



Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study

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Summary

Background Wuhan was the first epicentre of COVID-19 in the world, accounting for 80% of cases in China during the first wave. We aimed to assess household transmissibility of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and risk factors associated with infectivity and susceptibility to infection in Wuhan.

Methods This retrospective cohort study included the households of all laboratory-confirmed or clinically confirmed COVID-19 cases and laboratory-confirmed asymptomatic SARS-CoV-2 infections identified by the Wuhan Center for Disease Control and Prevention between Dec 2, 2019, and April 18, 2020. We defined households as groups of family members and close relatives who did not necessarily live at the same address and considered households that shared common contacts as epidemiologically linked. We used a statistical transmission model to estimate household secondary attack rates and to quantify risk factors associated with infectivity and susceptibility to infection, accounting for individual-level exposure history. We assessed how intervention policies affected the household reproductive number, defined as the mean number of household contacts a case can infect.

Findings 27 101 households with 29 578 primary cases and 57 581 household contacts were identified. The secondary attack rate estimated with the transmission model was 15.6% (95% CI 15.2–16.0), assuming a mean incubation period of 5 days and a maximum infectious period of 22 days. Individuals aged 60 years or older were at a higher risk of infection with SARS-CoV-2 than all other age groups. Infants aged 0–1 years were significantly more likely to be infected than children aged 2–5 years (odds ratio [OR] 2.20, 95% CI 1.40–3.44) and children aged 6–12 years (1.53, 1.01–2.34). Given the same exposure time, children and adolescents younger than 20 years of age were more likely to infect others than were adults aged 60 years or older (1.58, 1.28–1.95). Asymptomatic individuals were much less likely to infect others than were symptomatic cases (0.21, 0.14–0.31). Symptomatic cases were more likely to infect others before symptom onset than after (1.42, 1.30–1.55). After mass isolation of cases, quarantine of household contacts, and restriction of movement policies were implemented, household reproductive numbers declined by 52% among primary cases (from 0.25 [95% CI 0.24–0.26] to 0.12 [0.10–0.13]) and by 63% among secondary cases (from 0.17 [0.16–0.18] to 0.063 [0.057–0.070]).

Interpretation Within households, children and adolescents were less susceptible to SARS-CoV-2 infection but were more infectious than older individuals. Presymptomatic cases were more infectious and individuals with asymptomatic infection less infectious than symptomatic cases. These findings have implications for devising interventions for blocking household transmission of SARS-CoV-2, such as timely vaccination of eligible children once resources become available.

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Introduction

About a year into the COVID-19 pandemic, the global cumulative incidence of cases is still climbing, reaching more than 83.6 million as of Jan 1, 2021.¹ The resumption of economic activities depends on our understanding of important transmission venues such as households, workplaces, and schools for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), drivers of transmission, and availability of effective control measures. Households are major transmission venues for many

respiratory pathogens. The WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) suggested that most epidemiologically linked clusters in China were households and urged prioritisation of studies on risk factors for household transmission.² In resource-limited areas, including Wuhan in China early on in the epidemic, isolation of cases and quarantine of close contacts often occurred at home, enabling onwards transmission within households. Although children are less likely to develop severe disease than adults,² their

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Research in context

Evidence before this study

Households offer an ideal setting for assessing person-to-person transmissibility of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and risk factors for infectivity and susceptibility to infection. We searched PubMed and medRxiv for articles published between Dec 1, 2019, and Aug 20, 2020, using the search terms (“COVID-19” OR “SARS-CoV-2” OR “2019-nCoV”) AND (“household” OR “family”) AND (“transmissibility” OR “risk factors”). We identified 22 relevant articles. Secondary attack rate estimates varied across countries from 4.6% in Taiwan to 31.6% in Zhejiang Province, China, and were mostly based on studies with fewer than 300 households. Some studies found that older age groups were associated with increased susceptibility to infection or disease, and a study in Israel identified infants as a highly susceptible group. A study in Guangzhou found no effect of age on infectivity, probably due to a small sample size. A study in South Korea reported a high infection rate among household contacts of index cases aged 10–19 years old, but not in household contacts of younger index cases. A few studies confirmed efficient presymptomatic transmission of the virus. Two studies reported much lower infectivity of asymptomatic infections than symptomatic cases, with odds ratios of 0.028 and 0.25.

Added value of this study

Based on contact-tracing records from more than 27 000 households in Wuhan up to April 18, we found that

SARS-CoV-2 was transmitted with moderate efficiency within households at the very beginning of the pandemic, with an overall secondary attack rate of 15.6% (95% CI 15.2–16.0). Children and adolescents were less susceptible to infection, but more infectious once infected, than individuals aged 20 years or older. Children’s higher infectivity was affected by household size. Our study confirmed higher susceptibility of infants (aged 0–1 years) to infection than older children (≥ 2 years of age). Although children and adolescents were much less likely to have severe disease, they were as likely as adults to develop symptoms. We confirmed the high infectiousness of cases during the incubation period and found asymptotically infected individuals were about 80% less infectious than symptomatic cases. Finally, we found isolation of cases and quarantining of household contacts away from home effectively reduced household transmission.

Implications of all the available evidence

The high infectivity of children with SARS-CoV-2 infection highlights the need for careful planning of school reopening. Additionally, the susceptibility of infants supports caregivers of infants being prioritised for vaccination. When feasible, cases could be isolated and household contacts quarantined away from their homes to prevent household transmission, particularly when presymptomatic.

ability to transmit to household contacts is not well characterised, yet it is highly relevant for preventing transmission in schools and households.

