

Effectiveness of Containment Measures Against COVID-19 in Singapore

Implications for Other National Containment Efforts

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Background: We hypothesize that comprehensive surveillance of COVID-19 in Singapore has facilitated early case detection and prompt contact tracing and, with community-based measures, contained spread. We assessed the effectiveness of containment measures by estimating transmissibility (effective reproduction number, R_t) over the course of the outbreak.

Methods: We used a Bayesian data augmentation framework to allocate infectors to infectees with no known infectors and determine serial interval distribution parameters via Markov chain Monte Carlo sampling. We fitted a smoothing spline to the number of secondary cases generated by each infector by respective onset dates to estimate R_t and evaluated increase in mean number of secondary cases per individual for each day's delay in starting isolation or quarantine.

Results: As of April 1, 2020, 1000 COVID-19 cases were reported in Singapore. We estimated a mean serial interval of 4.6 days [95% credible interval (CI) = 4.2, 5.1] with a SD of 3.5 days (95%

CI = 3.1, 4.0). The posterior mean R_t was below one for most of the time, peaking at 1.1 (95% CI = 1.0, 1.3) on week 9 of 2020 due to a spreading event in one of the clusters. Eight hundred twenty-seven (82.7%) of cases infected less than one person on average. Over an interval of 7 days, the incremental mean number of cases generated per individual for each day's delay in starting isolation or quarantine was 0.03 cases (95% CI = 0.02, 0.05).

Conclusions: We estimate that robust surveillance, active case detection, prompt contact tracing, and quarantine of close contacts kept R_t below one.

Keywords: Bayesian; COVID-19; Reproduction number; Modeling; Outbreak containment

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Technical details of the code are available in the main text.

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On December 31, 2019, a cluster of viral pneumonia cases, subsequently identified as COVID-19, was reported in Wuhan, China. Thereafter, the number of infections rose exponentially in Wuhan,^{1–3} and cases were subsequently reported from all Chinese provinces and overseas, prompting the World Health Organization to declare a public health emergency of international concern,⁴ and on March 11, 2020, a pandemic.⁵ The rapid growth of cases globally fuels concern that the outbreak cannot be contained, especially as new countries discover autochthonous cases, and has led to debate on whether to bypass containment and seek to mitigate the impact of the pandemic.

The transmissibility of any pathogen can be characterized by the basic reproduction number, R_0 , the average number of secondary infections generated by a typically infectious individual in an entirely susceptible population.^{6,7} Exponential outbreak growth occurs when $R_0 > 1$, while disease extinction inevitably occurs when $R_0 < 1$. Over the outbreak's course, the effective reproduction number, R_t , the average number of secondary infections generated by a single infectious individual at since the onset of symptom t , is commonly used instead as the number of susceptible individuals decline or as public health control strategies (e.g., case isolation, quarantine of close contacts) are put in place to contain the outbreak and potentially drive R_t below one.

Using epidemic curves in Wuhan and other parts of China, modeling studies have initially estimated the R_0 of COVID-19—before travel restrictions imposed by China—to be between 1.4 and 6.5,⁸ raising concern that the virus may only be controlled once enough cases occur to reach herd immunity. The experience of some countries in Asia, however, speaks to the possibility that sufficient early effort may curtail transmission. Within China, extensive public health measures have been instituted to contain the outbreak, including a lockdown of Wuhan city and community-level containment measures across other cities.^{9,10} The joint World Health Organization – China mission on COVID-19 stated that the extraordinary public health containment measures had substantially blunted the epidemic's trajectory in China, contributing to a rapid decline in new cases in February.¹¹ However, these measures may be difficult to implement in most other countries, and countries with fewer cases could adopt less disruptive approaches. Japan, the Republic of Korea, Singapore, Taiwan, and Hong Kong (China) have all demonstrated successes in slowing the outbreak, and although their approaches are not identical, the rapid identification and isolation of infected individuals and timely quarantining of their close contacts is a key component of their strategies. At the same time, the spread of COVID-19 is accelerating in many countries, prompting discussion on the approaches needed to contain spread to reduce the impact on healthcare resources.

