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## Retrospective study identifies infection related risk factors in close contacts during COVID-19 epidemic



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### ABSTRACT

**Objectives:** This study aimed to compare the risk of infection of children with that of adults and to explore risk factors of infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by following up close contacts of COVID-19 patients.

**Method:** The retrospective cohort study was performed among close contacts of index cases diagnosed with COVID-19 in Guangzhou, China. Demographic characteristics, clinical symptoms and exposure information were extracted. Logistic regression analysis was employed to explore the risk factors. The restricted cubic spline was conducted to examine the dose-response relationship between age and SARS-CoV-2 infection.

**Results:** The secondary attack rate (SAR) was 4.4% in 1,344 close contacts. The group of household contacts (17.2%) had the highest SAR. The rare-frequency contact ( $p < 0.001$ ) and moderate-frequency contact ( $p < 0.001$ ) were associated with lower risk of infection. Exposure to index cases with dry cough symptoms was associated with infection in close contacts ( $p = 0.004$ ). Compared with children, adults had a significantly increased risk of infection ( $p = 0.014$ ). There is a linear positive correlation between age and infection ( $p = 0.001$ ).

**Conclusions:** Children are probably less susceptible to COVID-19. Close contacts with frequent contact with patients and those exposed to patients with cough symptoms are associated with an increased risk of infection.

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### Introduction

The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has posed a considerable health threat to people all over the world. World Health Organization (WHO) declared the outbreak as a Public Health Emergency of International Concern on January 30, 2020 (World Health Organization, 2020a). As of November 30, 2020, a total of 62,195,274 confirmed cases had been reported

worldwide, of which 1,453,355 have died (World Health Organization, 2020b). Therefore, exploring risk factors for COVID-19 and the susceptibility of people to this disease in different conditions is crucial to identify high-risk populations that require quarantine and targeted testing, as well as future vaccinations to effectively prevent transmission.

Several studies have reported family clustering in COVID-19 patients (Song et al., 2020; Xia et al., 2020; Qian et al., 2020). People living with confirmed patients were at a higher risk of infection than others (Li et al., 2020b). SARS-CoV-2 was more likely to be transmitted among household members through coughing, sneezing, or direct contact with virus contaminated surfaces. Studies suggested that smoking, obesity, male sex, and black ethnicity were risk factors for increased risk of infection (Ho et al., 2020; Petrakis et al., 2020; Engin et al., 2020). The elderly were considered to be susceptible to COVID-19 (Velavan and Meyer, 2020a). Older age was also recognized as an individual risk factor for more severe clinical outcomes of COVID-19, which was

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probably attributable to underlying comorbidities, such as cardiovascular diseases, diabetes and respiratory diseases (Velavan and Meyer, 2020b).

There is growing concern about the role of children in the spread of SARS-CoV-2 and the children's susceptibility to COVID-19. The clinical symptoms of infected children were generally more moderate than those of adults ((Dong et al., 2020). Children with mild symptoms or who are asymptomatic may not seek medical treatment, resulting in a lower reported incidence of cases among children than the actual situation. In this case, children, particularly asymptomatic ones with prolonged viral shedding, have the potential to be hidden drivers of the pandemic (Nikolai et al., 2020; Velavan et al., 2020; Kelvin and Halperin, 2020). However, some studies argued that children were far less important to the spread of SARS-CoV-2 than adults (Lee and Raszka, 2020; Rajmil, 2020). Children in a cluster were rarely index cases, and children with COVID-19 rarely caused outbreaks (Ludvigsson, 2020). Meanwhile, COVID-19 has shown a significantly low percentage of cases among children (Shim et al., 2020; Sun et al., 2020). No cases aged younger than 15 years were reported among the first 425 confirmed COVID-19 cases in Wuhan (Li et al., 2020a). Although confirmed cases of children have been reported since then (Xu et al., 2020; Wei et al., 2020), only 2% were under 20 years old among the 44,572 confirmed cases in China as of February 11, 2020 (Wu and McGoogan, 2020). This proportion was lower than that of the 0–20 year-old group among the total population in the country (24.1%) (National Bureau of Statistics of the People's Republic of China, 2012), which implied less susceptibility among children. However, the social activities of children are usually simpler than those of adults, especially as school suspensions have taken place in many places since the COVID-19 outbreak (Viner et al., 2020; Auger et al., 2020). The difference in exposure probability between adults and children might have contributed to the lower proportion of children's cases. The age difference of observed cases may be explained by the susceptibility to infection, the tendency of clinical symptoms, exposure probability, or all of the above. Therefore, whether children are less susceptible to SARS-CoV-2 remains uncertain.

Comparing the clinical difference between index cases and secondary cases can provide the clinical basis for studying the transmission and virulence of SARS-COV-2. Few studies have explored the differences in symptoms and clinical severity between index cases and secondary cases and the sample size of these studies was relatively small. A study (90 COVID-19 cases) by Chen et al. (2020a) showed no difference in symptoms between the index cases and secondary cases. However, there were more severe cases in the index cases than in secondary cases. Another study (Chen et al., 2020b) also found no difference in symptoms between the two groups, but secondary cases had shorter hospital stays than index cases.