Households are ideal settings for assessing transmissibility of a pathogen and associated determinants of susceptibility and infectivity. The household secondary attack rate is defined as the probability that an infected person will transmit the pathogen to a susceptible household member during their infectious period. A meta-analysis estimated the household secondary attack rate for SARS-CoV-2 as approximately 15–22%,³ higher than the estimated rates of 5–10% for SARS-CoV and 1–5% for Middle East respiratory syndrome coronavirus.⁴ Most studies neither distinguished between secondary and tertiary transmissions nor controlled for exposure history. Some household studies revealed that children were less susceptible to the virus than older adults, and that the transmissibility of SARS-CoV-2 was inversely related to household size.^{4–6} Whether infectivity differs by age is less clear,³ in part because when there are coprimary cases within a household, it is not possible to resolve which resulted in secondary infections. The relative importance of the presymptomatic (incubation) period versus the symptomatic period has been noted or quantified in some studies.^{4,7} However, few studies have assessed the relative infectivity of asymptomatic infections, although some

modelling studies have used values extrapolated from viral load data of mild and severe cases.^{3,8,9}

Here, we present an analysis of a large number of households extracted from contact tracing records in Wuhan, the first epicentre of the COVID-19 pandemic, where 80% of confirmed cases in China were reported. We estimated the transmission probability of SARS-CoV-2 within households and evaluated drivers for infectivity of cases and susceptibility of their household contacts, while adjusting for measured confounders and individual-level exposure history. We assessed the infectivity levels of both presymptomatic cases and asymptomatic infections. Finally, we estimated the effectiveness of case isolation and quarantine of household contacts away from home in reducing household transmission in Wuhan.

Methods

Study population

In response to the COVID-19 outbreak, the Wuhan Center for Disease Control and Prevention (CDC) conducted epidemiological investigations to trace the close contacts of ascertained cases, following the Prevention and Control Plan for COVID-19 issued by the National Health Commission of China.¹⁰ The retrospective cohort analysed here includes all

laboratory-confirmed or clinically confirmed cases and laboratory-confirmed asymptomatic infections identified between Dec 2, 2019, and April 18, 2020, in Wuhan, China, together with their household contacts. Data on demographics, clinical symptoms, laboratory test results, and time and location of quarantine or isolation were recorded for all investigated individuals.

Written informed consent was waived by the National Health Commission of China for outbreak investigations of notifiable infectious diseases. All identifiable personal information was removed from the data by Wuhan CDC before any analysis. The study was approved by the ethics committee of Wuhan CDC (WHCDCIRB-K-2020012).

Definitions

COVID-19 cases were defined according to the National Health Commission of China's Guidelines for Diagnosis and Management of COVID-19, with seven editions released over the study period (appendix 2 pp 3–4). Clinically confirmed cases were defined as suspected cases of COVID-19 with typical pneumonia manifestations who were negative for SARS-CoV-2 nucleic acid by real-time RT-PCR. Laboratory-confirmed cases were individuals with positive detection of SARS-CoV-2 nucleic acid by real-time RT-PCR using respiratory specimens, and included asymptomatic infection (appendix 2 p 3). For this study, a household contact of an identified case was broadly defined as a family member or close relative who had unprotected contact with the case within 2 days before the symptom onset or test-positive specimen collection of the case but did not necessarily live at the same address. For each household, the date with the earliest symptom onset (symptomatic infection) or the first test-positive specimen (asymptomatic infection) was designated as day 1. Primary cases were defined as cases (including asymptomatic infections) who had symptom onset or the first test-positive specimens collected on day 1 or day 2, enabling households to have coprimary cases. Later cases were classified as secondary cases.

Statistical analysis

Households that shared common contacts were considered epidemiologically linked and were merged into a single household for all analyses, although we retained the original household size for analyses of household size as a risk factor (appendix 2 pp 7–8). We evaluated the overall household secondary attack rate in the primary analysis but also distinguished individuals who lived at the same address from those who did not in a sensitivity analysis.

Characteristics of primary cases, secondary cases, and uninfected or untested household contacts were compared using the χ^2 test for discrete variables and Wilcoxon rank sum test for continuous variables. The observed secondary attack rate was calculated as the proportion of secondary infections among all household contacts, assuming untested contacts were uninfected.

Total numbers of confirmed COVID-19 cases, proportions of confirmed cases among the population (ie, community-level attack rates), total numbers of contact-traced households, and average observed household secondary attack rates were mapped at the community level in Wuhan using ArcGIS (version 10.2; Esri, Redlands, CA, USA). Population data were obtained from the Hubei Health Statistics and Information Platform. A generalised estimating equation (GEE) regression model with a logistic link function and an exchangeable correlation structure for each household was used to assess individual-level and household-level risk factors for infection of household contacts. Both the observed secondary attack rate and GEE model were restricted to households with a single primary case. Both assumed that all secondary cases were infected by the primary case, and that all household contacts were equally exposed to the primary case. All descriptive analyses and the GEE modelling were done using R (version 3.6.1).

See Online for appendix 2

To account for individual-level exposure history and potential tertiary transmission, we also used a chain-binomial transmission model to estimate the secondary attack rate. This model was also used to evaluate determinants of infectivity and susceptibility to infection (appendix 2 pp 11–17). Here, both infectivity and susceptibility refer to a combination of biological effects (eg, immune response or viral shedding) and physical exposure, and our analysis cannot distinguish one mechanism from another. We assumed that each susceptible individual was exposed to any infected household members as well as a non-specific external force of infection, and that two household members had contact with each other when neither was isolated or quarantined at centralised facilities. Households with only primary cases but no exposed household contacts were excluded from the transmission analyses. A Monte Carlo expectation maximisation algorithm was used to account for uncertainties in the infection date of asymptomatic infections (appendix 2 pp 13–14).¹¹ We performed analyses under several plausible assumptions about the distributions of the incubation and infectious periods based on the literature (appendix 2 pp 9–11, 23).^{12,13} We report results assuming a mean incubation period of 5 days and a maximum infectious period of 22 days for the primary analysis. We compared household reproductive numbers, defined as the mean number of household contacts an infectious person can infect, across three time windows—before Jan 24, 2020 (before lockdown), Jan 24–Feb 10 (moderate control), and after Feb 10 (strong control)—to assess the effectiveness of general interventions such as case isolation, quarantine of close contacts, and restriction of human movement in communities (panel).

From Feb 23, 2020, all household contacts were tested for SARS-CoV-2 regardless of symptom status. Before then, a substantial number of household contacts without symptoms were not tested, creating uncertainty in their infection status. We used a two-step imputation

Panel: Timeline of key control events during the outbreak of COVID-19 in Wuhan, China

Dec 2, 2019

Symptom onset of the earliest case recorded in surveillance.

Dec 30, 2019–Jan 1, 2020

Active case finding began, the National Health Commission and WHO were notified, and Huanan Seafood Market was closed.

