)	0(0)	
Expectoration	5(14.7)	8(16.7)	0(0)	
Hemoptysis	1(2.9)	0(0)	0(0)	
Sore throat	3(8.8)	10(20.8)	0(0)	
Nasal obstruction	3(8.8)	4(8.3)	1(1.1)	
Runny nose	1(2.9)	3(6.3)	1(1.1)	
Sneeze	1(2.9)	1(2.1)	1(1.1)	
Headache	7(20.6)	10(20.8)	0(0)	
Muscle aches or fatigue	11(32.4)	15(31.8)	2(2.1)	
Diarrhea	4(11.8)	7(14.6)	2(2.1)	

Data are n (%) or median (IQR), unless otherwise specified. ^aP values indicated differences between secondary cases and noncases. P values ≤0.05 marked in bold was considered statistically significant.

^bEducation level information of 2 noncases were missing. Abbreviations: BMI, body mass index.

Table 2. Secondary Infection Rate (SIR) and Odds Ratio (OR) for Association with COVID-19 by Characteristics of Index patients, Contacts and Households.

Risk factor	No. of secondary cases of COVID-19 n=48	No. of household contacts n=143 ^a	SIR (95% CI), %	OR(95% CI)	P value
Overall	48	148	32.4(22.4-44.4)		
Index case characteristics					
Age, years					0.14
≤55	18	72	25(12.8-43.1)	Ref	
>55	30	71	42.3(27-59.2)	2.2(0.75-6.38)	
Sex					0.78
Man	27	77	35.1(20-53.9)	Ref	
Female	21	66	31.8(19.5-47.4)	0.86(0.31-2.38)	
Smoking					0.81
Yes	15	42	35.7(18.4-57.9)	1.14(0.38-3.43)	
No	33	101	32.7(20.7-47.5)	Ref	
BMI, Kg/M ²					0.11
<24	24	69	34.8(22.5-49.5)	Ref	
24-28	13	58	22.4(9.6-44.1)	0.54(0.17-1.75)	
>28	11	16	68.8(55.8-79.3)	4.13(1.81-9.40)	
Education level					0.17
Elementary and below	3	12	25(7.5-57.8)	Ref	
Secondary education	34	78	43.6(28.6-59.9)	2.32(0.49-11)	
Higher education	11	53	20.8(8.5-42.5)	0.79(0.14-4.53)	
Direct exposure to Wuhan and its surrounding areas					0.12
Yes	46	124	37.1(25.6-50.3)	5.01(0.63-39.92)	
No	2	19	10.5(1.6-46.6)	Ref	
Initial symptom Fever					0.72
Yes	24	76	31.6(18.6-48.3)	0.83(0.30-2.3)	
No	24	67	35.8(21-54)	Ref	
Initial symptom Coughing					0.07
Yes	23	47	48.9(29.4-68.8)	2.72(0.94-7.89)	
No	25	96	26(15.3-40.6)	Ref	
Fever					0.79
Yes	42	123	34.1(22.9-47.6)	1.21(0.30-4.95)	
No	6	20	30(10.5-61)	Ref	
Coughing					0.05
Yes	39	91	42.9(30.5-56.1)	3.58(1-12.9)	
No	9	52	17.3(6.1-40.1)	Ref	
Household contact characteristics					
Age, years					0.05
0-3	4	10	40(13.8-73.5)	1.13(0.29-4.48)	
4-18	1	21	4.8(0.6-28.1)	0.09(0.01-0.73)	
19-60	30	81	37(24.2-52)	Ref	
>60	13	31	41.9(23.5-62.9)	1.23(0.51-2.98)	
Sex					0.37
Man	19	63	30.2(18.5-45.1)	Ref	
Female	29	80	36.3(24.6-49.7)	1.32(0.71-2.44)	
BMI, Kg/M ²					0.71
<18.5	8	27	29.6(14.9-50.2)	0.88(0.38-2.04)	
18.5-23.9	20	62	32.3(20.2-47.3)	Ref	
24-27.9	15	43	34.9(19.1-54.8)	1.13(0.45-2.8)	
>28	5	11	45.5(27.2-65)	1.75(0.58-5.27)	
Smoking					0.55
Yes	7	25	28(11.7-53.3)	0.73(0.25-2.15)	
No	41	118	34.7(23.9-47.5)	Ref	
Relationship to index case					0.12
Spouse	12	23	52.2(32.5-71.2)	3.66(1.28-10.5)	
First-degree relative	22	59	37.3(22.3-55.2)	2(0.81-4.93)	
others	14	61	23(12.5-38.3)	Ref	
Exposure hours after index case onset ^b					0.12
<72	16	69	23.2(11.4-41.5)	Ref	
>120	30	72	41.7(26.8-58.3)	2.37(0.79-7.07)	
Direct exposure to Wuhan and its surrounding areas					<0.01
Yes	36	70	51.4(36.8-65.8)	5.38(1.62-17.9)	
No	12	73	16.4(6.9-34.5)	Ref	
Education level ^c					0.59
Elementary and below	9	34	26.5(14-44.3)	Ref	
Secondary education	20	53	37.7(22.8-55.5)	1.68(0.65-4.35)	
Higher education	19	54	35.2(22.5-50.4)	1.51(0.59-3.85)	
Underlying medical conditions					<0.01
Yes	25	43	58.1(40.3-74.1)	4.65(1.93-11.21)	
No	23	100	23(13.3-36.7)	Ref	
Physical contact					0.01
Yes	29	60	48.3(33-64)	3.15(1.44-6.89)	
No	19	83	22.9(13-37)	Ref	
Shared meal					0.12
Yes	40	103	38.8(26.8-52.4)	2.54(0.87-7.42)	
No	8	40	20(8.3-40.7)	Ref	