Singapore, with 1000 cases as of April 1, 2020, has taken a unique approach of enhanced surveillance, active case detection, and individual-level containment of spread, together with border controls and community measures that allowed the general population of about 5.7 million inhabitants to continue their daily activities with precautions.^{12,13} This article describes the COVID-19 outbreak in Singapore and assesses the effectiveness of these measures by calculating the R_t in Singapore over the course of the local outbreak. These data have implications for other countries seeking to contain the spread of COVID-19.

METHODS

Singapore's case definition for suspected COVID-19 cases was established on January 2, 2020 based on clinical and epidemiologic criteria, and evolved over time as more information became available globally (eTable 1; <http://links.lww.com/EDE/B725>). In addition, Singapore set up an enhanced surveillance system on January 31, 2020 to detect COVID-19 among (1) severely ill patients in intensive care and deaths with possibly infectious cause, (2) all hospitalized patients with pneumonia, which was later expanded to include patients with pneumonia in primary care, and (3) patients with influenza-like illness (ILI) in sentinel primary care clinics. Doctors could also exercise discretion to test patients they suspected for clinical or epidemiologic reasons. A confirmed case was defined as a person with a respiratory sample that tested positive for SARS-CoV-2 using real-time reverse

transcriptase-polymerase chain reaction tests targeting the N and ORF1ab genes,¹⁴ or seropositivity on a recently developed assay.¹¹

All confirmed cases were interviewed to establish their activity maps from 14 days before symptom onset until isolation in hospital and to identify interactions with other cases or exposure to travelers to affected regions. Contact tracing was conducted to identify their close contacts. Close contacts with recent or current fever or respiratory symptoms were referred directly to hospitals for isolation and testing as part of active case finding. Close contacts who are well were placed under mandatory quarantine at either their homes or designated government quarantine facilities for 14 days from their last date of exposure. Other contacts who had limited interactions with a COVID-19 case were placed on phone surveillance. Both groups were monitored daily for development of symptoms by public health officials, and contacts with fever or respiratory symptoms were referred to hospitals. For some of the larger clusters, further testing of asymptomatic close contacts through respiratory and/or blood samples were performed to identify additional cases.

Temperature and health screening were instituted for all inbound travellers at all ports of entry. Advisories were issued against travel to severely affected countries or regions and residents returning from these areas were subject to a 14-day home self-quarantine while short-term visitors were not allowed to enter or transit through Singapore. The public were also advised to maintain good personal hygiene, and to seek medical attention early and avoid close contact with others when unwell. Schools remained open and implemented precautionary measures such as reduction of mass assemblies, inter-class and inter-school activities, and staggered meal times. Workplaces were encouraged to implement business continuity plans, such as staggered work hours, segregated teams and telecommuting. Large-scale events were postponed or cancelled, and public venues were instructed to limit the number of patrons at any one time (eTable 2; <http://links.lww.com/EDE/B725>).

Estimating the Serial Interval and Effective Reproduction Number

In summary, we estimated the effective reproduction number, R_t , by adapting the method of Wallinga and Teunis¹⁵ to account for the situation when epidemiologic links between some, but not all, cases were known or suspected. Our approach incorporates additional epidemiologic data from cluster investigations, similar to that of Hens et al,¹⁶ but we simultaneously estimate the parameters of the serial interval (i.e., time from symptom onset in an infector to symptom onset in an infectee) distribution and probabilistically distribute infected cases (infectee) to known infector(s), if epidemiologic links exist, or to any case with symptoms onset before the infectee. The estimation of the latter was achieved through Bayesian data augmentation—an approach adopted by

Cauchemez et al,¹⁷ and this allows us to determine the number of secondary cases generated by each infector j , R_j . A spline interpolation of all R_j against the onset date of each infector j then serves as an estimate to the R_t . We performed these steps iteratively to evaluate the mean and 95% credible intervals of the serial interval and R_t . The following paragraphs document the process in detail.