Jan 23, 2020

Lockdown of Wuhan was declared. All public transportation within the city and inbound and outbound transportation were suspended.

Jan 24, 2020

Patients with fever were required to self-report to community health-care centres. Individuals with mild symptoms but not identified as suspected cases were told to isolate either at home or in designated facilities. Severe or suspected COVID-19 cases were admitted to hospital.

Feb 2, 2020

The government required district-level centralised isolation and treatment of all confirmed cases, suspected cases, and feverish patients with pneumonia symptoms; quarantine of close contacts of cases at designated facilities; and reporting of asymptomatic infections.

Feb 11–13, 2020

Tightened management of all residential communities and restricted within-community movement were initiated. Communities initiated door-to-door symptom screening.

Feb 20–22, 2020

Body temperature of each resident was monitored twice a day. Discharged patients who had been admitted with COVID-19 were told to isolate for an additional 14 days at home. A 3-day campaign was initiated on Feb 20 to test (real-time PCR) all confirmed cases, suspected cases, feverish individuals, and close contacts of cases.

April 22, 2020

Public ground transportation fully returned to normal.

April 26, 2020

National Health Commission declared no hospitalised cases in Wuhan.

approach with the first step imputing infection status and the second step imputing a time interval that is informative about the potential infection time of each imputed asymptomatic infection (appendix 2 pp 17–18). The imputation involves regression models based on characteristics of the household contacts, the primary cases, and the household itself that are related to whether asymptomatic household contacts were tested or not and were potentially related to the infection outcome

(appendix 2 pp 24–25). For both the GEE analysis and the chain-binomial transmission analysis, the results were averaged over 300 sets of imputed data. Households with members with missing ages were excluded from all age-related analyses.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

From Dec 2, 2019, to April 18, 2020, 29 405 households with at least one clinically confirmed or laboratory-confirmed COVID-19 case were identified. After merging epidemiologically linked households, we obtained 27 101 households with 29 578 primary cases, including coprimary cases. These primary cases had 57 581 household contacts, consisting of 10 367 secondary cases, 29 658 test-negative contacts, and 17 556 untested contacts (table 1). The median household size (before merging) was three people (IQR 2–4), and 72·7% (21 385/29 405) of the households had two or three household members. Large households tended to be younger and were more often detected later in the epidemic (appendix 2 p 26). The median age among all cases was 56 years (43–66), and 20 760 (52·0%) cases were female. Age data were missing for 1112 test-negative or untested contacts in 806 households. Primary cases and secondary cases shared similar age and sex profiles (table 1). Compared with uninfected or untested contacts, secondary cases were older, more likely to be female, and more likely to live in smaller households (table 1). Secondary cases were more likely to be laboratory confirmed than primary cases (table 1).

The cases included in this study accounted for 76·7% (39 945/52 070) of all reported cases in Wuhan as of April 18 (appendix 2 p 20). The majority of reported cases had symptom onset between Jan 24 and Feb 10 (table 1). More cases were reported and more infected households were contact traced in densely populated districts in central Wuhan such as Wu-Chang, Jiang-Han, Jiang-An, Qiao-Kou, Han-Yang, and Hong-Shan (figure). The community-level attack rates showed a similar distribution, with higher rates in central Wuhan, but average observed household secondary attack rates were spatially more evenly distributed (figure).

Secondary cases were less severe clinically than primary cases, with more asymptomatic cases (4·2% vs 1·9%) and fewer severe or critical cases (13·9% vs 19·2%; table 1). Clinical severity was missing for 280 cases and was assumed to be mild for these cases in all subsequent analyses. Among the 4903 primary and secondary cases with symptoms recorded, the most common systemic symptoms were fever (in 2970 [60·6%]), fatigue (in 1325 [27·0%]), and myalgia (in 626 [12·8%]), and the most

	All cases (n=39 945)	Primary cases (n=29 578)	Secondary cases (n=10 367)	Test-negative or untested contacts* (n=47 214)	p value
Age, years					<0.0001†
Median (IQR)	56 (43–66)	57 (44–66)	55 (39–66)	43 (28–58)	..
<20	908 (2.3%)	413 (1.4%)	495 (4.8%)	7744/46 102 (16.8%)	..
20–59	22 642 (56.7%)	16 892 (57.1%)	5750 (55.5%)	27 749/46 102 (60.2%)	..
≥60	16 395 (41.0%)	12 273 (41.5%)	4122 (39.8%)	10 609/46 102 (23.0%)	..
Sex					<0.0001†
Female	20 760 (52.0%)	15 417 (52.1%)	5343 (51.5%)	22 674 (48.0%)	..
Male	19 185 (48.0%)	14 161 (47.9%)	5024 (48.5%)	24 540 (52.0%)	..
Household size					<0.0001†
2	16 519 (41.4%)	13 115 (44.3%)	3404 (32.8%)	8857 (18.8%)	..
3–4	17 366 (43.5%)	12 550 (42.4%)	4816 (46.5%)	22 598 (47.9%)	..
5–6	4989 (12.5%)	3276 (11.1%)	1713 (16.5%)	11 864 (25.1%)	..
>6	1071 (2.7%)	637 (2.2%)	434 (4.2%)	3895 (8.2%)	..
Clinical severity‡					<0.0001§
Asymptomatic	1006 (2.5%)	567 (1.9%)	439 (4.2%)	NA	..
Mild	20 326 (50.9%)	14 928 (50.5%)	5398 (52.1%)	NA	..
Moderate	11 504 (28.8%)	8416 (28.5%)	3088 (29.8%)	NA	..
Severe	6193 (15.5%)	4895 (16.5%)	1298 (12.5%)	NA	..
Critical	916 (2.3%)	772 (2.6%)	144 (1.4%)	NA	..
Case type					<0.0001¶
Clinical	11 441 (28.6%)	8844 (29.9%)	2597 (25.1%)	NA	..
Laboratory confirmed	28 504 (71.4%)	20 734 (70.1%)	7770 (74.9%)	NA	..
Epidemic phase (based on onset of primary case)					<0.0001¶
Before Jan 24	7599 (19.0%)	7146 (24.2%)	453 (4.4%)	11 869 (25.1%)	..
Jan 24–Feb 10	25 073 (62.8%)	18 595 (62.9%)	6478 (62.5%)	27 685 (58.6%)	..
After Feb 10	7273 (18.2%)	3837 (13.0%)	3436 (33.1%)	7660 (16.2%)	..

