SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study

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Summary

Background The proportion of asymptomatic carriers and transmission risk factors of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among household and non-household contacts remains unclear. In Singapore, extensive contact tracing by the Ministry of Health for every diagnosed COVID-19 case, and legally enforced quarantine and intensive health surveillance of close contacts provided a rare opportunity to determine asymptomatic attack rates and SARS-CoV-2 transmission risk factors among community close contacts of patients with COVID-19.

Methods This retrospective cohort study involved all close contacts of confirmed COVID-19 cases in Singapore, identified between Jan 23 and April 3, 2020. Household contacts were defined as individuals who shared a residence with the index COVID-19 case. Non-household close contacts were defined as those who had contact for at least 30 min within 2 m of the index case. All patients with COVID-19 in Singapore received inpatient treatment, with access restricted to health-care staff. All close contacts were quarantined for 14 days with thrice-daily symptom monitoring via telephone. Symptomatic contacts underwent PCR testing for SARS-CoV-2. Secondary clinical attack rates were derived from the prevalence of PCR-confirmed SARS-CoV-2 among close contacts. Consenting contacts underwent serology testing and detailed exposure risk assessment. Bayesian modelling was used to estimate the prevalence of missed diagnoses and asymptomatic SARS-CoV-2-positive cases. Univariable and multivariable logistic regression models were used to determine SARS-CoV-2 transmission risk factors.

Findings Between Jan 23 and April 3, 2020, 7770 close contacts (1863 household contacts, 2319 work contacts, and 3588 social contacts) linked to 1114 PCR-confirmed index cases were identified. Symptom-based PCR testing detected 188 COVID-19 cases, and 7582 close contacts completed quarantine without a positive SARS-CoV-2 PCR test. Among 7518 (96·8%) of the 7770 close contacts with complete data, the secondary clinical attack rate was 5·9% (95% CI 4·9–7·1) for 1779 household contacts, 1·3% (0·9–1·9) for 2231 work contacts, and 1·3% (1·0–1·7) for 3508 social contacts. Bayesian analysis of serology and symptom data obtained from 1150 close contacts (524 household contacts, 207 work contacts, and 419 social contacts) estimated that a symptom-based PCR-testing strategy missed 62% (95% credible interval 55–69) of COVID-19 diagnoses, and 36% (27–45) of individuals with SARS-CoV-2 infection were asymptomatic. Sharing a bedroom (multivariable odds ratio [OR] 5·38 [95% CI 1·82–15·84]; p=0·0023) and being spoken to by an index case for 30 min or longer (7·86 [3·86–16·02]; p<0·0001) were associated with SARS-CoV-2 transmission among household contacts. Among non-household contacts, exposure to more than one case (multivariable OR 3·92 [95% CI 2·07–7·40], p<0·0001), being spoken to by an index case for 30 min or longer (2·67 [1·21–5·88]; p=0·015), and sharing a vehicle with an index case (3·07 [1·55–6·08]; p=0·0013) were associated with SARS-CoV-2 transmission. Among both household and non-household contacts, indirect contact, meal sharing, and lavatory co-usage were not independently associated with SARS-CoV-2 transmission.

Interpretation Targeted community measures should include physical distancing and minimising verbal interactions. Testing of all household contacts, including asymptomatic individuals, is warranted.

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Introduction

The COVID-19 pandemic has resulted in 1 119 431 deaths as of Oct 21, 2020.[1] There is concern about the high rate of complications and mortality from reported COVID-19 cases, which has triggered community-wide lockdowns in an attempt to contain disease spread.[2–4]

The full spectrum of disease severity and mortality from COVID-19 and the risk factors that result in infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are unknown because of the limitations of routine case detection and surveillance systems.[5] Symptom-based testing strategies based on

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For the Mandarin translation of the abstract see Online for appendix 1

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Research in context

Evidence before this study

As of Aug 4, 2020, our search of PubMed using keywords "COVID-19" OR "SARS-CoV-2" AND "secondary attack rate" yielded 17 articles in English that have estimated the secondary attack rate in various groups. Of these studies, 11 (from mainland China, Hong Kong, Taiwan, and South Korea) examined secondary attack rates among community cohorts, while the others were limited to specific close-contact settings. The various community cohort studies analysed 27 to 585 index cases and 106 to 4007 close contacts, and reported household attack rates ranging from 7·6% to 23%. None of the studies examined seroprevalence. Three studies identified independent exposure risk factors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: being in the same household and travelling together with an index case (a study in Shenzhen, China), age older than 18 years and spousal relationship with an index case (a study in Wuhan, China), and age 60 years or older (a study in Guangzhou, China).

Added value of this study

We used contact tracing data from 7770 close contacts (1863 household contacts, 2319 work contacts, and 3588 social contacts) of PCR-confirmed COVID-19 cases who were placed under 2-week quarantine and referred for PCR testing if symptomatic. Additionally, a subset of 1150 close contacts (524 household contacts, 207 work contacts, and 419 social contacts) consented for serology testing after completion of quarantine and were assessed by a detailed symptom and risk factor questionnaire. Extensive contact tracing, thorough follow-up of contacts during and after quarantine, and low community prevalence enabled clear case–contact relationships to be established and rigorous asymptomatic case identification. Using Bayesian modelling, we estimated that the symptom-based PCR testing strategy missed more than half of SARS-CoV-2 positive close contacts and that more than a third of SARS-CoV-2-positive close contacts were asymptomatic. The risk factor analysis identified longer duration of verbal interaction and sharing a bedroom as independent exposure risk factors of SARS-CoV-2 transmission to household close contacts. For non-household close contacts, the exposure risk factors independently associated with SARS-CoV-2 transmission were longer duration of verbal interaction, sharing a vehicle, and having contact with more than one index case. Among both household and non-household contacts, indirect contact, meal-sharing, and lavatory co-usage were not independently associated with SARS-CoV-2 transmission.

Implications of all the available evidence

The available findings, including those from our study, support physical distancing and minimising verbal interactions as part of community measures for prevention of SARS-CoV-2 transmission. In view of the substantial prevalence of asymptomatic infections, routine testing of close contacts regardless of symptoms will reduce missed diagnoses. Household close contacts, who are at high risk of SARS-CoV-2 transmission, should be prioritised for routine testing. Detection of SARS-CoV-2-positive household close contacts would prompt either relocation of the person out of the household or implementation of physical distancing and other infection prevention measures within the household.

reverse-transcription PCR tests are unlikely to identify asymptomatic infections or relatively mild cases that do not present to the health-care system.[6,7] As such, seroprevalence studies are important to determine the extent of infection in the community to influence public health strategies.