In China, close contacts of all confirmed COVID-19 cases were traced by the local Center for Disease Control and Prevention (CDC) to investigate the exposure history, test SARS-CoV-2 nucleic acid and follow up on the health status. These valuable data provide a rare opportunity for us to explore the susceptibility of children to SARS-CoV-2, examine risk factors of infection and the difference of the severity of the symptoms between index and secondary cases in a prospective view by following up close contacts of COVID-19 patients.

## Methods

### Study design and participants

A retrospective cohort study was performed among close contacts of index cases diagnosed with COVID-19 in Guangzhou,

China before March 5, 2020. Based on the *Guidelines for Investigation and Management of Close Contacts of COVID-19 Cases* (Chinese Center for Disease Control and Prevention, 2020), close contacts refer to individuals who have not taken effective protection during interaction with COVID-19 confirmed cases (within one meter, e.g., sharing a meal, living in the same household, socializing, working, and traveling, etc.) within two days before the onset of symptoms of the confirmed cases. The definition of close contacts is described in Supplementary Appendix A. The index case was defined as the confirmed COVID-19 case who was the first person exposed to other sources of infection in a cluster. When the exposure time cannot be determined, the index case was defined as the case with the earliest onset of symptoms in a cluster. To study children's susceptibility to SARS-CoV-2, only the clusters including children were selected in this study. In this study, children referred to individuals aged 14 years or younger. Otherwise, people were classified as adults. As of March 5, 2020, 3410 close contacts of 391 index cases were identified in Guangzhou, of which 1344 close contacts of 100 index cases meet the criteria mentioned above, that is, there were children among the close contacts of these 100 index patients.

### Data sources and variables

Since COVID-19 has been listed as a category B notifiable infectious disease in China, such cases must be reported online through the online direct reporting system. Once a confirmed case was identified, the local CDC would be informed to initiate a detailed field investigation, including contact tracing, and finally form an epidemiological investigation report. The detailed description of contact tracing, monitoring and testing has been reported in previous studies (Luo et al., 2020; Jing et al., 2020). Briefly, all close contacts were quarantined at designated facilities for 14 days counting from the last unprotected contact with COVID-19 patients. During the quarantine period, nasal swabs were collected from each contact at least twice for reverse transcription-polymerase chain reaction (RT-PCR) testing by the Guangzhou CDC or county-level CDC, once at the beginning of the quarantine and the other near the 14th day. In addition, monitoring of clinical symptoms was performed daily by trained CDC staff. If nasal swabs were tested positive or any symptom was noticed, the contact was sent to the designated hospital for evaluation and diagnosis of infection. Individuals whose sample tested negative and did not present any symptom were dismissed after the quarantine.

Demographic characteristics, symptoms in the first clinical assessment, clinical severity, and comorbidities of cases as well as the demographic characteristics, contact frequency, and exposure history of close contacts were extracted from epidemiological investigation reports. The clinical severity of all cases was updated as the disease progressed, with the most severe stage as the final severity determination.

The clinical severity was classified as asymptomatic, mild, moderate, and severe. Cases who had no symptoms but tested positive for SARS-CoV-2 were designated as asymptomatic. Mild cases were those who had mild symptoms without sign of pneumonia on chest imaging. Cases with fever, respiratory symptoms, and imaging signs of pneumonia by computed tomography (CT) were diagnosed as moderate. Severe cases referred to those who had one of the following conditions: (i) respiratory distress, respiratory frequency  $\geq 30$ /min; (ii) oxygen saturation  $\leq 93\%$ ; (iii) arterial oxygen partial pressure/oxygen concentration  $\leq 300$  mmHg; or (iv) respiratory failure, shock, or other organ dysfunction. We classified the exposure situation of close contacts into the following categories. The contact who lived in the same household with a confirmed case was considered as

household exposure. The family members who closely interacted with cases but did not live with them were listed as non-household relatives. Vehicle exposure referred to when the contact and the confirmed case had used the same vehicle within one meter. Health care exposure included other patients in the same hospital ward, medical staff, and hospital workers without appropriate protection measures. Non-health care work exposure or social life exposure included friends, colleagues, individuals who had provided business or life services to patients, and other casual close contacts.

**Statistical methods**

Continuous variables were expressed as median and interquartile range (IQR), analyzed with the Wilcoxon rank-sum test. Categorical variables were described as counts and percentages, analyzed by the chi-square test or Fisher's exact test. Spearman's rank correlation coefficient was calculated to analyze the correlation between the clinical severity of index cases and secondary cases. The secondary attack rate (SAR), risk ratio (RR), and its 95% confidence intervals (CI) were calculated to assess the infection risk. Then, a stepwise multiple logistic regression was adopted with variable showing  $P < 0.1$  in univariate analysis to identify further characteristics or factors associated with infection. The restricted cubic spline nested in the logistic regression was used to explore the dose-response relationship between age and infection. All analyses were conducted using R Statistical Software 3.6.3. In addition to univariate analysis ( $p < 0.1$ ), a two-tailed  $p < 0.05$  was considered as the level of significance.