Shared living room					<0.01
Yes	23	43	53.5(38.8-67.6)	3.45(1.75-6.8)	
No	25	100	25(15.1-38.5)	Ref	
Shared vehicle					<0.01
Yes	34	73	46.6(31.2-62.6)	3.49(1.45-8.4)	
No	14	70	20(10.7-34.3)	Ref	
Household level characteristics					
Number of contacts in household					0.26
1	2	5	40(10-80)	Ref	
2	8	14	57.1(27.4-82.5)	2(0.22-17.84)	
3	8	12	66.7(41.4-85)	3(0.38-23.76)	
4	11	28	39.3(20.6-61.8)	0.97(0.13-7.24)	
5	5	19	26.3(6.2-66)	0.54(0.05-6.3)	
≥6	14	65	21.5(9.6-41.5)	0.41(0.05-3.12)	
Household activities after index case onset					
No protective measures of contacts ^d					0.02
Yes	39	86	45.3(32.3-59.1)	4.43(1.37-14.34)	
No	9	57	15.8(6.2-34.6)	Ref	
Index case indoor isolation					0.98
Yes	32	95	33.7(21.5-48.5)	1.02(0.34-3.08)	
No	16	48	33.3(16.6-55.7)	Ref	
Index case living along					0.88
Yes	5	16	31.3(8.9-67.8)	0.89(0.17-4.52)	
No	43	127	33.9(22.9-46.9)	Ref	
Index case wearing mask					0.36
Yes	18	65	27.7(15.1-45.2)	0.61(0.22-1.72)	
No	30	78	38.5(23.9-55.4)	Ref	
Ventilation and disinfection					0.29
Yes	15	58	25.9(11.8-47.7)	0.55(0.18-1.7)	
No	33	85	38.8(26.1-53.3)	Ref	
Separate dining					0.28
Yes	17	64	26.6(14.2-44.1)	0.56(0.2-1.57)	
No	31	79	39.2(24.7-56)	Ref	
Hours spending at home of index case, hours ^e					0.87
< 72	20	63	31.7(16-53.2)	Ref	
≥72	26	77	33.8(21.8-48.2)	1.1(0.37-3.22)	
Index onset to admission time, days ^f					0.72
≤3	14	37	37.8(17.3-63.9)	Ref	
3-5	17	56	30.4(14.9-52)	0.72(0.18-2.91)	
>5	17	41	41.5(24.6-60.6)	1.16(0.31-4.35)	

P values ≤ 0.05 marked in bold was considered statistically significant. ^a A total of 5 noncases were excluded for analyses due to missing data. ^b Data on exposure hours after index case onset of 2 secondary cases were missing. ^c Education level information of 2 noncases were missing. ^d Protective measures of contacts included wearing masks when contact with index case, hand hygiene after contact with index case and avoiding contact with the index case. ^e Data on hours spending at home of index case of 2 secondary cases were missing. ^f Data on index onset to admission time of 9 noncases were missing. Abbreviations: BMI, body mass index; CI, confidence interval; COVID-19, Coronavirus Disease 2019; OR, odds ratio; SIR, secondary infection rate.

Table 3. Multivariable Models for Risk Factors Associated with COVID-19 by Characteristics of Index Patients, Contacts and Households.