Additionally, understanding individual-level exposure risk factors that lead to SARS-CoV-2 infection is important to formulate targeted public health measures, as community-wide measures such as lockdowns are associated with severe adverse socioeconomic consequences and are not sustainable in the long term. Exposure risk factors have been studied in specific situations, such as an outbreak in a long-term care facility[8] and as a result of singing activities.[9] In the general community, a study of close contacts from Guangzhou, China, determined symptom severity as a factor correlating with SARS-CoV-2 transmission.[10]

We systematically investigated the overall prevalence of SARS-CoV-2 infection and epidemiological risk factors among exposed individuals in Singapore, an island city-state in southeast Asia with a population of 5·8 million people. Since the identification of the first imported COVID-19 case in Singapore on Jan 23, 2020, contact tracing and active case finding was done for every COVID-19 case detected in the community to identify all close contacts, who were then prospectively monitored under 14-day quarantine at home. Contacts who reported symptoms were admitted to the hospital for COVID-19 testing by PCR. This closely monitored cohort of contacts provided a unique opportunity to determine attack rates on the basis of symptom-based PCR tests and follow-up serological surveys, coupled with questionnaires to determine the prevalence of asymptomatic infection. As unique index–contact pairs were known, individual-level exposure risk factors associated with SARS-CoV-2 infection could be determined by use of exposure-risk questionnaires to inform targeted community prevention strategies.

Methods

Case definitions and COVID-19 management

In this retrospective cohort study, we analysed close contacts of confirmed COVID-19 cases identified in Singapore between Jan 23 and April 3, 2020. Since Jan 2, 2020, surveillance for COVID-19 in Singapore has been done according to regularly updated Ministry of Health criteria for suspected COVID-19, which are circulated to all physicians in Singapore (appendix 2 pp 1, 2). In

See Online for appendix 2

brief, COVID-19 testing was mandated for individuals with acute respiratory illness and relevant epidemiological exposures (travel to high-risk areas or close contact with a person with confirmed COVID-19). From Jan 31, 2020, all inpatients with clinical or radiological features of pneumonia were tested.[11] Additionally, physicians could exercise clinical judgment and test individuals who did not overtly fulfil suspected COVID-19 criteria. Physicians were required by law, under the Infectious Diseases Act, to report all COVID-19 cases to the Ministry of Health. Confirmed COVID-19 cases were defined as individuals with positive detection of SARS-CoV-2 nucleic acid by real-time RT-PCR of respiratory specimens.[12]

Contact tracing was done by the Ministry of Health for every diagnosed COVID-19 case.[13] Household contacts were defined as individuals who shared the same residential address as the index case, regardless of duration or proximity of contact. Among non-household contacts, the Ministry of Health defined close contacts as individuals who had contact for at least 30 min within a 2 m distance from the index case—these individuals were considered at high risk of exposure to SARS-CoV-2 and developing infection, and were placed under strict quarantine by law.[13,14] Other contacts who were with the index case for 10–30 min within 2 m were deemed lower-risk contacts and placed under health surveillance by telephone; we excluded these individuals from the present analysis as there were few infections in this group. Work contacts were defined as individuals who came into close contact with the index case at work, from 2 days before the onset of symptoms to isolation of the case, to account for pre-symptomatic transmission.[15] Social contacts were defined as individuals who came into close contact with the index case, from 2 days before onset of symptoms to isolation of the case, through social activities. Transport contacts—those in any mode of transportation and not in any of the previous categories—and uncategorised contacts were excluded from the analyses.

Close contacts were placed under legally enforced quarantine for 14 days from the last day of exposure. During quarantine, they were not allowed to leave their residence or assigned location. Public health officials assessed all contacts via telephone for fever or respiratory symptoms thrice daily. Symptomatic contacts were transferred to hospital via a dedicated ambulance for clinical evaluation and COVID-19 testing. The National Centre for Infectious Diseases was the designated national screening centre but in some cases contacts were transferred to other hospitals (eg, paediatric cases were transferred to KK Women and Children's Hospital). All individuals diagnosed with COVID-19 were admitted to hospital and remained in isolation until they were discharged, following at least two consecutive negative PCR tests on respiratory specimens collected 24 h apart.

This work was completed as part of an outbreak investigation under the Singapore Infectious Diseases Act and approved by the Ministry of Health.[16] All data and samples collected were de-identified before analysis, and only public health officers appointed by the Ministry of Health and with clearance were granted access to personally identifiable information.

Epidemiological risk factor and seroprevalence determination

Comprehensive data on the index case and close contacts were extracted from the Ministry of Health's contact tracing database. For index cases, demographic information, date of symptom onset, and date of hospital admission were obtained. For close contacts, demographic information, COVID-19 status based on PCR confirmation, contact type, and contact information were obtained.

All household, work, and social contacts identified between Jan 23, 2020 (date of identification of the first COVID-19 case in Singapore) and April 3, 2020, were approached for informed consent via telephone, to participate in a risk factor questionnaire (appendix 2 pp 3–6) and a one-time blood draw for SARS-CoV-2 serology testing. Contacts diagnosed with COVID-19 via symptom-based testing during quarantine were only asked to answer the risk factor questionnaire and were not approached for serology testing. We excluded individuals who were younger than 4 years, unable to answer the risk factor questionnaire because of inability to identify the index case that they were exposed to, and unable to travel to designated clinic locations for blood draw. For individuals younger than 21 years, assent was obtained and then consent was obtained from at least one parent or guardian. Close contacts were classified as uncontactable after a minimum of three unsuccessful call attempts.

Consenting individuals answered the 70-point risk-factor questionnaire, adapted from the WHO household transmission investigation protocol.[17] The questionnaire was filled out either by telephone interview or through an online web-based application. It covered demographic information, relationship with the known COVID-19 index case or cases, exposure attributes during contact with the case or cases during the defined time interval, medical history (previous diagnosis of severe acute respiratory syndrome [SARS] or Middle East respiratory syndrome, or both, and chronic medical illness), and travel history. The date of onset and type of clinical symptoms experienced by the individual, if any, were also recorded. The questionnaire assessed specifically for fever (measured temperature of ≥38°C), cough, sore throat, shortness of breath, runny or blocked nose, diarrhoea, abdominal discomfort, muscle ache, fatigue, and other symptoms. Under other symptoms, individuals were asked to specify any additional symptoms not listed above. Asymptomatic individuals were defined as those who reported no symptoms at all. The relevant time interval for transmission risk factors was defined as the period 2 weeks before the start of the individual's quarantine or admission to hospital for a COVID-19 diagnosis (or the earlier date if both were applicable) until discharge from quarantine or hospital.