**Results**

*Demographics and baseline characteristics of close contacts*

The epidemiology characteristics of 1,344 close contacts of 100 index cases were analyzed. Among the 1,344 close contacts, 50.1%

(647/1344) were males, and 16.1% (216/1344) were children. Household accounted for the largest proportion of exposure settings (19.9%, 267/1344). Differences were observed in the distribution of exposure setting ( $p < 0.001$ ), contact frequency ( $p < 0.001$ ), clinical severity of index cases ( $p = 0.035$ ), and age of index cases ( $p = 0.006$ ) between child and adult contacts (Table 1).

*Demographics and clinical characteristics of index and secondary patients with COVID-19*

A total of 59 cases were detected among the total close contacts, with SAR of 4.4% (95% CI: 3.4%–5.6%). The 100 index cases, with a median age of 48.0 (IQR: 35.8–62.0) years and 51.0% (51/100) being male, were all symptomatic. In the primary clinical evaluation, fever (87.0%, 87/100) and dry cough (46.0%, 46/100) were the most common symptoms. A total of 33.0% (33/100) of index cases had comorbidities. Among the 59 cases detected in close contacts, the median age was 43.0 (IQR: 31.0–60.5) years; 40.7% (24/59) were male, and one case was asymptomatic. In the primary clinical assessments, fever (45.8%, 27/59) and dry cough (27.1%, 16/59) were the most common symptoms. A total of 18.6% (11/59) of cases had comorbidities (Table 2).

The proportions of fever ( $p < 0.001$ ), dry cough ( $p = 0.029$ ), sore throat ( $p = 0.019$ ), and myalgia ( $p = 0.030$ ) in index cases were higher than those in cases detected among the close contacts. Three secondary cases were severe cases, belonging to three different clusters, and the index cases of two clusters were also severe cases. There was no correlation between the clinical severity of index cases and secondary cases (spearman's correlation coefficient =  $-0.007$ ,  $p = 0.956$ ) (Supplementary Figure 1). Among 59 secondary cases, the proportion of females ( $p = 0.011$ ) in adults was higher than that in children. However, no differences were found in fever ( $p = 0.741$ ), dry cough ( $p = 0.713$ ), sore throat ( $p > 0.999$ ), and myalgia ( $p > 0.999$ ) (Table 2). The proportions of symptoms of shiver, expectoration, nasal congestion, rhinorrhea, headache, fatigue, joint sore, shortness of breath, dyspnoea, chest

**Table 1**  
Demographics and baseline characteristics of close contacts by age group.

Characteristic	All close contacts (n = 1344) (n(%))	Adults (n = 1128) (n(%))	Children (n = 216) (n(%))	p-value
Gender of close contacts				0.442
Male	674 (50.1)	560 (49.6)	114 (52.8)	
Female	670 (49.9)	568 (50.4)	102 (47.2)	
Exposure setting				<b>&lt;0.001</b>
Household	267 (19.9)	178 (15.8)	89 (41.2)	
Non-household relatives	261 (19.4)	200 (17.7)	61 (28.3)	
Vehicle	265 (19.7)	230 (20.4)	35 (16.2)	
Health care	210 (15.6)	205 (18.2)	5 (2.3)	
Non-health care work or social life	341 (25.4)	315 (27.9)	26 (12.0)	
Contact frequency				<b>&lt;0.001</b>
Often	333 (24.8)	231 (20.5)	102 (47.2)	
Moderate	440 (32.7)	384 (34.0)	56 (25.9)	
Rare	571 (42.5)	513 (45.5)	58 (26.9)	
Clinical severity of index case				<b>0.035</b>
Mild	299 (22.2)	244 (21.6)	55 (25.5)	
Moderate	908 (67.6)	759 (67.3)	149 (69.0)	
Severe	137 (10.2)	125 (11.1)	12 (5.5)	
Age of index case, year				<b>0.006</b>
≤40	349 (26.0)	279 (24.7)	70 (32.4)	
41–60	460 (34.2)	380 (33.7)	80 (37.0)	
>60	535 (39.8)	469 (41.6)	66 (30.6)	
Fever (index cases)				0.506
Yes	1134 (84.4)	948 (84.0)	186 (86.1)	
No	210 (15.6)	180 (16.0)	30 (13.9)	
Dry cough (index cases)				0.947
Yes	691 (51.4)	579 (51.3)	112 (51.9)	
No	653 (48.6)	549 (48.7)	104 (48.1)	

Bold indicates statistically significant values.  
Adults, age >14 years; Children, age ≤14 years.