NA=not applicable. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Including 8619 asymptomatic contacts who might have been tested but whose laboratory test records were missing; these individuals were treated as untested in all analyses. Age data were missing for 1112 test-negative or untested household contacts. † χ^2 test comparing secondary cases to uninfected contacts. ‡Severity categories were measured at the time of clinical assessment or laboratory testing. Mild cases include 280 cases for whom severity was missing. A total of 2060 cases died. § χ^2 test comparing proportion of asymptomatic infections between secondary and primary cases. ¶ χ^2 test comparing secondary with primary cases.

Table 1: Demographic and clinical characteristics of cases and test-negative or untested contacts of SARS-CoV-2-infected households in Wuhan, China, from Dec 2, 2019, to April 18, 2020

common respiratory symptoms were dry cough (in 1776 [36.2%]), shortness of breath (in 846 [17.3%]), productive cough (in 661 [13.5%]), and chest tightness or pain (in 633 [12.9%]; appendix 2 p 27). Radiological evidence of pulmonary abnormality was confirmed in 3247 (66.2%) of 4903 cases. Secondary cases had lower rates of systemic or respiratory symptoms but a higher rate of radiological evidence than primary cases (appendix 2 p 27). Using data after Feb 22, 2020, when most household contacts were laboratory tested, we estimated the proportion of secondary cases who developed symptoms after infection (pathogenicity) to be 84.0% (95% CI 81.7–86.1; 913/1087; appendix 2 p 28). Young adults aged 20–39 years were less likely to develop symptoms upon infection than those aged 60 years or older (78.8%, 95% CI 73.0–83.8 [186/236] vs 87.5%, 83.9–90.6 [351/401]). The pathogenicity of infection in children and adolescents (84.7%, 76.0–91.2 [83/98]) resembled that of adults aged 40 years or older, although

symptomatic cases among children and adolescents were much less likely to be severe or critical than for those aged 60 years or older (2.4%, 95% CI 0.3–8.4 [two of 83] vs 18.8%, 14.9–23.3 [66/351]). Neither pathogenicity nor disease severity differed between the two sexes (appendix 2 p 28).

For the 24985 households that had only a single primary case, the overall observed secondary attack rate was 16.0% (95% CI 15.7–16.3; table 2). The secondary attack rate estimated by the chain-binomial transmission model was similar, 15.6% (15.2–16.0), under the assumption of a mean incubation period of 5 days and a maximum infectious period of 22 days (table 3; appendix 2 p 30). The model-estimated secondary attack rate for contacts living at the same residential address was 16.1% (15.6–16.5), higher than the 12.6% (11.4–13.9) rate estimated for contacts from the same household but living in different residences—eg, grandparents and grandchildren (appendix 2 p 31).

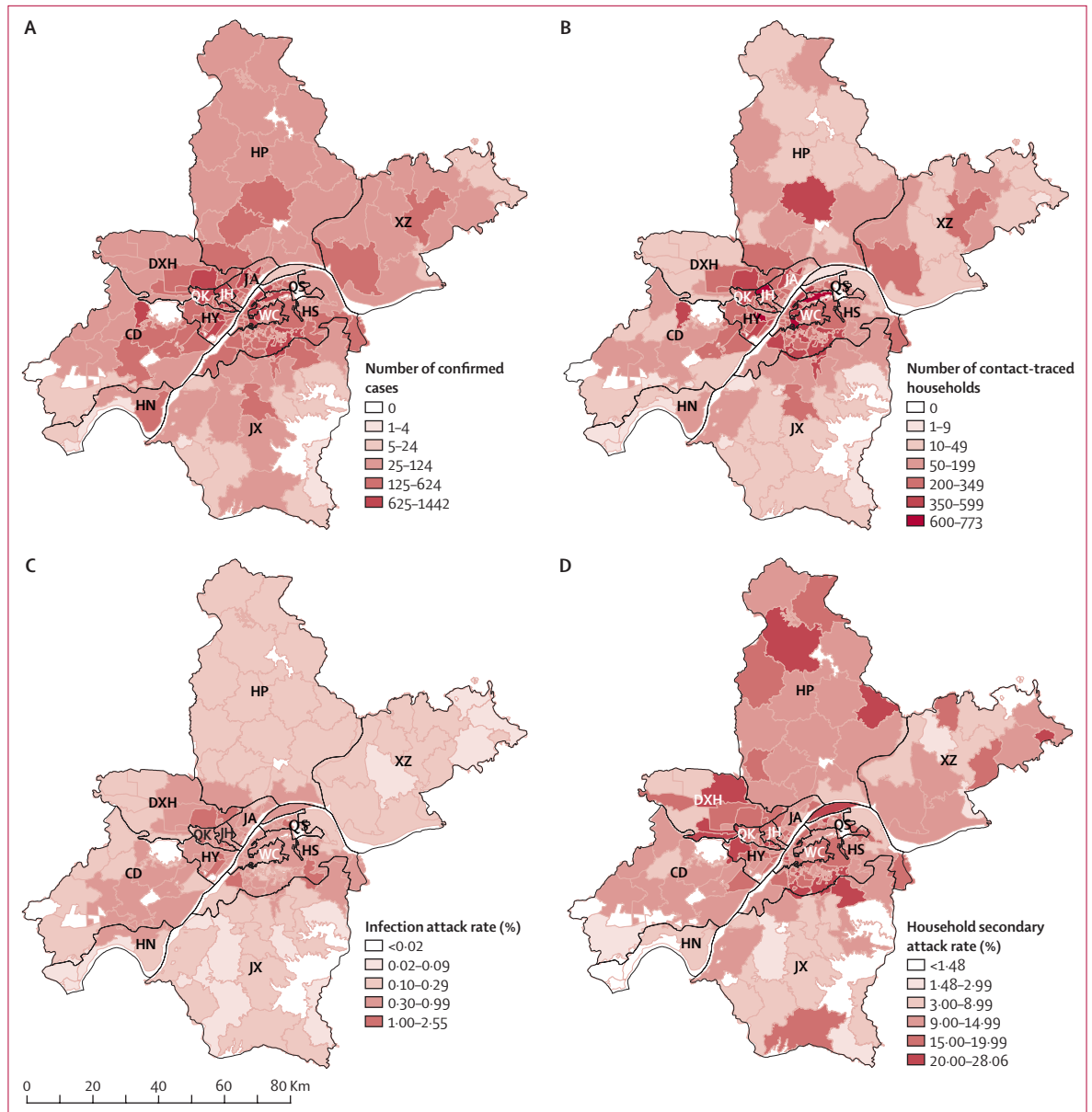


Figure: Spatial distribution of all confirmed COVID-19 cases and the retrospective cohort of contact-traced households reported during Dec 2, 2019–April 18, 2020, at the community level in Wuhan, China