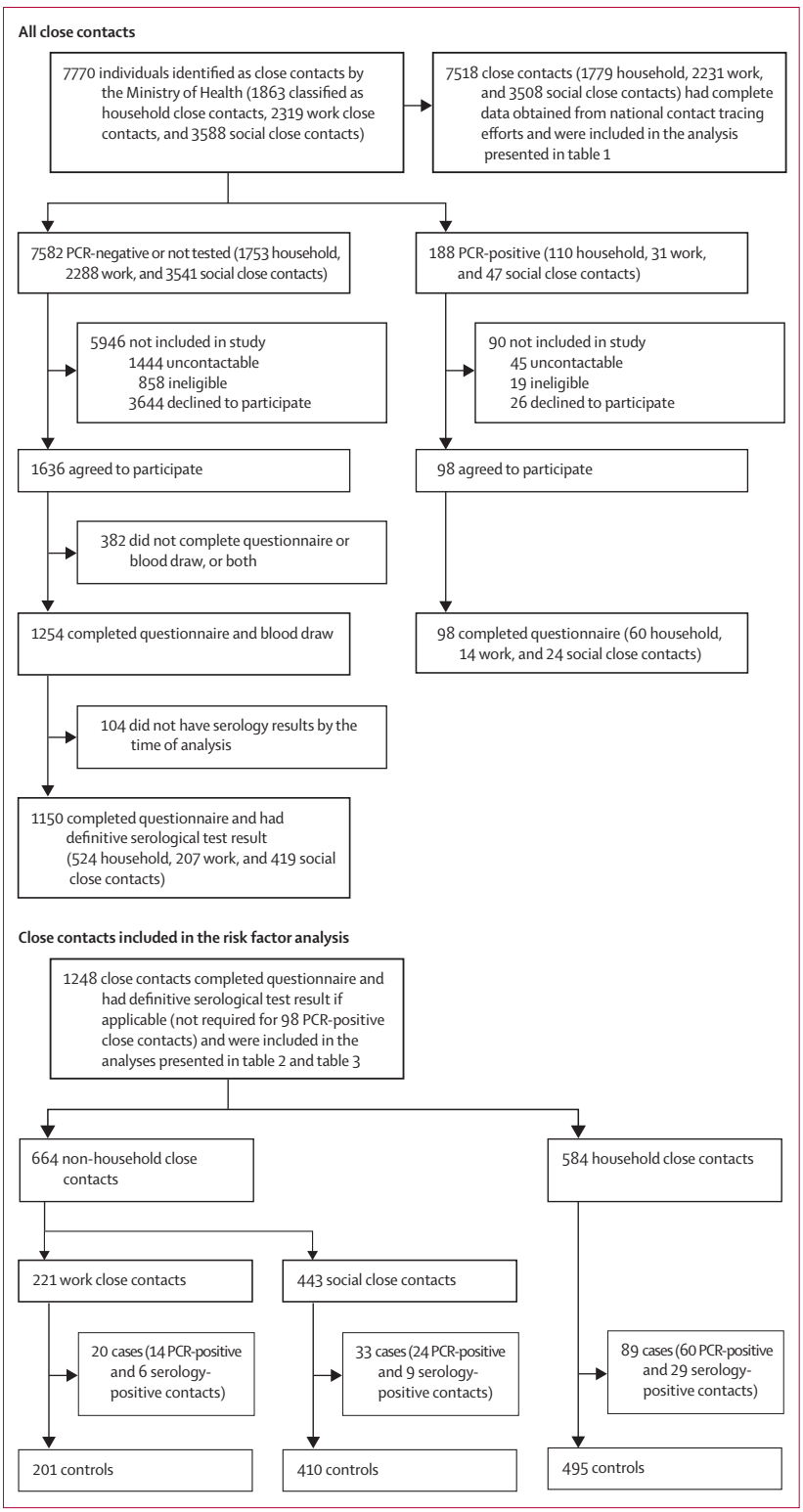

Figure 1: **Disposition of individuals identified by the Ministry of Health as close contacts of COVID-19 cases**

Consenting individuals who completed quarantine without a positive SARS-CoV-2 PCR test underwent blood draw for serology. To avoid blood samples being taken too soon for seroconversion to be detected, the appointment for blood draw was given at least 2 weeks after the quarantine end date, contingent on the participant's availability. Information about the median time interval from entering quarantine to the date of serology testing was collected. Blood samples were processed at Singapore's National Centre for Infectious Diseases. Serum samples were tested with a surrogate viral neutralising assay for detection of neutralising antibodies to SARS-CoV-2.[18] A positive serological test result was concluded if the surrogate viral neutralising assay for a particular sample resulted in inhibition of 30% or greater (98·9% sensitivity and 100·0% specificity), as previously reported and validated by Tan and colleagues[18] (serological methods are described in appendix 2 p 6).

Statistical analysis and modelling

As defined by WHO, the secondary clinical attack rate was derived from symptom-based PCR test results of close contacts, stratified by household, work, and social categories, with the R software (version 3.5.0 [64 bit]). We tested for clustering in secondary attack rates within location types by comparing binomial and beta-binomial models, using the likelihood ratio test (detailed in appendix 2 p 9).

We used Bayesian inference to fit a model accounting for PCR testing and serological sensitivities, probabilities of symptoms if infected or not, and participation in serological testing, to data on the number of PCR-confirmed or serologically confirmed infections among residential, work, and social contacts, and overall. The approach, described in full in appendix 2 (pp 9–22), was motivated by the need to accommodate contacts who did not consent for serology and the risk of false negative results from the tests, resulting in incomplete data. The method involved identifying 16 combinations of true infection status, symptom presence, testing and test outcomes, and the associated probabilities of each under a probability tree model (appendix 2 pp 9–10). As not all combinations could be uniquely determined from the data, categories were merged by summing probabilities, and a multinomial distribution for the number of participants in each category or merged category used to define a likelihood function for the parameters, which included the probability of infection, the symptomatic fraction among both infected and uninfected individuals, the proportions of symptomatic contacts tested with PCR and serology, and the sensitivity of both assays. Uniform prior distributions were assumed for all parameters except for the sensitivity of the serological assay, which was given a beta prior to match previous performance.[18] The posterior distribution of the parameters was sampled with a Markov chain Monte Carlo sampler as described in appendix 2 (pp 11–12), and other estimands were derived

through operations to the parameter samples. Convergence was assessed visually (traceplots are provided in appendix 2 pp 13–19). Details of the Bayesian model used and the R code are also provided in appendix 2 (pp 20–22).