**Table 2**  
Demographics and clinical characteristics of index and secondary patients with COVID-19.

Characteristics	Index patients (n = 100)	Patients in close contacts			p-value <sup>a</sup>	p-value <sup>b</sup>
		Total secondary cases (n = 59)	Secondary cases in adults (n = 49)	Secondary cases in children (n = 10)		
Age, years	48.0 [35.8, 62.0]	43.0 [31.0, 60.5]	54.00 [35.0, 62.0]	6.0 [1.5, 10.8]	0.136 <sup>c</sup>	–
Gender					0.273	<b>0.011<sup>d</sup></b>
Male	51 (51.0)	24 (40.7)	16 (32.7)	8 (80.0)		
Female	49 (49.0)	35 (59.3)	33 (67.3)	2 (20.0)		
Occupation					>0.999 <sup>d</sup>	>0.999 <sup>d</sup>
Health care worker	3 (3.0)	1 (1.7)	1 (2.0)	0 (0.0)		
Other	97 (97.0)	58 (98.3)	48 (98.0)	10 (100.0)		
Clinical severity					0.087 <sup>d</sup>	>0.999 <sup>d</sup>
Asymptomatic	0 (0.0)	1 (1.7)	1 (2.0)	0 (0.0)		
Mild	27 (27.0)	25 (42.4)	20 (40.8)	5 (50.0)		
Moderate	66 (66.0)	30 (50.8)	25 (51.0)	5 (50.0)		
Severe	7 (7.0)	3 (5.1)	3 (6.1)	0 (0.0)		
Signs and symptoms						
Fever	87 (87.0)	27 (45.8)	23 (46.9)	4 (40.0)	< <b>0.001</b>	0.741 <sup>d</sup>
Highest temperature	38.0 [37.6, 38.5]	38.0 [37.5, 38.2]	38.0 [37.6, 38.3]	37.8 [37.5, 38.0]	0.181 <sup>c</sup>	0.392 <sup>c</sup>
Dry cough	46 (46.0)	16 (27.1)	14 (28.6)	2 (20.0)	<b>0.029</b>	0.713 <sup>d</sup>
Sore throat	20 (20.0)	3 (5.1)	3 (6.1)	0 (0.0)	<b>0.019</b>	>0.999 <sup>d</sup>
Myalgia	16 (16.0)	2 (3.4)	2 (4.1)	0 (0.0)	<b>0.030</b>	>0.999 <sup>d</sup>
<b>Any Comorbidity</b>	33 (33.0)	11 (18.6)	11 (22.4)	0 (0.0)	0.077	0.183 <sup>d</sup>

Data were displayed by median [Interquartile range] or n (%); Bold indicates statistically significant values.

Adult, age >14 years; Children, age ≤14 years.

<sup>a</sup> Index patients vs. total secondary cases.

<sup>b</sup> Secondary cases in adults vs. secondary cases in children.

<sup>c</sup> Wilcoxon Rank-sum test.

<sup>d</sup> Fisher's exact test.

distress, chest pain, nausea, vomiting, and diarrhea did not differ among index cases and secondary cases, nor did they differ among adult and child secondary cases. See Supplementary Table 1 for the specific number of symptoms and comorbidities in each group.

#### Secondary attack rate in close contacts

The SAR of children and adults was 4.6% (10/216, 95% CI: 2.2%–8.4%) and 4.3% (49/1128, 95% CI: 3.2%–5.7%), respectively, and no differences were found between the two groups ( $p = 0.851$ ) (Table 3). The SAR of adults aged 60 years or older and adults aged 15–59 years was 10.1% (19/188, 95% CI: 6.2%–15.3%) and 3.2% (30/935, 95% CI: 2.2%–4.6%), respectively. There was no significant difference in infection risk found between children and adults aged 15–59 years (RR = 0.69, 95% CI: 0.33–1.44,  $p = 0.411$ ). Compared with children, the infection risk in adults aged 60 years or older increased (RR = 2.18, 95% CI: 0.99–4.82,  $p = 0.053$ ).

The group of household contacts and often-frequency contact had the highest risk of infection, with SAR of 17.2% (46/267, 95% CI: 12.9%–22.3%) and 16.8% (56/333, 95% CI: 13.0%–21.3%), respectively. Compared with the household group, the infection risk in the group of non-household relatives (RR = 0.20, 95% CI: 0.10–0.42,  $p < 0.001$ ), vehicle (RR = 0.02, 95% CI: 0–0.16,  $p < 0.001$ ), health care (RR = 0.03, 95% CI: 0–0.20,  $p < 0.001$ ), and non-health care work or social life (RR = 0.03, 95% CI: 0.01–0.14,  $p < 0.001$ ) decreased. Moderate contact (RR = 0.01, 95% CI: 0–0.10,  $p < 0.001$ ) and rare contact (RR = 0.02, 95% CI: 0.01–0.09,  $p < 0.001$ ) were associated with decreased risk of infection compared with often-frequency contact. The clinical severity of index cases was not associated with the risk of infection in close contacts. Compared with the mild group, the risk of infection was not significantly increased in the moderate group ( $p = 0.771$ ) and severe group ( $p = 0.201$ ). Exposure to index cases with symptoms of fever (RR = 5.28, 95% CI: 1.28–21.79,  $p = 0.008$ ) or dry cough (RR = 1.99, 95% CI: 1.14–3.47,  $p = 0.010$ ) was associated with an increased risk of infection (Table 3).