(A) Distribution of all clinically or laboratory confirmed COVID-19 cases in Wuhan. (B) Distribution of all contact-traced households included in this study. (C) The community-level infection attack rate (ie, the cumulative number of confirmed cases as a percentage of the total population) in each district in Wuhan. (D) The observed household secondary attack rate (ie, the proportion of secondary infections among household contacts) among households with a single primary case included in this study. In B and D, the community of each household was determined by the community of the primary case, or the case with the earliest symptom onset if there were coprimary cases. CD= Cai-Dian. DXH= Dong-Xi-Hu. HN= Han-Nan. HP= Huang-Pi. HS=Hong-Shan. HY=Han-Yang. JA=Jiang-An. JH=Jiang-Han. JX= Jiang-Xia. QK=Qiao-Kou. QS= Qing-Shan. WC=Wu-Chang. XZ= Xin-Zhou.

Based on the chain-binomial model adjusted for all covariates, household transmissibility of SARS-CoV-2 was inversely associated with household size (table 3; appendix 2 p 32). The GEE model showed a similar household size effect (table 2). Compared with Jan 24–Feb 10, 2020, odds of daily household transmission between an infectious individual and a

susceptible individual was lower after Feb 10 (table 3). A greater reduction was seen in the observed household secondary attack rate, from near 20% in the periods before Feb 10 to 4.1% after (table 2).

In general, both the observed secondary attack rate and model-estimated odds of infection (with regard to susceptibility) increased with age of the household contacts

(tables 2, 3). Individuals aged 60 years or older were the most susceptible age group to SARS-CoV-2 infection. The least susceptible age group was children aged 2–5 years. The transmission model estimated that individuals younger than 20 years were about 66–84% (ORs ranging from 0.16 to 0.34) less susceptible than adults aged 60 years or older, and adults aged 20–59 years were 31–49% (ORs ranging from 0.51 to 0.69) less susceptible (table 3). Infants (aged 0–1 years) were more susceptible to infection than toddlers (2–5 years; OR 2.20, 95% CI 1.40–3.44) and elementary-school-aged children (6–12 years; 1.53, 1.01–2.34). Female contacts were slightly more susceptible than male contacts (table 3). The GEE model yielded similar ORs, although it estimated slightly larger differences in susceptibility between older contacts (≥ 60 years) and younger ones (table 2).

According to the transmission model, cases younger than 20 years were more likely to infect others than cases older than 60 years (table 3). Sex and disease severity did not seem to have an appreciable impact on infectivity, although disease severity was statistically associated with onwards transmission in the transmission model (table 3). Clinically diagnosed cases were less infectious than laboratory-confirmed cases (table 3). The GEE and transmission models produced largely concordant results regarding infectivity across age groups, except that the GEE model identified primary cases younger than 20 years old as being less infectious than older ones, whereas the transmission model suggested the opposite (tables 2, 3). The GEE model also found individuals older than 80 years to be similar to those aged 60–79 years in terms of both infectivity and susceptibility to infection (table 2), and these two age groups were thus combined for transmission modelling.

Both models found infected individuals who remained asymptomatic during the whole infection course to be much less infectious than symptomatic cases. The GEE model estimated an OR of 0.34 (95% CI 0.21–0.54) for asymptomatic individuals versus patients with mild and moderate disease (table 2). The transmission model estimated an OR of 0.42 (0.17–1.04) for asymptomatic versus symptomatic individuals up to Feb 1, which decreased to 0.21 (0.14–0.31) afterwards (table 3). Asymptomatic infections were formally required to be reported in Wuhan from Feb 1, which suggests greater ascertainment bias before Feb 1. For this reason, the estimated relative infectivity after Feb 1 is probably more accurate, implying that an asymptotically infected individual was associated with about 80% lower infectivity than a symptomatic case after symptom onset. When allowing infectivity to differ before and after symptom onset among symptomatic cases, the transmission model estimated the presymptomatic (incubation) period was more infectious than the symptomatic period (table 3).

When exploring how the effective household reproductive numbers changed over the pandemic