Infector–infectee pairs were established through epidemiological investigations, and we categorized the infectees as follows: (1) infectee with one or more linked potential infectors who developed symptoms before the infectee and before isolation; (2) infectee with travel history to a country with ongoing COVID-19 outbreak in the preceding 14 days or reported frequent interactions with travellers from China in Singapore, but with no epidemiologic links to other cases in Singapore; (3) infectee with no known infector but who were associated to a known cluster of cases; (4) infectee with no known infector and who were not associated to any cluster of cases. With $n = 1000$ observed cases as of March 15, 2020, an $n \times n$ adjacency matrix, A , was created wherein $a_{ij} = 1$ if there is a known or possible contact from infector j to infectee i and 0 otherwise.

We used a Bayesian data augmentation framework to infer the infector–infectee pairs in categories (1), (3) and (4). We assumed a gamma distribution with shape $\mu\sigma^{-1}$ and rate $\mu\sigma^{-2}$ for the serial interval. We evaluated the posterior distribution of (μ, σ) using a custom-built Markov Chain Monte Carlo algorithm,¹⁸ with a Metropolis–Hastings step for these moments and a Gibbs step to sample infectors for each infectee. For the latter, we sampled the infector proportional to $a_{ij} \Gamma(t_i - t_j | \mu, \sigma)$ where $\Gamma(\cdot)$ is a discretized version of the gamma distribution and t_i and t_j is the calendar time of symptom onset of infectee i and infector j . We excluded 21 asymptomatic cases from the analysis as their serial interval was undefined.

For each iteration of the Markov Chain Monte Carlo algorithm, we evaluated the number of secondary cases for each infector j , R_j , and fitted a smoothing spline¹⁹ of R_j against the onset dates of infector j to obtain a posterior smoothed estimate of R_t over the course of the outbreak thus far. As the outbreak is still ongoing, we accounted for potential underestimation of recent values of R_t by determining the proportion of the unobserved serial interval distribution for each individual, in each iteration, to evaluate the expected number of unobserved cases, U_j , for a infector j with observed O_j secondary cases. The assumed probability mass and expected value of U_j is:

$$P(U_j | \mu, \sigma, O_j, T_j) \propto \binom{U_j + O_j}{U_j} q_j^{U_j} (1 - q_j)^{O_j}$$

$E(U_j) = \sum_{U_j=1}^{\infty} P(U_j | \mu, \sigma, O_j, T_j) \cdot U_j$ where q_j is the probability of an infectee having onset T_j days after data truncation, derived from $\Gamma(t | \mu, \sigma)$. We also fitted a negative

binomial distribution to the inferred distribution of secondary cases in each iteration to account for over-dispersion and evaluated the posterior mean and dispersion parameter.

We aggregated the mean number of secondary cases among individuals with the same duration from onset to isolation or quarantine over all iterations to derive the posterior distribution. We also fitted a linear model to the inferred number of secondary cases per individual at each iteration to determine the posterior distribution of the increase in R_t per day’s delay in starting isolation or quarantine.

We took uniform improper prior distributions over the parameter support for all parameters. We assessed convergence through visual inspection of trace plots and the Gelman–Rubin convergence statistic.²⁰ We ran multiple chains with burn-in of 1000 iterations each to obtain a total of 108,000 draws from the posterior, and did analysis in R.²¹

RESULTS

Case Ascertainment

As of April 1, 2020, 1000 confirmed cases of COVID-19 were reported in Singapore (Figure 1 and Table). There were 22 cases imported from China (including seven who traveled to Singapore on two dedicated evacuation flights from Wuhan) and nine cases who reported frequent contact with travelers from China in Singapore. With the exception of cases evacuated from Wuhan,²² there were no known imported cases from China since January 31, 2020 and 508 imported cases were identified after March 3, 2020. At the time of writing, there were 20 reported clusters of which one household cluster was associated with COVID-19 transmission linked to two church clusters. Three other clusters were described in detail elsewhere.²³

The cases in Singapore were detected as follows: (1) 695 met the suspect case definition, of whom 302 were identified to be symptomatic when contact traced and referred for assessment while 41 had first symptom onset during quarantine, (2) 55 through enhanced surveillance of pneumonia, severely ill patients in intensive care, and ILI in sentinel primary care clinics, and (3) 250 through clinical discretion, mostly due to unresolving respiratory tract symptoms with no other known pathogenic cause, or having potential contact with visitors from China due to their occupation.