#### Association between potential risk factors and infection

Stepwise multiple logistic regression analysis was conducted based on the following factors: age of close contacts, exposure setting, contact frequency and symptoms of index cases (fever and dry cough). Results showed that rare-frequency contact (OR = 0.01, 95% CI: 0–0.04,  $p < 0.001$ ) and moderate-frequency contact (OR = 0.01, 95% CI: 0–0.05,  $p < 0.001$ ) were associated with lower risk of infection. Adult close contacts (OR = 2.40, 95% CI: 1.19–5.26,  $p = 0.020$ ) and those exposed to index cases with dry cough symptoms (OR = 2.43, 95% CI: 1.31–4.64,  $p = 0.004$ ) were associated with increased possibility to be infected (Table 4).

In the sensitivity analysis, the cutoff values of age groups of close contacts in multivariate regression were changed. Results showed that compared with children, the risk of infection was significantly higher in adults over 60 years old (OR = 5.52, 95% CI: 2.34–13.72,  $p < 0.001$ ), but not in those aged 15–59 years (OR = 1.77, 95% CI: 0.84–3.99,  $p = 0.147$ ).

Then, the restricted cubic spline analysis was applied to further examine the association between age and SARS-CoV-2 infection. After adjustment for contact frequency, contacts' gender and exposure setting, and index cases' symptoms (fever and cough), age was positively associated with infection in a linear manner ( $p$  for overall = 0.001,  $p$  for nonlinear = 0.405) (Figure 1).

#### Discussion

In this retrospective cohort study, 59 cases with COVID-19 were detected among 1344 close contacts, with an attack rate of 4.4%. The SAR in close contacts reported by other studies varied at 11.7% (Bi et al., 2020), 11.2% (Kwok et al., 2020), and 0.7% (Cheng et al., 2020) in Shenzhen, Hong Kong, and Taiwan, respectively. The present study found that secondary cases generally exhibited less severe symptoms than index cases, with fewer signs of fever, dry cough, sore throat, and myalgia, which may indicate that the

**Table 3**  
Secondary attack rate by different characteristics.

	No. of contacts (n = 1344)	No. of secondary cases (n = 59)	No. of uninfected contacts (n = 1285)	Secondary attack rate (95% CI), %	p-value	RR (95% CI)
Age of case in contacts, year						
≤14 (Children)	216	10	206	4.6 (2.2,8.4)	–	reference
>14 (Adults)	1128	49	1079	4.3 (3.2,5.7)	0.851	0.94 (0.47,1.88)
Gender of case in contacts						
Male	674	24	650	3.6 (2.3,5.3)		reference
Female	670	35	635	5.2 (3.7,7.2)	0.137	1.47 (0.86,2.49)
Exposure setting						
Household	267	46	221	17.2 (13.0,22.3)	–	reference
Non-household relatives	261	9	252	3.5 (1.6,6.4)	<0.001	<b>0.20 (0.10,0.42)</b>
Vehicle	265	1	264	0.4 (0,2.1)	<0.001	<b>0.02 (0,0.16)</b>
Health care	210	1	209	0.5 (0,2.6)	<0.001	<b>0.03 (0,0.20)</b>
Non-health care work or social life	341	2	339	0.6 (0.1,2.1)	<0.001	<b>0.03 (0.01,0.14)</b>
Contact frequency						
Often	333	56	277	16.8 (12.9,21.3)	–	reference
Moderate	440	1	439	0.2 (0,1.3)	<0.001	<b>0.01 (0,0.10)</b>
Rare	571	2	569	0.4 (0,1.3)	<0.001	<b>0.02 (0.01,0.09)</b>
Clinical severity of index case						
Mild	299	13	286	4.4 (2.3,7.3)	–	reference
Moderate	908	36	872	4.0 (2.8,5.5)	0.771	0.91 (0.48,1.74)
Severe	137	10	127	7.3 (3.6,13.0)	0.201	1.68 (0.72,3.93)
Age of index case, year						
≤60	809	31	778	3.8 (2.6,5.4)	–	reference
>60	535	28	507	5.2 (3.5,7.5)	0.275	1.37 (0.81,2.30)
Fever (index cases)						
No	210	2	208	1.0 (0.1,3.4)	–	reference
Yes	1134	57	1077	5.0 (3.8,6.5)	<b>0.008</b>	<b>5.28 (1.28,21.79)</b>
Dry cough (index cases)						
No	653	19	634	2.9 (1.8,4.5)	–	reference
Yes	691	40	651	5.8 (4.2,7.8)	<b>0.010</b>	<b>1.99 (1.14,3.47)</b>

Bold indicates statistically significant values. Abbreviations: RR, Risk ratio; CI, Confidence interval.

virulence of SARS-CoV-2 decreased in the transmission process. There was no correlation between the clinical severity of index cases and secondary cases, which may be because the clinical severity is mainly affected by host factors, such as age, comorbidities and immune function (Hoiland et al., 2020; Velavan and Meyer, 2020b; Zhang et al., 2020). Recent studies have reported that children tend to be asymptomatic or have mild