	Primary cases	Household contacts	Secondary cases	Secondary attack rate (95% CI)	Odds of infection of household contacts (95% CI)*
Overall	24 985	52 822	8447	16.0% (15.7–16.3)	..
Household size					
2	11 504	12 050	3270	27.1% (26.3–27.9)	1 (ref)
3–4	10 322	24 961	3647	14.6% (14.2–15.1)	0.56 (0.53–0.59)
5–6	2669	12 076	1231	10.2% (9.7–10.8)	0.42 (0.39–0.46)
>6	490	3735	299	8.0% (7.2–8.9)	0.39 (0.34–0.46)
Epidemic phase (based on onset of primary case)					
Before Jan 24	6462	13 968	2674	19.1% (18.5–19.8)	1.14 (1.07–1.21)
Jan 24–Feb 10	15 152	31 127	5453	17.5% (17.1–18.0)	1 (ref)
After Feb 10	3371	7727	320	4.1% (3.7–4.6)	0.25 (0.22–0.29)
Age of contacts, years†					
≤ 1	NA	264	16	6.1% (3.5–9.7)	0.32 (0.21–0.50)
2–5	NA	2018	55	2.7% (2.1–3.5)	0.15 (0.12–0.19)
6–12	NA	2693	125	4.6% (3.9–5.5)	0.23 (0.19–0.27)
13–19	NA	2263	141	6.2% (5.3–7.3)	0.27 (0.23–0.32)
20–39	NA	13 639	1627	11.9% (11.4–12.5)	0.48 (0.45–0.51)
40–59	NA	16 369	2828	17.3% (16.7–17.9)	0.65 (0.61–0.69)
60–79	NA	11 783	2985	25.3% (24.5–26.1)	1 (ref)
≥ 80	NA	1389	337	24.3% (22.0–26.6)	1.03 (0.90–1.17)
Sex of contacts					
Female	NA	25 682	4357	17.0% (16.5–17.4)	1.11 (1.05–1.18)
Male	NA	27 140	4090	15.1% (14.7–15.5)	1 (ref)
Age of primary case, years					
<20	327	793	46	5.8% (4.3–7.7)	0.66 (0.48–0.90)
20–39	4373	10 476	1350	12.9% (12.3–13.5)	0.97 (0.90–1.05)
40–59	9908	20 596	3114	15.1% (14.6–15.6)	0.98 (0.92–1.04)
60–79	9248	18 539	3489	18.8% (18.3–19.4)	1 (ref)
≥ 80	1129	2418	448	18.5% (17.0–20.1)	0.96 (0.84–1.09)
Sex of primary case					
Female	13 093	27 358	4259	15.6% (15.1–16.0)	0.96 (0.91–1.02)
Male	11 892	25 464	4188	16.5% (16.0–16.9)	1 (ref)
Clinical severity of primary case					
Asymptomatic	524	1367	27	2.0% (1.3–2.9)	0.34 (0.21–0.54)
Mild or moderate	19 556	41 030	6495	15.8% (15.5–16.2)	1 (ref)
Severe or critical	4905	10 425	1925	18.5% (17.7–19.2)	1.01 (0.94–1.08)
Ascertainment of primary case					
Clinical	7599	15 215	2028	13.3% (12.8–13.9)	0.72 (0.67–0.76)
RT-PCR	17 386	37 607	6419	17.1% (16.7–17.5)	1 (ref)

Untested contacts were treated as uninfected in the calculations. Secondary attack rates are not based on the transmission model. Odds ratios are calculated from a multivariable generalised estimating equation model. NA=not applicable. †Age was missing for 1027 contacts in 744 single-primary-case households; these households were excluded from the estimation of observed secondary attack rates by age group and from the multivariate generalised estimating equation model.

Table 2: Estimates of observed secondary attack rates among households with a single primary case

periods, we found a decrease from 0.25 (95% CI 0.24–0.26) up to Feb 10 to 0.12 (0.10–0.13) after among primary cases, marking a 52% reduction (table 4). The reduction was more substantial for secondary cases, from around 0.17 (0.16–0.18) to 0.063 (0.057–0.070), a 63% reduction.

	Mean incubation period: 5 days		Mean incubation period: 7 days	
	Maximum infectious period: 13 days	Maximum infectious period: 22 days*	Maximum infectious period: 13 days	Maximum infectious period: 22 days
Secondary attack rate				
Overall	10.4% (10.1–10.7)	15.6% (15.2–16.0)	12.3% (11.9–12.6)	17.1% (16.7–17.5)
Odds of household transmission				
Household size (vs two people)				
3–4	0.60 (0.57–0.63)	0.59 (0.56–0.62)	0.59 (0.56–0.62)	0.58 (0.55–0.61)
5–6	0.41 (0.38–0.43)	0.40 (0.37–0.42)	0.39 (0.37–0.42)	0.39 (0.36–0.41)
>6	0.32 (0.29–0.36)	0.31 (0.28–0.35)	0.31 (0.28–0.35)	0.30 (0.27–0.34)
Epidemic phase (vs Jan 24–Feb 10)				
Before Jan 24	0.74 (0.69–0.79)	0.72 (0.68–0.77)	0.79 (0.74–0.84)	0.77 (0.73–0.82)
After Feb 10	0.86 (0.77–0.96)	0.86 (0.77–0.95)	0.63 (0.56–0.70)	0.62 (0.56–0.69)
Odds of infection for an exposed household contact (susceptibility)				
Age group, years (vs ≥60)				
0–1	0.34 (0.23–0.51)	0.34 (0.23–0.51)	0.34 (0.23–0.51)	0.34 (0.23–0.51)
2–5	0.16 (0.13–0.19)	0.16 (0.13–0.20)	0.16 (0.13–0.19)	0.16 (0.13–0.19)
6–12	0.22 (0.19–0.26)	0.22 (0.19–0.26)	0.22 (0.19–0.26)	0.22 (0.19–0.26)
13–19	0.27 (0.23–0.31)	0.27 (0.23–0.31)	0.27 (0.23–0.31)	0.27 (0.23–0.31)
20–39	0.50 (0.48–0.53)	0.51 (0.48–0.54)	0.50 (0.48–0.53)	0.50 (0.48–0.53)
40–59	0.69 (0.65–0.72)	0.69 (0.66–0.72)	0.68 (0.65–0.72)	0.69 (0.65–0.72)
Female sex (vs male)	1.11 (1.06–1.16)	1.11 (1.07–1.16)	1.11 (1.06–1.16)	1.11 (1.06–1.16)
Odds of onwards transmission for an infective case (infectivity)				
Age group, years (vs ≥60)				
<20	1.65 (1.32–2.05)	1.58 (1.28–1.95)	1.41 (1.13–1.77)	1.38 (1.11–1.72)
20–39	1.12 (1.02–1.22)	1.10 (1.02–1.20)	1.08 (0.99–1.17)	1.07 (0.99–1.16)
40–59	1.02 (0.95–1.09)	1.02 (0.95–1.09)	1.02 (0.95–1.08)	1.02 (0.96–1.09)
Female sex (vs male)	0.97 (0.91–1.04)	0.98 (0.92–1.04)	0.97 (0.91–1.03)	0.97 (0.91–1.03)
Disease severity: severe or critical (vs mild or moderate)	0.91 (0.84–0.98)	0.92 (0.85–0.98)	0.94 (0.88–1.01)	0.94 (0.88–1.00)
Diagnosis: clinical (vs RT-PCR)	0.75 (0.70–0.80)	0.75 (0.70–0.80)	0.73 (0.69–0.78)	0.74 (0.69–0.78)
Asymptomatic infection (vs symptomatic)				
Up to Feb 1	0.88 (0.36–2.14)	0.42 (0.17–1.04)	0.61 (0.28–1.33)	0.29 (0.13–0.65)
From Feb 2	0.53 (0.38–0.76)	0.21 (0.14–0.31)	0.39 (0.27–0.56)	0.16 (0.11–0.24)
Before symptom onset (vs after symptom onset)	0.76 (0.68–0.85)	1.42 (1.30–1.55)	1.46 (1.31–1.63)	2.92 (2.67–3.19)