We used univariable and multivariable logistic regression models, implemented with Stata, version 15.0, to assess the association between transmission risk factors and SARS-CoV-2 infection among household contacts and non-household (work and social) contacts. Cases included both PCR-confirmed cases and individuals with a positive SARS-CoV-2 serology result. Controls were defined as individuals who completed quarantine without a COVID-19 diagnosis and had a negative serology test. We selected variables that were representative of different potential modes of SARS-CoV-2 transmission for the multivariable regression analysis and included variables with an exposure prevalence of more than 10%, a greater effect size on univariable analysis, and which were significant ($p<0·05$). The Wald χ^2 test was done for all risk factors with a two-sided α level of 0·05. R software (version 3.5.0 [64 bit]) was used for analysis, unless otherwise specified.

Role of the funding source

The sponsor 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 the corresponding author had final responsibility for the decision to submit for publication.

Results

Between Jan 23 and April 3, 2020, there were 1114 PCR-confirmed COVID-19 index cases in the community in Singapore. 13 026 close contacts of these cases were identified, of whom 1863 were household contacts, 2319 were work contacts, 3588 were social contacts, 2626 were transport contacts, and 2630 were uncategorised. Transport and uncategorised close contacts were excluded from the analysis. Of 7770 close contacts (24·0% household, 29·8% work, and 46·2% social), 7582 completed quarantine without a COVID-19 diagnosis by symptom-based PCR testing, and 188 symptomatic contacts were identified as positive cases. 1150 (15·2%) of the 7582 contacts without a COVID-19 diagnosis completed serological testing and the exposure risk questionnaire by the time of analysis. 98 (52·1%) of the 188 contacts with a COVID-19 diagnosis completed the exposure risk questionnaire (figure 1).

Of the 7770 close contacts, 7518 (96·8%) with complete data obtained as part of national contact tracing efforts, regardless of participation in the study's risk assessment questionnaire and serology testing, including national case number (or numbers) of linked index case (or cases), age of index case (or cases), symptom duration of index case (or cases) before hospital admission, age of contact, sex of contact, and symptom-based PCR result of contact were analysed. 84 (4·5%) of 1863 household contacts, 88 (3·8%) of 2319 work contacts, and 80 (2·2%) of 3588 social contacts had one or more relevant fields with missing data and were excluded from this analysis (table 1). The median age of close contacts was 33 years (IQR 21–49) and 3922 (52·2%) were female. The median interval between symptom onset and admission to hospital for the index case was 5 days (IQR 2–7). Among household contacts (n=1779) there were 578 unique contact groups, with a median of three contacts per group (IQR 2–4). Among work contacts (n=2231) there were 225 contact groups, with a median of five contacts per group (IQR 2–12); and among social contacts (n=3508) there were 346 contact groups, with a median of three contacts per group (IQR 1–7).

Of the 1779 household contacts analysed, 468 (26·3%) underwent symptom-based SARS-CoV-2 PCR testing. Symptom-based PCR testing was done for 332 (14·9%) of 2231 work contacts and 458 (13·1%) of 3508 social contacts.

	Household (n=1779)	Work (n=2231)	Social (n=3508)
Median age of contacts, years (IQR)	35 (22–53)	38 (30–49)	28 (10–47)
Number of female contacts (%)	1046 (58·9%)	1064 (47·7%)	1832 (52·2%)
Number of unique index cases linked to all contacts	581	225	347
Median age of unique index cases linked to all contacts, years (IQR)	39 (26–54)	39 (30–50)	39 (27–54)
Number of female cases among unique index cases linked to all contacts (%)	244 (42·0%)	71 (31·6%)	151 (43·5%)
Median time, in days, from symptom onset to hospital admission of index case due to COVID-19 (IQR)*	4 (2–7)	5 (4–7)	5 (2–7)
Number of unique contact groups†‡	578	225	346
1 contact	131	36	102
2 contacts	113	33	60
3 contacts	334	156	184
Median number of contacts in each contact group (IQR)‡	3 (2–4)	5 (2–12)	3 (1–7)
Mean number of contacts in each contact group (SD)‡	3 (2)	10 (17)	10 (26)
Number of cases among contacts detected by symptom-based PCR screening§	105	30	45
Secondary clinical attack rate (95% CI)	5·9% (4·9–7·1)	1·3% (0·93–1·9)	1·3% (0·95–1·7)
Number of contact groups with no cases among contacts detected by symptom-based PCR screening (%)	499/578 (86·3%)	206/225 (91·6%)	312/346 (90·2%)
Number of contact groups with cases among contacts detected by symptom-based PCR screening (%)	79/578 (13·7%)	19/225 (8·4%)	34/346 (9·8%)
1 case	63	12	26
2 cases	13	3	6
3 cases	3	4	2

*Median for all unique index cases linked to all contacts. †Contact group refers to a group consisting of one or more index cases and their close contacts. ‡Number of contacts, excluding the linked index case (or index cases). §PCR-based assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral nucleic acid.

Table 1: **Characteristics of close contact groups included in analysis**

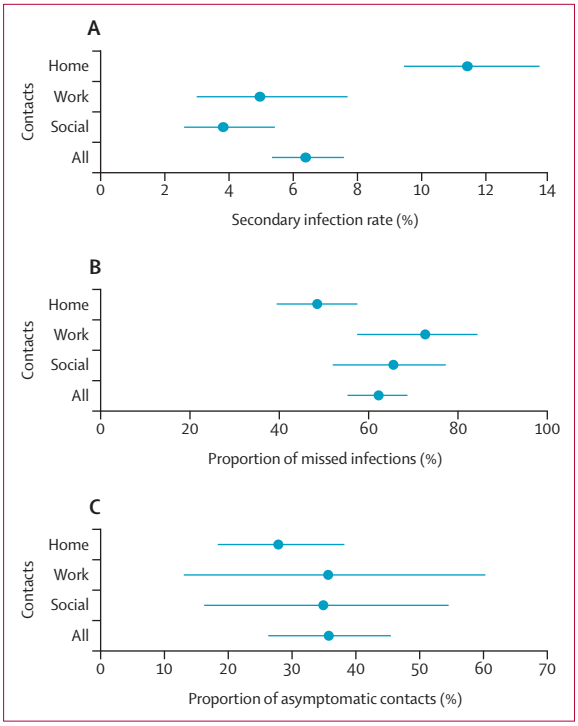

Figure 2: **Bayesian modelling estimates of secondary infection rates, proportion of missed infections, and proportion of asymptomatic contacts, among all contacts**

(A) Overall secondary infection rate among 1779 home, 2231 work, and 3508 social contacts. (B) Proportion of infections missed by symptom-based PCR among estimated infected contacts. (C) Proportion of infected contacts estimated to be asymptomatic, among home, work, or social contacts of a case, or among all contacts. Dots are posterior means and lines are 95% credible intervals.