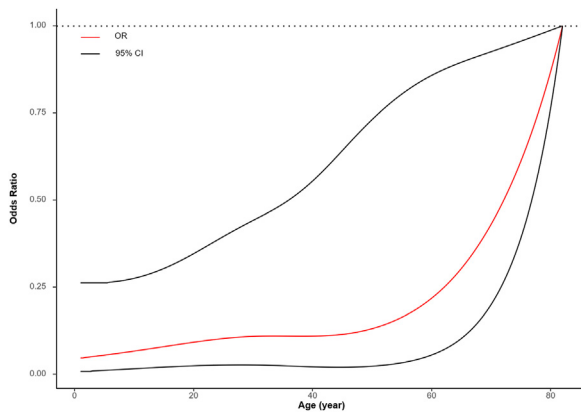
**Table 4**  
Multivariate analysis of association between potential risk factors and infection.

Characteristic	OR	95% CI	p-value
Age of case in contacts, year			
≤14 (Children)	reference	–	–
>14 (Adults)	<b>2.54</b>	<b>1.26–5.60</b>	<b>0.014</b>
Contact frequency			
Often	reference	–	–
Moderate	<b>0.01</b>	<b>0–0.04</b>	< <b>0.001</b>
Rare	<b>0.01</b>	<b>0–0.05</b>	< <b>0.001</b>
Fever (index cases)			
No	reference	–	–
Yes	2.89	0.83–18.30	0.157
Dry cough (index case)			
No	reference	–	–
Yes	<b>2.42</b>	<b>1.35–4.49</b>	<b>0.004</b>

Bold indicates statistically significant values. Abbreviations: OR, Odd ratio; CI, Confidence interval.

symptoms compared with adults (Xu et al., 2020; Dong et al., 2020). However, our study found no difference in the severity between children and adults among 59 secondary cases, which may be due to the small number of cases (10 cases in children).

The results showed that among the 1,344 close contacts, differences occurred in exposure patterns and contact frequency between the children and adult groups. The adults' exposure patterns were more diverse, but family exposure (including household and non-household relatives contact) accounted for the majority among the children. Frequent interactions between family members may explain that the often-contact accounts for the majority of children's contact frequency (47.2%), which was higher than that for adults (20.5%). The group of household contact (17.2%) and the group of often-frequency contact (16.8%) had the highest SAR. A similar attack rate (16.3% for household contact) was reported in the recent study that included 392 household contacts (Li et al., 2020b). Our results provide further time-series evidence for the easy spread of COVID-19 in households. It is worth noting that in terms of management, centralized quarantine should be adopted as much as possible to avoid the further spread of the epidemic among family members due to the difficulty of implementing household quarantine measures. No correlation was observed between household contact and infection in multivariate analysis, whereas the frequency of exposure was associated with increased risk. Therefore, we speculated that the high SAR of household contact was probably due to frequent contact among household members.



**Figure 1.** Dose-response relationship between age and the risk of being infected with SARS-CoV-2. Models are adjusted for contact frequency, contacts' gender and exposure setting, and index cases' symptoms (fever and cough).

Multivariate results showed that the dry cough symptoms in index cases were associated with an increased risk of infection in close contacts. This result was not surprising because interpersonal transmission generally occurs through droplets produced when an infected person coughs or sneezes. Thus, close contacts of index cases with dry cough symptoms need close medical attention, such as increasing nucleic acid testing to detect the infection as early as possible during the quarantine period.

Some studies had suggested that children were not susceptible to COVID-19 (Li et al., 2020b; Xu et al., 2020). However, among the 1,344 close contacts in this study, no difference in SAR was found between adults and children. We noted that the proportions of household contact and often-frequency contact in the children's group were higher than those in the adult group. The exposure bias may lead to a similar SAR in the children and adult groups. After other factors in multivariate analysis were adjusted, adults were correlated with an increased risk of infection compared with children. However, sensitivity analysis showed no significant difference in the infection risk observed between adults aged 15–59 years and children. Considering the results, we speculate that although children may not be susceptible to SARS-CoV-2, the difference between the susceptibility of children and adults aged 15–59 years was small, so that the sample size of our study was insufficient to detect the difference. Meanwhile, the elderly had a high risk of infection. The present study showed that close contacts aged 60 years or older were associated with an increased risk of infection. Thus, when compared with whole adults, the children were less susceptible to the virus. Additionally, RCS shows a linear positive relationship between age and infection risk, which also indicates that children may be less susceptible to SARS-CoV-2. A study by Patel and Verma (2020) showed that the expression of ACE2 in the nasal epithelium was age-dependent, and ACE gene expression was lower in children, which may explain their non-susceptibility to COVID-19.