Data are secondary attack rate (95% CI) or odds ratio (95% CI). Overall secondary attack rates, regardless of characteristics of the infector, infectee, or household, were estimated with a separate model with fewer covariates than the model used to estimate odds ratios (appendix p 30), as some covariates will change the interpretation of the secondary attack rate. Estimates of baseline daily transmission probabilities within households and from an external source, as well as estimates of daily transmission probabilities between different age groups within households, are shown in the appendix (pp 32–33). *Primary analysis.

Table 3: Model-based estimates of secondary attack rates and odds ratios reflecting covariate effects on susceptibility and infectivity

The model-estimated secondary attack rate was moderately sensitive to assumptions around incubation and infectious periods, varying from 10.4% (95% CI 10.1–10.7) to 17.1% (16.7–17.5), with larger estimates associated with a longer incubation period or a longer infectious period (table 3). An extension of the infectious period to 27 days (21 days after symptom onset) led to a further increase in the secondary attack rate estimate to 17.8% (17.4–18.2; appendix 2 p 34). This sensitivity results from the fact that how the transmission model allocates secondary infections between the external force of infection and infectious household members depends on the durations of the incubation and infectious periods. Most findings about risk factors are robust to varying assumptions about

the natural history of disease (table 3). The estimated infectivity of asymptomatic infections versus symptomatic infections varied moderately (ORs 0.16–0.53) on or after Feb 2, whereas that of presymptomatic infections versus symptomatic infections varied more notably (ORs 0.76–2.92), between the extreme values for the incubation and infectious periods (table 3). When primary cases were defined as those with the earliest symptom onset or test-positive specimen collection date in their households (excluding the following day), the estimate of secondary attack rate increased slightly to 17.0% (16.6–17.4; appendix 2 p 35). Limiting analysis to the 15922 households with all contacts tested, which accounted for about 60% of all households, the estimates

	Mean incubation period: 5 days		Mean incubation period: 7 days	
	Maximum infectious period: 13 days	Maximum infectious period: 22 days*	Maximum infectious period: 13 days	Maximum infectious period: 22 days
Primary				
Before Jan 24	0.19 (0.18–0.20)	0.25 (0.24–0.26)	0.24 (0.23–0.25)	0.29 (0.28–0.30)
Jan 24–Feb 10	0.21 (0.20–0.22)	0.25 (0.24–0.26)	0.25 (0.24–0.26)	0.28 (0.27–0.28)
After Feb 10	0.12 (0.11–0.13)	0.12 (0.10–0.13)	0.10 (0.092–0.12)	0.10 (0.089–0.11)
Secondary				
Before Jan 24	0.14 (0.13–0.14)	0.17 (0.16–0.18)	0.17 (0.16–0.18)	0.20 (0.19–0.21)
Jan 24–Feb 10	0.15 (0.14–0.15)	0.17 (0.16–0.18)	0.18 (0.17–0.18)	0.19 (0.19–0.20)
After Feb 10	0.064 (0.058–0.071)	0.063 (0.057–0.070)	0.056 (0.050–0.062)	0.055 (0.049–0.061)

Data in parentheses are 95% CIs. Epidemic phases are defined by intervention policy (lockdown from Jan 23 to April 7, 2020, and tightened community management since Feb 11; panel). *Primary analysis.

Table 4: Estimates of effective household reproductive numbers for primary cases and secondary cases in different epidemic stages in 2020

of risk factors' effects were qualitatively similar, but the estimated secondary attack rates increased—eg, to 20.6% (95% CI 20.0–21.2) under the assumption of a mean incubation period of 5 days and a maximum infectious period of 22 days—suggesting households with more secondary cases were more likely to have complete testing (appendix 2 p 36). When the effect of age on infectivity was stratified by household size, the higher infectivity of children than adults was mainly limited to households with more than three members (appendix 2 p 37). The transmission model provided satisfactory goodness-of-fit to the data, especially under the longer infectious period (appendix 2 p 22).

Discussion

We characterised the transmissibility of SARS-CoV-2 within households and associated risk factors in Wuhan, China, based on a large amount of household contact-tracing data available from early in the COVID-19 pandemic. Using a statistical transmission model, we found individuals older than 60 years were more likely to be infected than the younger population, especially those younger than 20 years. Additionally, infants were more likely to be infected than older children. Once infected, children and adolescents were as likely as adults to develop symptoms, although much less likely to have severe disease. In addition, children and adolescents were more likely to infect others than were older age groups. Individuals with asymptomatic infection were less likely to infect others than were symptomatic cases. Symptomatic cases were more infectious during the incubation period than during the symptomatic period.

The estimated household secondary attack rate of SARS-CoV-2 in Wuhan is similar to that in Guangzhou (15.6% vs 15.5%) found by a previous study using comparable methods.⁴ Moreover, our observed household secondary attack rate in Wuhan (16.0%) was similar to that in Guangzhou (13.2%) and Shenzhen (14.9%), but lower than that in Beijing (23%) and Zhejiang province (31.6%).^{5,6,14,15} Secondary attack rate estimates in

mainland China have tended to be higher than those for other locations—eg, 10.5% in the USA and 4.6% in Taiwan.^{16,17} The heterogeneity in household secondary attack rates across different regions is probably due to differences in control measures, surveillance practices, and crowdedness in households.