The secondary clinical attack rate was 5·9% (95% CI 4·9–7·1) among 1779 household contacts, 1·3% (0·9–1·9) among 2231 work contacts, and 1·3% (1·0–1·7) among 3508 social contacts (table 1). Sex of the contact and symptom duration of the index case before admission to hospital were not significantly associated with the secondary clinical attack rate (appendix 2 pp 7–8). Contacts younger than 30 years were less likely to be diagnosed as COVID-19 positive than were those aged 30 years or older. Among work contacts, men were more likely than women to be diagnosed as COVID-19 positive.

499 (86·3%) of the 578 household contact groups had no cases detected by symptom-based PCR screening. 206 (91·6%) of the 225 work contact groups and 312 (90·2%) of the 346 social contact groups had no symptom-based PCR-detected cases. Of the contact groups with contacts detected as SARS-CoV-2 positive by symptom-based PCR testing, most (63 of 79 household contact groups, 12 of 19 work contact groups, and 26 of 34 social contact groups) had only one case per group. There was evidence of clustering of secondary infection in homes and workplaces ($p<0·0001$ for both) but not among social contacts ($p=0·40$), with the SD of the number of secondary infections being inflated in households of three by 15%, and by 28% in households of four, compared with what the SD would be if secondary infections were statistically independent (appendix 2 p 9).

Among the 7582 close contacts who completed quarantine without a COVID-19 diagnosis, 1150 (15·2%) consented to serological testing and completed the study questionnaire: 524 (30·0%) of 1753 household contacts, 207 (9·0%) of 2288 work contacts, and 419 (11·8%) of 3541 social contacts (figure 1). The median age of the contacts was 35 years (IQR 26–51) and 623 (54·2%) were female. 44 (3·8%) contacts were SARS-CoV-2 seropositive. PCR-negative individuals did not differ in probability to participate in serology from untested individuals, nor did men differ from women (appendix 2 p 9). Only among social contacts, older individuals were more likely to consent for serological testing and completing the questionnaire (odds ratio [OR] 1·13 per decade of age [95% CI 1·08–1·19]; $p<0·0001$; appendix 2 p 9). The median time interval from entering quarantine to the date of serology testing was 32 days (IQR 26–37) for household contacts, 92 days (IQR 75–104) for work contacts, and 51 days (IQR 33—64) for social contacts.

Serology results were positive for 29 (5·5%) of 524 household contacts, six (2·9%) of 207 work contacts, and nine (2·1%) of 419 social contacts (figure 1). Among the 44 serology-positive contacts, 29 (65·9%) were asymptomatic. Of the 15 symptomatic contacts, seven had negative symptom-based PCR test results during quarantine and eight were not tested. Of the eight not tested, six reported fever or respiratory symptoms, or both, one reported only diarrhoea, and one reported only abdominal discomfort. Of the 29 household serology-positive contacts, 19 (65·5%) were asymptomatic.

Using Bayesian modelling adjusting for differential testing rates among consenting and non-consenting contacts and the sensitivity of the tests, the overall secondary infection rate was 11 (95% credible interval [95% CrI] 9–14) per 100 household contacts, four (3–5) per 100 social contacts, and five (3–8) per 100 work contacts (figure 2A). Bayesian modelling estimated that the symptom-based testing strategy missed 62% (95% CrI 55–69) of SARS-CoV-2 infections (figure 2B). Additionally, among household contacts, symptom-based testing missed 48% (95% CrI 39–57) of SARS-CoV-2 infections. 36% (95% CrI 27–45) of household contacts with SARS-CoV-2 infection were asymptomatic (figure 2C). There was a lower rate of missed diagnoses among household contacts than among social and work contacts (the model is described in detail in appendix 2 pp 9–12).

The median age of household contacts (n=584; figure 1B) was 38 years (IQR 26–53), and 338 (57·9%) were female (table 2). Exposure risk factors associated with SARS-CoV-2 infection on both univariable and multivariable analysis were sharing of a bedroom (multivariable OR 5·38 [95% CI 1·82–15·84]; $p=0·0023$) and being spoken to by a COVID-19 case, with the highest risk if the case spoke for 30 min or longer (multivariable OR 7·86 [95% CI

	Cases (n=89)	Controls (n=495)	Univariable analysis		Multivariable analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age group						
≤35 years	37 (41·6%)	238 (48·1%)	Ref	..	Ref	..
>35 years	52 (58·4%)	257 (51·9%)	1·30 (0·82–2·06)	0·26	0·99 (0·54–1·83)	0·98
Sex						
Female	49 (55·1%)	289 (58·4%)	Ref	..	Ref	..
Male	40 (44·9%)	206 (41·6%)	1·15 (0·73–1·80)	0·56	1·26 (0·73–2·18)	0·41
Number of COVID-19 cases individual came into contact with						
Contact with single COVID-19 case	66 (74·2%)	418 (84·4%)	Ref	..	Ref	..
Contact with more than one COVID-19 case	23 (25·8%)	77 (15·6%)	1·89 (1·11–3·22)	0·019	1·65 (0·86–3·19)	0·14
Relationship with COVID-19 case*						
Not a family member of any COVID-19 case	5 (5·6%)	91 (18·4%)	Ref	..	Ref	..
Family member of a COVID-19 case but not spouse nor partner	37 (41·6%)	311 (62·8%)	2·17 (0·83–5·67)	0·12	1·52 (0·53–4·32)	0·44
Spouse or partner of a COVID-19 case	47 (52·8%)	93 (18·8%)	9·20 (3·50–24·17)	<0·0001	1·63 (0·45–5·93)	0·46
Indirect contact						
Did not receive any object directly from any COVID-19 case or touch the same surface or surfaces immediately after any COVID-19 case, or both	11 (12·4%)	188 (38·0%)	Ref	..	Ref	..
Received an object handed over by a COVID-19 case or touched the same surface or surfaces immediately after a COVID-19 case, or both	78 (87·6%)	307 (62·0%)	4·34 (2·25–8·37)	<0·0001	1·67 (0·77–3·64)	0·20
Sharing of meals						
Did not share a meal with any COVID-19 case	17 (19·1%)	228 (46·1%)	Ref	..	Ref	..
Shared a meal without involving any of the following: eating from the same plate, drinking from the same cup, or eating with the same utensils	26 (29·2%)	141 (28·5%)	2·47 (1·30–4·72)	0·0060	1·03 (0·48–2·21)	0·93
Shared a meal involving one or more of the following: eating from the same plate, drinking from the same cup, or eating with the same utensils	46 (51·7%)	126 (25·5%)	4·90 (2·69–8·90)	<0·0001	1·29 (0·60–2·80)	0·52
Sharing of bedroom and toilet						
Did not share a bedroom with any COVID-19 case and did not use the same toilet as any COVID-19 case	19 (21·4%)	296 (59·8%)	Ref	..	Ref	..
Used the same toilet as a COVID-19 case but did not share a bedroom	12 (13·5%)	105 (21·2%)	1·78 (0·84–3·79)	0·14	1·11 (0·49–2·54)	0·80
Shared a bedroom with a COVID-19 case but did not use the same toilet	13 (14·6%)	28 (5·7%)	7·23 (3·23–16·18)	<0·0001	5·38 (1·82–15·84)	0·0023
Shared a bedroom and used the same toilet as a COVID-19 case	45 (50·6%)	66 (13·3%)	10·62 (5·84–19·33)	<0·0001	5·05 (1·85–13·79)	0·0016
Sharing of vehicle						
Did not take the same vehicle as a COVID-19 case	31 (34·8%)	277 (56·0%)	Ref	..	Ref	..
Took the same vehicle as a COVID-19 case	58 (65·2%)	218 (44·0%)	2·38 (1·48–3·81)	0·00030	0·84 (0·46–1·52)	0·56
Longest duration that a COVID-19 case spoke to individual						
Individual was not spoken to by a COVID-19 case	21 (23·6%)	331 (66·9%)	Ref	..	Ref	..
COVID-19 case spoke for <30 min	32 (36·0%)	124 (25·1%)	4·07 (2·26–7·32)	<0·0001	3·91 (2·09–7·34)	<0·0001
COVID-19 case spoke for ≥30 min	36 (40·5%)	40 (8·1%)	14·19 (7·55–26·64)	<0·0001	7·86 (3·86–16·02)	<0·0001