Our study has several limitations. First, tracking all contacts of a confirmed case is difficult. We only quarantine individuals who had close contact with a COVID-19 case; thus, the SAR may be slightly higher. Second, the sample size of infected persons in the close contacts cohort might be too small to find differences in the clinical characteristics between adults and children. And it also caused the lower limits of the confidence intervals to be zero in some places after being rounded to two decimal places. Third, based on the setting of the index cases in this study, we could not rule out the possibility that a person who developed symptoms late, rather than the index case who we set, caused the infection of other cases in the cluster.

In summary, the findings of our study suggested that children are probably less susceptible to COVID-19, and the group of household contacts had the highest SAR. Close contacts with frequent contact with COVID-19 patients and those with exposure to patients with cough symptoms are associated with an increased risk of infection.

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## Conflict of interest

We declare no conflict of interest.

## Ethical statement

This work obtained ethical approval from the Institutional Review Board of the School of Public Health at Sun Yat-sen University (L2020001) in line with guidelines for the protection of human subjects. Analytical datasets were constructed in an anonymised manner.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijid.2020.12.011>.

## References

- Auger KA, Shah SS, Richardson T, Hartley D, Hall M, Warniment A, et al. Association between statewide school closure and COVID-19 incidence and mortality in the US. *JAMA* 2020;324(9):859, doi:<http://dx.doi.org/10.1001/jama.2020.14348>.
- Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis* 2020;20(8):911–9, doi:[http://dx.doi.org/10.1016/S1473-3099\(20\)30287-5](http://dx.doi.org/10.1016/S1473-3099(20)30287-5).
- Chen Q, Huang T, Chen M, He W, Shi Z, Lv M, et al. Clinical characteristics of COVID-19 in first and second generation cases, Chengdu. *Modern Prev Med (in Chinese)* 2020a;47(15):2843–7.
- Chen L, Yang X, Zheng N, Cai T, Hu Y, Gu J, et al. Clinical characteristics of 67 discharged cases of coronavirus disease 2019. *Chin J Nosocomiol (in Chinese)* 2020b;30(13):1942–6, doi:<http://dx.doi.org/10.11816/cn.ni.2020.200526>.
- Cheng H, Jian S, Liu D, Ng T, Huang W, Lin H, et al. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. *JAMA Intern Med* 2020;180(9):1156, doi:<http://dx.doi.org/10.1001/jamainternmed.2020.2020>.
- Chinese Center for Disease Control and Prevention. Guidelines for investigation and management of close contacts of COVID-19 cases. *China CDC Weekly* 2020;2(19):329–31, doi:<http://dx.doi.org/10.46234/ccdcw2020.084>.
- Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;e20200702, doi:<http://dx.doi.org/10.1542/peds.2020-0702>.
- Engin AB, Engin ED, Engin AB. Two important controversial risk factors in SARS-CoV-2 infection: obesity and smoking. *Environ Toxicol Phar* 2020;78:103411, doi:<http://dx.doi.org/10.1016/j.etap.2020.103411>.
- Ho FK, Celis-Morales CA, Gray SR, Katikireddi SV, Niedzwiedz CL, Hastie C, et al. Modifiable and non-modifiable risk factors for COVID-19: results from UK Biobank. *medRxiv* 2020;357, doi:<http://dx.doi.org/10.1101/2020.04.28.20083295> [Preprint]. May 2, 2020 [cited 2020 May 20].
- Hoiland RL, Fergusson NA, Mitra AR, Griesdale DEG, Devine DV, Stukas S, et al. The association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19. *Blood Adv* 2020;4(20):4981–9, doi:<http://dx.doi.org/10.1182/bloodadvances.2020002623>.
- Jing Q, Liu M, Zhang Z, Fang L, Yuan J, Zhang A, et al. Household secondary attack rate of COVID-19 and associated determinants in Guangzhou, China: a retrospective cohort study. *Lancet Infect Dis* 2020;20(10):1141–50, doi:[http://dx.doi.org/10.1016/S1473-3099\(20\)30471-0](http://dx.doi.org/10.1016/S1473-3099(20)30471-0).