Risk factor	aOR(95% CI)	P value
Model 1. Including index case factors only		
Initial symptom Coughing		0.03
Yes	3.27(1.22-8.75)	
No	Ref	
Lymphocyte count, $\times 10^9$ per L		0.07
≤ 1.5	2.97(0.96-9.17)	
> 1.5	Ref	
Model 2. Including contact factors only		
Underlying medical conditions		0.01
Yes	6.10(2.05-18.15)	
No	Ref	
Exposure hours after index case onset		0.09
≤ 72 h	Ref	
> 72 h	2.79(0.85-9.16)	
Direct exposure to Wuhan and its surrounding areas		0.04
Yes	3.15(0.97-10.18)	
No	Ref	
Physic contact		0.06
Yes	2.31(1.05-5.06)	
No	Ref	
Shared vehicle		<0.01
Yes	3.78(1.57-9.11)	
No	Ref	
Model 3. Including household factors only		
No protective measures of contacts after index onset ^a		0.02
Yes	4.43(1.37-14.34)	
No	Ref	
Model 4. Including index case, contact and household factors		
Contact underlying medical conditions		0.03
Yes	5.99(1.81-19.83)	
No	Ref	
Contact direct exposure to Wuhan and its surrounding areas		0.01
Yes	4.14(1.25-13.68)	
No	Ref	
No protective measures of contacts after index onset		0.02
Yes	4.95(1.59-15.39)	
No	Ref	
Shared vehicle		0.02
Yes	4.37(1.80-10.58)	
No	Ref	

^aIn household level multivariate analysis, only one variable with P value less than 0.1 was eligible for further analyses.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

Figure legends:

Figure 1. Distribution of Probable or Confirmed Cases of COVID-19 by Date of Onset, Admission and Diagnosis, Zhuhai, China, 8 January–20 February 2020 (n=104)

Figure 2. Estimated cumulative distribution functions of the Incubation Period and Serial Interval of COVID-19 Infection.

Kaplan-Meier cumulative incidence of the second cases with respect to the incubation period (A) and serial interval(B) is shown by black lines, with a plot of estimates of the cumulative distribution function of log-normal distributions fit to the data represented by thick cyan and magenta lines respectively, along with 10,000 parametric bootstrapped sample estimates of the cumulative distribution function depicted by cyan and magenta shading respectively. Horizontal lines indicate the 95% CIs for the 5th, 50th, and 95th percentiles of these fitted distributions. The estimated median incubation period of COVID-19 was 4.3 days (95%CI; 3.4-5.3 days), with symptoms developing in 95% of the infected persons by 15.3 days (95%CI; 10.4 to 21.1 days) and in 5% by 1.2 days (95%CI; 0.76 to 1.8). The estimate of the dispersion parameter was 2.2 (95%CI; 1.8 to 2.5), and the estimated mean incubation period was 5.8 days. Accordingly, the serial interval of household secondary cases was estimated to be 5.1 days (95%CI; 4.3 to 6.2 days); distributions that were fit to the observed data implied that the serial interval was less than 14.8 days in 95% of cases (95%CI; 11 to 19.2 days) and less than 1.8 days in 5% of cases (95%CI; 1.4 to 2.4 days). The estimate of the dispersion parameter was 1.9 (95%CI; 1.65 to 2.2), and the estimated mean serial interval was 6.3 days.

Figure 1

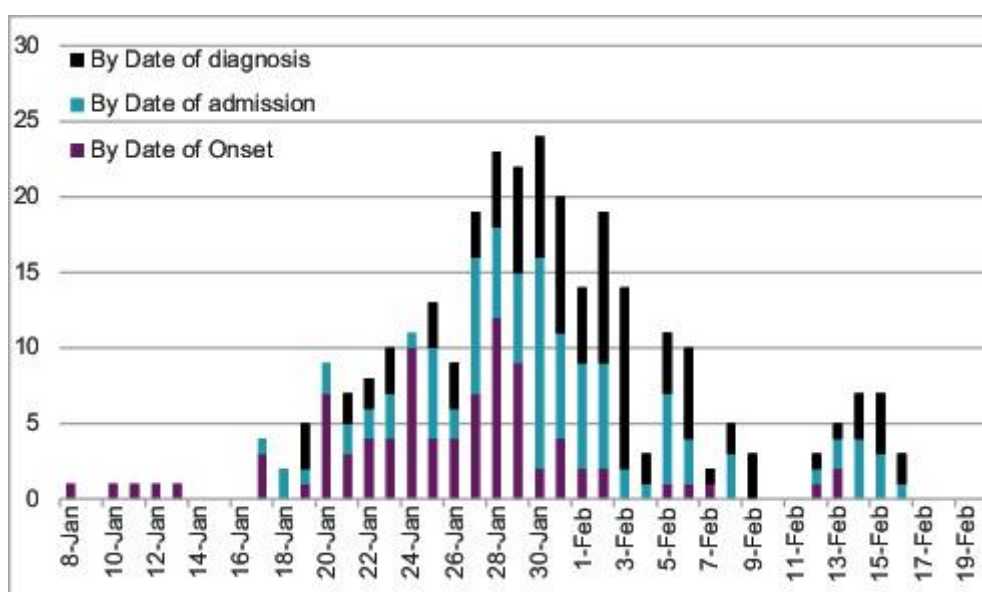


Figure 2