Data are n (%) unless otherwise stated; the number of individuals with the particular exposure variable is expressed as a percentage of the total number of the group (case or control). *Refers to status of the individual or contact in relation to the linked index case (or cases).

Table 2: **Univariable and multivariable analysis of risk factors for acquisition of COVID-19 among household contacts who participated in the risk assessment questionnaire (and serology testing if applicable)**

3·86–16·02]; p<0·0001). Exposure risk factors significantly associated with SARS-CoV-2 infection only on univariable analysis were having contact with more than one COVID-19 case, being a spouse or partner of a case, receiving an object handed over by a case or touching the same surface immediately after a case (or both), sharing a meal with a case, using the same toilet as a case, and sharing the same vehicle as a case.

The median age of work and social contacts (n=664) was 35 years (IQR 26–50) and 330 (49·7%) were female.

	Cases (n=53)	Controls (n=611)	Univariable analysis		Multivariable analysis	
			Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age group						
≤35 years	29 (54·7%)	317 (51·9%)	Ref	..	Ref	..
>35 years	24 (45·3%)	294 (48·1%)	0·89 (0·51–1·57)	0·69	0·69 (0·37–1·29)	0·25
Sex						
Female	24 (45·3%)	306 (50·1%)	Ref	..	Ref	..
Male	29 (54·7%)	305 (49·9%)	1·21 (0·69–2·13)	0·50	1·52 (0·82–2·83)	0·19
Number of COVID-19 cases the individual came into contact with						
Contact with single COVID-19 case	29 (54·7%)	516 (84·5%)	Ref	..	Ref	..
Contact with more than one COVID-19 case	24 (45·3%)	95 (15·5%)	4·50 (2·51–8·06)	<0·0001	3·92 (2·07–7·40)	<0·0001
Direct contact						
Did not have direct physical contact with any COVID-19 case	31 (58·5%)	428 (70·1%)	Ref	..	Ref	..
Had direct physical contact with a COVID-19 case	22 (41·5%)	183 (29·9%)	1·66 (0·94–2·94)	0·083	1·10 (0·55–2·19)	0·79
Indirect contact						
Did not receive any object directly from any COVID-19 case or touch the same surface or surfaces immediately after any COVID-19 case, or both	20 (37·7%)	354 (57·9%)	Ref	..	Ref	..
Received an object handed over by a COVID-19 case or touched the same surface or surfaces immediately after a COVID-19 case, or both	33 (62·3%)	257 (42·1%)	2·27 (1·27–4·05)	0·0054	1·24 (0·62–2·46)	0·55
Sharing of meals						
Did not share a meal with any COVID-19 case	24 (45·3%)	404 (66·1%)	Ref	..	Ref	..
Shared a meal without involving any of the following: eating from the same plate, drinking from the same cup, or eating with the same utensils	11 (20·8%)	101 (16·5%)	1·83 (0·87–3·87)	0·11	1·04 (0·44–2·46)	0·92
Shared a meal involving one or more of the following: eating from the same plate, drinking from the same cup, or eating with the same utensils	18 (34·0%)	106 (17·4%)	2·86 (1·50–5·46)	0·0015	1·45 (0·63–3·31)	0·38
Sharing of toilet						
Did not use the same toilet as a COVID-19 case	39 (73·6%)	519 (84·9%)	Ref	..	Ref	..
Used the same toilet as a COVID-19 case	14 (26·4%)	92 (15·1)	2·03 (1·06–3·88)	0·033	1·03 (0·48–2·18)	0·95
Sharing of vehicle						
Did not take the same vehicle as any COVID-19 case	29 (54·7%)	505 (82·7%)	Ref	..	Ref	..
Took the same vehicle as a COVID-19 case	24 (45·3%)	106 (17·4%)	3·94 (2·21–7·04)	<0·0001	3·07 (1·55–6·08)	0·0013
Longest duration that a COVID-19 case spoke to individual						
Individual was not spoken to by a COVID-19 case	13 (24·5%)	281 (46·0%)	Ref	..	Ref	..
COVID-19 case spoke for <30 min	19 (35·9%)	196 (32·1%)	2·10 (1·01–4·34)	0·047	2·50 (1·15–5·44)	0·021
COVID-19 case spoke for ≥30 min	21 (39·6%)	134 (21·9%)	3·39 (1·65–6·97)	0·0009	2·67 (1·21–5·88)	0·015
Mask worn by COVID-19 case or cases						
COVID-19 case or cases did not wear a mask during all contact episodes	45 (84·9%)	548 (89·7%)	Ref	..	..	..
COVID-19 case or cases wore a mask during all contact episodes	8 (15·1%)	63 (10·3%)	1·55 (0·70–3·43)	0·28	Not included†	..
Mask worn by individual						
Individual did not wear a mask during all contact episodes	47 (88·7%)	564 (92·3%)	Ref	..	..	..
Individual wore a mask during all contact episodes	6 (11·3%)	47 (7·7%)	1·53 (0·62–3·77)	0·35	Not included†	..