- Kelvin AA, Halperin S. COVID-19 in children: the link in the transmission chain. *Lancet Infect Dis* 2020;20(6):633–4, doi:[http://dx.doi.org/10.1016/S1473-3099\(20\)30236-X](http://dx.doi.org/10.1016/S1473-3099(20)30236-X).
- Kwok KO, Wong VWY, Wei WI, Wong SYS, Tang JW. Epidemiological characteristics of the first 53 laboratory-confirmed cases of COVID-19 epidemic in Hong Kong, 13 February 2020. *Eurosurveillance* 2020;25(16), doi:<http://dx.doi.org/10.2807/1560-7917.ES.2020.25.16.2000155> pii=2000155.
- Lee B, Raszka WJ. COVID-19 transmission and children: the child is not to blame. *Pediatrics* 2020;146(2), doi:<http://dx.doi.org/10.1542/peds.2020-004879>.
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020a;382(13):1199–207, doi:<http://dx.doi.org/10.1056/NEJMoa2001316>.
- Li W, Zhang B, Lu J, Liu S, Chang Z, Cao P, et al. The characteristics of household transmission of COVID-19. *Clin Infect Dis* 2020b;(April), doi:<http://dx.doi.org/10.1093/cid/ciaa450>.
- Ludvigsson JF. Children are unlikely to be the main drivers of the COVID-19 pandemic – a systematic review. *Acta Paediatr* 2020;109(8):1525–30, doi:<http://dx.doi.org/10.1111/apa.15371>.
- Luo L, Liu D, Liao X, Wu X, Jing Q, Zheng J, 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;, doi:<http://dx.doi.org/10.7326/M20-2671>.
- National Bureau of Statistics of the People's Republic of China. The 6th National Population Census. 2012. <http://www.stats.gov.cn/tjsj/pcsj/rkpc/6rp/notepyr-ightch.htm>.
- Nikolai LA, Meyer CG, Kreamsner PG, Velavan TP. Asymptomatic SARS Coronavirus 2 infection: invisible yet invincible. *Int J Infect Dis* 2020;100:112–6, doi:<http://dx.doi.org/10.1016/j.ijid.2020.08.076>.
- Patel AB, Verma A. Nasal ACE2 levels and COVID-19 in children. *JAMA* 2020;323(23):2386, doi:<http://dx.doi.org/10.1001/jama.2020>.
- Petrakis D, Margina D, Tsarouhas K, Tekos F, Stan M, Nikitovic D, et al. Obesity a risk factor for increased COVID19 prevalence, severity and lethality (Review). *Mol Med Rep* 2020;22(1):9–19, doi:<http://dx.doi.org/10.3892/mmr.2020.11127>.
- Qian G, Yang N, Ma AHY, Wang L, Li G, Chen X, et al. COVID-19 transmission within a family cluster by presymptomatic carriers in China. *Clin Infect Dis* 2020;71:861–2, doi:<http://dx.doi.org/10.1093/cid/ciaa316>.
- Rajmil L. Role of children in the transmission of the COVID-19 pandemic: a rapid scoping review. *BMJ Paediatr Open* 2020;4(1):e722, doi:<http://dx.doi.org/10.1136/bmjpo-2020-000722>.
- Shim E, Tariq A, Choi W, Lee Y, Chowell G. Transmission potential and severity of COVID-19 in South Korea. *Int J Infect Dis* 2020;93:339–44, doi:<http://dx.doi.org/10.1016/j.ijid.2020.03.031>.
- Song R, Han B, Song M, Wang L, Conlon CP, Dong T, et al. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. *J Infect* 2020;81:e26–30, doi:<http://dx.doi.org/10.1016/j.jinf.2020.04.018>.
- Sun K, Chen J, Viboud C. Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowdsourced data: a population-level observational study. *Lancet Digit Health* 2020;2(4):e201–8, doi:[http://dx.doi.org/10.1016/S2589-7500\(20\)30026-1](http://dx.doi.org/10.1016/S2589-7500(20)30026-1).
- Velavan TP, Meyer CG. The COVID-19 epidemic. *Trop Med Int Health* 2020a;25(3):278–80, doi:<http://dx.doi.org/10.1111/tmi.13383>.
- Velavan TP, Meyer CG. Mild versus severe COVID-19: laboratory markers. *Int J Infect Dis* 2020b;95:304–7, doi:<http://dx.doi.org/10.1016/j.ijid.2020.04.061>.
- Velavan TP, Pollard AJ, Kreamsner PG. Herd immunity and vaccination of children for COVID-19. *Int J Infect Dis* 2020;98:14–5, doi:<http://dx.doi.org/10.1016/j.ijid.2020.06.065>.
- Viner RM, Russell SJ, Croker H, Packer J, Ward J, Stansfield C, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. *Lancet Child Adolesc Health* 2020;4(5):397–404, doi:[http://dx.doi.org/10.1016/S2352-4642\(20\)30095-X](http://dx.doi.org/10.1016/S2352-4642(20)30095-X).
- Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang Z. Novel coronavirus infection in hospitalized infants under 1 year of age in China. *JAMA* 2020;323(13):1313, doi:<http://dx.doi.org/10.1001/jama.2020.2131>.
- World Health Organization (WHO). Coronavirus (COVID-19) Events as They Happen. 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>.
- World Health Organization (WHO). Situation Reports. 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. *JAMA* 2020;323(13):1239, doi:<http://dx.doi.org/10.1001/jama.2020.2648>.
- Xia X, Wu J, Liu H, Xia H, Jia B, Huang W. Epidemiological and initial clinical characteristics of patients with family aggregation of COVID-19. *J Clin Virol* 2020;127:104360, doi:<http://dx.doi.org/10.1016/j.jcv.2020.104360>.
- Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med* 2020;26(4):502–5, doi:<http://dx.doi.org/10.1038/s41591-020-0817-4>.
- Zhang X, Tan Y, Ling Y, Lu G, Liu F, Yi Z, et al. Viral and host factors related to the clinical outcome of COVID-19. *Nature* 2020;583(7816):437–40, doi:<http://dx.doi.org/10.1038/s41586-020-2355-0>.