It has been reported that children are less, and elderly adults are more, prone to severe clinical outcomes from COVID-19,^{18,19} and several studies have found that older age groups are more likely to get infected.^{4,20,21} Similar to this study, a study in Bnei Brak, Israel, observed a higher risk of infection among infants aged 0–1 years than in older children.²⁰ A possible explanation for this finding is that infants have weaker innate immune systems and closer contact with parents than older children. We also found that SARS-CoV-2 was less likely to cause symptoms upon infection among young adults in their 20s and 30s, but its pathogenicity in children and adolescents was similar to that in adults aged 40 years or older. Similar levels of pathogenicity in children were noticed before in China and South Korea based on a much smaller number of observations, but no comparison was made with other age groups in those studies.^{22,23}

Using the transmission model, we found that cases younger than 20 years were nearly 60% more likely to infect others than cases aged 60 years or older. This finding seems to contradict the observed secondary attack rates of the two groups and the GEE-based odds ratio estimates (table 2). The observed secondary attack rate and the GEE model did not account for individual-level exposure history and should be interpreted as unconditional results—ie, not adjusted for the amount of exposure. By contrast, the chain-binomial model evaluated how risk factors change transmission probability per daily exposure. In addition, GEE-based estimates did not consider tertiary transmissions from secondary cases to household contacts. We found children with SARS-CoV-2 infection, particularly those who were secondary cases, were more likely than adults to infect household members who were actually exposed

to them during their infectious periods (appendix 2 pp 18–19, 29). This fact, together with the much faster isolation of child cases (appendix 2 p 38), which implied a short duration of exposure of contacts to infected children, supports the higher infectivity of children than adults suggested by the chain-binomial model. A survey during the early epidemic phase in Wuhan found higher contact frequency between the age groups 0–20 years and 30–50 years than between any other age groups, which could explain in part the higher infectivity of children.²⁴ The infectivity of children could be modified by other factors, which merits further investigation. For example, the higher infectivity of children than of adults was mainly limited to households with more than three members in our study. Moreover, a recent study in South Korea reported a high infection rate among household contacts of index cases aged 10–19 years but not among household contacts of younger index cases.²⁵

Using the transmission model on data available after Feb 1, we estimated that individuals with asymptomatic infections were about 80% less likely to infect others than symptomatic cases. While it has long been speculated that individuals with asymptomatic infection can transmit the disease, strong epidemiological evidence has been scarce, and a reliable assessment of the relative infectivity of asymptomatic infections versus symptomatic infections was lacking before this study.^{3,26,27} A study in Anhui province of China compared secondary attack rates among general contacts between 131 individuals with asymptomatic infections and 16 symptomatic cases, with an OR of 0.25.²⁸ All 16 symptomatic cases tested positive before symptom onset, implying the possibility of selection bias. A recent meta-analysis estimated household secondary attack rates to be 19.9% for symptomatic index cases and 0.7% for asymptomatic ones, suggesting an OR of 0.028, which is much lower than our estimate of 0.21.³ Some modelling studies extrapolated the relative infectivity of asymptomatic or subclinical infections from viral load dynamics of mild and severe cases, and their results tended to be lower than our estimates.^{8,9}

Our results show the importance of isolating cases and quarantining household contacts outside of the home to prevent onwards transmission within households. During the period Jan 24–Feb 10, when many people with mild COVID-19 were isolated at home, the observed secondary attack rate and the model-estimated effective reproductive number within households remained essentially unchanged compared with before Jan 24 (tables 2, 4). When massive case isolation and quarantine of household contacts at designated places reached full coverage near mid-February, both the observed household secondary attack rate and household effective reproductive numbers were substantially reduced, consistent with a previous modelling study.²⁹ Such dramatic reduction in household transmissibility of the virus was mainly driven

by the reduced number of days of exposure of household contacts to the cases due to the interventions (appendix 2 pp 21, 29). The daily transmission probability between an infectious case and an exposed household contact was, however, less affected by the interventions (table 3). More dramatic reduction in transmissibility for secondary cases than for primary cases was expected, as the household contacts were still exposed to primary cases during their incubation period before isolation or quarantine occurred (appendix 2 pp 21, 29).

Our study has several limitations. Although we have imputed asymptomatic infections among untested contacts in the early stage, bias cannot be ruled out as there was no protocol for laboratory testing and there could be unmeasured confounders not adjusted for in the imputation. Asymptomatic infections might still have been under-detected even after household contacts were universally tested. The overall proportion of asymptomatic infections after Feb 22 was 16%, somewhat lower than the 18% or 32% observed (depending on whether abnormal lung CT is counted as a clinical sign) in the outbreak on the *Diamond Princess* cruise.^{30,31} The GEE analysis was applied only to households with a single primary case, but these households tended to have more secondary cases aged 60 years or older (appendix 2 p 39), which might affect the generalisability of the GEE results. In addition, our data do not offer strong evidence in favour of any particular scenario of the incubation and infectious periods, and the variation in results across the different assumptions should be considered as part of the uncertainty in these estimates. Finally, we merged epidemiologically linked households, but the mixing pattern between these households could be more complex than what was assumed.

Our study has implications for forecasting and control of the global pandemic of SARS-CoV-2. Differential susceptibility and infectivity between age groups, as well as other epidemiological parameters estimated in this study, are key inputs for modelling studies projecting the future trajectory of the pandemic. The relatively high infectivity of children in households should be considered carefully when making decisions around school reopenings, as infected children can pass the virus to their family members. Finally, given the vulnerability of infants to infection, their caregivers should be prioritised for vaccination.

Contributors

FL, X-BY, H-JW, P-LL, Y-HP, Y-QY, SL, and GL contributed to the epidemiological investigation and collected the data. YY, S-QX, and Y-YL conceived the statistical analysis plan. M-JL, Y-YL, FL, L-QF, and QL accessed, verified, and analysed data under the supervision of YY and S-QX. Y-YL and YY drafted the manuscript. All authors contributed to interpretation of results and critical revision.

Declaration of interests

We declare no competing interests

Data sharing

Data for plotting the main figure and figure S1 are available online for download. Individual-level data will not be made publicly available with

For the figure data see https://ufloida-my.sharepoint.com/:f/g/personal/yangyang_ufl_edu/Ei-U0gqXRhNDixONBcXlmBkBCtSBHdm4LhZOQvdUjh2FA

this Article. Requests for sharing of deidentified individual-level data or aggregated household data for scientific research can be directed to FL (lifang@whcdc.org). All proposals will be subject to scientific review and institutional review board approval at Wuhan CDC, and all approved data requestors will need to sign a data use agreement.

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