Data are n (%), unless otherwise stated; the number of individuals with the particular exposure variable is expressed as a percentage of the total number of the group (case or control). As mask wearing was not significant in the univariable analysis, it was not included in the multivariable analysis.

Table 3: **Univariable and multivariable analysis of risk factors for acquisition of COVID-19 among non-household (work and social) contacts**

Exposure risk factors associated with SARS-CoV-2 infection on both univariable and multivariable analysis were having contact with more than one COVID-19 case (multivariable OR 3·92 [95% CI 2·07–7·40]; p<0·0001), being spoken to by the index case for 30 min or longer (2·67 [1·21–5·88]; p=0·015), and sharing the same vehicle as a case (3·07 [1·55–6·08]; p=0·0013). 115 of (88·5%) of 130 contacts who shared the same vehicle as a

COVID-19 case took the same car. Of the 24 cases who took the same vehicle as a COVID-19 case, 14 took the same car only, six took the same car and other forms of transport, and four took other forms of transport only. Of the 106 controls, 88 took the same car only, seven took the same car and other forms of transport, and 11 took other forms of transport only. Cars include both private vehicles and taxis, and vans (n=3). Other forms of transport include aircraft, buses, trains, and lorries or unspecified company transport, or both (n=1). Exposure risk factors significantly associated with SARS-CoV-2 infection only on univariable analysis were having direct physical contact with a COVID-19 case, receiving an object handed over by a case or touching the same surface immediately after a case (or both), sharing a meal with a case, and using the same toilet as a case (table 3).

Discussion

This retrospective study explored transmission risk factors for COVID-19 and the proportion of asymptomatic cases that would have been missed by testing symptomatic individuals only. Our findings show that attack rates among household contacts are higher than among non-household contacts; moreover, among both household and non-household close contacts, close physical proximity, and increased duration of verbal interaction are epidemiological risk factors for SARS-CoV-2 transmission. Bayesian estimates determined that the symptom-based testing approach did not identify more than half of contacts with SARS-CoV-2 infection and that more than a third of infections were asymptomatic.

Singapore's comprehensive approach to COVID-19 control, much of which was prepared following the 2003 SARS epidemic, is likely to have contributed to the low secondary attack rate among household and non-household contacts during the study period.[19] Clear leadership was provided by the Multi-Ministry Task Force, which includes the Ministry of Health, established to coordinate the multi-sectoral response for COVID-19 control. The network of more than 800 public health preparedness clinics was activated and extended medical leave of up to 5 days was provided for patients with respiratory symptoms. All individuals who tested positive for SARS-CoV-2 infection were admitted to isolation wards in hospitals, regardless of symptom severity, to prevent onward transmission.[20] Active contact tracing for rapid quarantine of close contacts of SARS-CoV-2 positive individuals was implemented as described in this study.[13] Travellers or returning residents from overseas were placed under a mandatory 14-day stay-at-home notice, initially at home and later in designated hotels. Symptomatic cases with stay-at-home notices underwent SARS-CoV-2 testing.[21]

We identified higher symptomatic secondary clinical attack rates (5·9%) and seroprevalence (5·5% [29 of 524]) in household contacts than in work contacts (secondary clinical attack rate 1·3% and seroprevalence 2·9% [six of 207]) and social contacts (secondary clinical attack rate 1·3% and seroprevalence 2·1% [nine of 419]), which corroborate with previous studies.[22,23] The increased risk of transmission in the household setting might be because of closer and more prolonged interactions than those experienced by work or social contacts. Priority for quarantine measures should therefore be given to household contacts. It is also important to note the clustering of transmission events in the household, with most cases not transmitting to other members of the household and yet some cases transmitting to multiple household contacts. Our study also suggests that clustering of transmission events occurs in workplace settings, and additional studies are needed to determine factors associated with increased SARS-CoV-2 transmission in these settings.

Close physical proximity and increased duration of verbal interaction were independent risk factors for SARS-CoV-2 transmission among both household and non-household contacts. Clusters linked to activities where verbal interaction and singing occurred for prolonged periods in close congregation have been reported.[9,11] As countries emerge from lockdowns, wearing of masks and physical distancing[24,25] to reduce close contact and minimising direct (especially verbal) work and social interactions are feasible components of a sustainable strategy to prevent community transmission.[26,27]

In our study, more than half of contacts with SARS-CoV-2 infection remained undiagnosed by symptom-based PCR testing, and 36% of infections were estimated to be asymptomatic. Onward transmission has been documented from asymptomatic SARS-CoV-2 cases, especially in the household setting, thus highlighting the importance of early diagnosis of asymptomatic infection.[28–30] Detection of asymptomatic contacts with active SARS-CoV-2 infection is crucial both to determine contact-related secondary transmission events early and to avoid release of potentially infectious individuals from quarantine. To address these issues, Singapore has initiated routine PCR testing of all close contacts at both the beginning and end of their quarantine period, regardless of symptoms.

In most household settings, especially where the COVID-19 index case remains undiagnosed, physical distancing and avoidance of direct verbal interaction is difficult to achieve. Our estimates suggest that with the existing symptom-based PCR testing approach, approximately half of household contacts with SARS-CoV-2 infections would remain undiagnosed. Asymptomatic infections or infections with symptoms other than fever or acute respiratory symptoms could have been missed in the present study as the public health officers focused on fever and respiratory symptoms to refer close contacts for PCR testing. Additionally, some individuals with fever and respiratory symptoms remained undiagnosed, possibly because they did not report their symptoms to public health officers. Routinely testing household close contacts of confirmed COVID-19 cases, regardless of symptoms, is

likely to help in reducing missed COVID-19 diagnoses. Detection of a COVID-19-positive household close contact would trigger either relocation of the COVID-19-positive person out of the household or be a basis for the household to practice physical distancing, ideally physical separation of the infected person in a separate room for a period of 14 days.[31]

This study had some limitations. Recall bias for symptoms during quarantine could have been present, although this bias would have been mitigated by thrice-daily temperature monitoring and access to Ministry of Health officers for symptom reporting and referral for testing. Because not all contacts consented for serological testing, there is a risk that those who were tested differed in terms of demographic or other characteristics from those who did not undergo testing; if true, this would bias our estimates. We did not find substantial demographic differences between the two groups, but it is possible that other factors that were not measured, such as perceived risk of infection, might have influenced the decision to consent for serology. Dormitory-dwelling migrant workers accounted for less than 1% of the study population as this study predated the outbreak in migrant worker dormitories in Singapore.[32] Hence, we were unable to determine the attack rate among dormitory-dwelling migrant workers. We were also unable to assess the effectiveness of community face mask use as the prevalence of mask use was low at that time. In Singapore, mask wearing was made mandatory for all people (above the age of 2 years) leaving their home from April 14, 2020. On the basis of previous knowledge of other droplet-transmitted respiratory viruses, surgical mask wearing would be expected to be effective in preventing SARS-CoV-2 transmission.[24]

In conclusion, the household attack rate and individual-level transmission risk factors of SARS-CoV-2 suggest that physical distancing and minimising direct verbal interactions would help reduce community transmission. For prevention of transmission to household contacts, early identification of COVID-19 index cases and contacts is important. In view of the significant number of missed diagnoses in a symptom-based testing strategy, testing of all household contacts, including asymptomatic individuals, is recommended.

Contributors

OTN and KM conceived of and led the study. JP, LDW, and MYA were involved in data collection. OTN, KM, VK, and JP accessed and verified the data. OTN, KM, ARC, VK, JP, KZL, JS, WNC, and CT were involved in data analysis, data interpretation, and writing of the manuscript in consultation with MC, LML, SV, PYC, THL, RJL, SPS, MI-CC, ZS, LK, RP, L-FW, Y-SL and VJML.

Declaration of interests

We declare no competing interests.

Data sharing

Individual-level participant data that underlie the results reported in this Article, after de-identification (in the text, tables, figures, and appendix 2), are regarded as sensitive and will not be shared. The study methods, statistical analysis plan, and analytical code are available in detail in the main Article and appendix 2.

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References

1 WHO. WHO coronavirus disease (COVID-19) dashboard. 2020. https://covid19.who.int (accessed Oct 6, 2020).
2 Hsiang S, Allen D, Annan-Phan S, et al. The effect of large-scale anti-contagion policies on the COVID-19 pandemic. *Nature* 2020; **584:** 262–67.
3 Lai S, Ruktanonchai NW, Zhou L, et al. Effect of non-pharmaceutical interventions to contain COVID-19 in China. *Nature* 2020; **585:** 410–13.
4 Flaxman S, Mishra S, Gandy A, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature* 2020; **584:** 257–61.
5 Flahault A. Has China faced only a herald wave of SARS-CoV-2? *Lancet* 2020; **395:** 947.
6 Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med* 2020; **382:** 2081–90.
7 Gudbjartsson DF, Helgason A, Jonsson H, et al. Spread of SARS-CoV-2 in the Icelandic population. *N Engl J Med* 2020; **382:** 2302–15.
8 McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a long-term care facility in King County, Washington. *N Engl J Med* 2020; **382:** 2005–11.
9 Hamner L, Dubbel P, Capron I, et al. High SARS-CoV-2 attack rate following exposure at a choir practice — Skagit County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 606–10.
10 Luo L, Liu D, Liao X, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. *Ann Intern Med* 2020; published online Aug 13. https://doi.org/10.7326/M20-2671.
11 Yong SEF, Anderson DE, Wei WE, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. *Lancet Infect Dis* 2020; **20:** 809–15.
12 Sun Y, Koh V, Marimuthu K, et al. Epidemiological and clinical predictors of COVID-19. *Clin Infect Dis* 2020; **71:** 786–92.
13 Ng Y, Li Z, Chua YX, et al. Evaluation of the effectiveness of surveillance and containment measures for the first 100 patients with COVID-19 in Singapore—January 2–February 29, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 307–11.
14 WHO. Coronavirus disease (COVID-19) advice for the public. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public (accessed Sept 9, 2020).
15 Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic transmission of SARS-CoV-2—Singapore, January 23–March 16, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 411–15.
16 Singapore Statutes Online. Infectious Diseases Act (Chapter 137). Revised edition. July 31, 2003. https://sso.agc.gov.sg/Act/IDA1976 (accessed Sept 17, 2020).
17 WHO. Household transmission investigation protocol for 2019-novel coronavirus (COVID-19) infection. Feb 28, 2020. https://www.who.int/publications/i/item/household-transmission-investigation-protocol-for-2019-novel-coronavirus-(2019-ncov)-infection (accessed March 30, 2020).

18 Tan CW, Chia WN, Qin X, et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2–spike protein–protein interaction. *Nat Biotechnol* 2020; **38:** 1073–78.

19 Lee VJ, Chiew CJ, Khong WX. Interrupting transmission of COVID-19: lessons from containment efforts in Singapore. *J Travel Med* 2020; **27:** taaa039.

20 Dickens BL, Koo JR, Wilder-Smith A, Cook AR. Institutional, not home-based, isolation could contain the COVID-19 outbreak. *Lancet* 2020; **395:** 1541–42.

21 Chiew CJ, Li Z, Lee VJ. Reducing onward spread of COVID-19 from imported cases: quarantine and 'stay at home' measures for travellers and returning residents to Singapore. *J Travel Med* 2020; **27:** taaa049.

22 Cheng H-Y, Jian S-W, Liu D-P, 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:** 1156–63.

23 Bi Q, Wu Y, Mei S, 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:** 911–19.

24 Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet* 2020; **395:** 1973–87.

25 Wang Y, Tian H, Zhang L, et al. Reduction of secondary transmission of SARS-CoV-2 in households by face mask use, disinfection and social distancing: a cohort study in Beijing, China. *BMJ Glob Health* 2020; **5:** e002794.

26 WHO. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed. Interim guidance. June 29, 2020. https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2020.4 (accessed July 16, 2020).

27 US Centers for Disease Control and Prevention. Infection control guidance for healthcare professionals about coronavirus (COVID-19). June 3, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html (accessed July 16, 2020).

28 Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020; **323:** 1406–07.

29 Chau NVV, Thanh Lam V, Thanh Dung N, et al. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. *Clin Infect Dis* 2020; published online June 4. https://doi.org/10.110/2020.04.27.20082347.

30 Liu J, Huang J, Xiang D. Large SARS-CoV-2 outbreak caused by asymptomatic traveler, China. *Emerg Infect Dis* 2020; **26:** 2260–63.

31 WHO. Considerations for quarantine of contacts of COVID-19 cases. Interim guidance. Aug 19, 2020. https://www.who.int/publications/i/item/considerations-for-quarantine-of-individuals-in-the-context-of-containment-for-coronavirus-disease-(covid-19) (accessed Oct 9, 2020).

32 Ministry of Health, Singapore. Covid-19 situation report: data updated as of Oct 6, 2020. https://covidsitrep.moh.gov.sg (accessed Oct 6, 2020).