Modeling Results

Infector–infectee pairs determined using Bayesian data augmentation are presented in Figure 2. The estimated mean serial interval was 4.6 days [95% credible interval (CI) = 4.2, 5.1] with a SD of 3.5 days (95% CI = 3.1, 4.0) (Figure 3).

Since confirmation of the first COVID-19 case in Singapore on January 23, 2020, the estimated posterior mean R_t was below 1 most of the time and peaked on week 9 of 2020 at 1.1 (95% CI = 1.0, 1.3) (Figure 4), after accounting for right truncation of data due to the unobserved serial interval of the

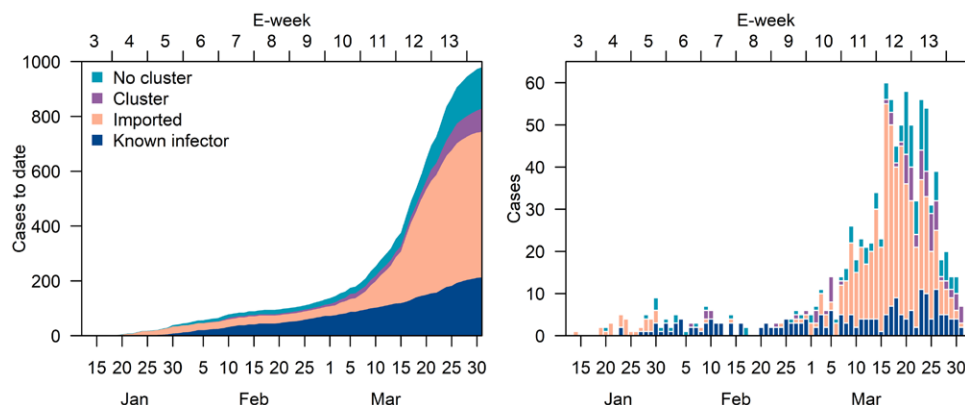


FIGURE 1. Cases by infectee category (A) cumulative cases over time, (B) cases by onset date. (Dark blue) Infectee with one or more linked potential infectors who developed symptoms before the infectee and before isolation; (Pink) infectee with travel history to a country with ongoing COVID-19 outbreak in the preceding 14 days or reported frequent interactions with travellers from China in Singapore, but with no epidemiologic links to other cases in Singapore; (Purple) infectee with no known infector but who were associated to a known cluster of cases; (Turquoise) infectee with no known infector and who were not associated to any cluster of cases.

TABLE. Characteristics of Individuals Who Tested Positive for SARS-CoV-2 in Singapore

	N (%)
Infectee category	
Infectee with one or more linked potential infectors who developed symptoms before the infectee and before isolation	222 (22.2)
Infectee with travel history to a country with ongoing COVID-19 outbreak in the preceding 14 days or reported frequent interactions with travellers from China in Singapore, but with no epidemiological links to other cases in Singapore	539 (53.9)
Infectee with no known infector but who were associated to a known cluster of cases	89 (8.9)
Infectee with no known infector and who were not associated to any cluster of cases	150 (15.0)
Primary detection method	
Case definition	695 (69.5)
Enhanced surveillance of pneumonia, severely ill patients in ICU, and ILI in sentinel primary care clinics	55 (5.5)
Clinical discretion	250 (25.0)

recent cases. Of the 1000 cases, we estimated 830 of the cases had fewer than one onward transmission, 117 cases generated at least one but less than two secondary cases, while 53 generated at least two secondary cases (Figure 4). One of the cases was estimated to have infected six persons of which one subsequently infected another six persons. They were associated with the family 1 and church 2 cluster, respectively (Figure 2). The former was symptomatic during a Chinese New Year gathering while the latter was symptomatic when attending church staff meetings on two occasions.

Forty-one cases developed a first symptom after quarantine or isolation in hospital and 508 of the cases were isolated

within 4 days since their symptom onset (Figure 5). From the data, a delay of 7 days from onset to isolation would result in 0.8 secondary cases per symptomatic case (95% CI = 0.7, 0.9). For each day’s delay in isolating a symptomatic case, approximately 0.03 secondary cases (95% CI = 0.02, 0.05) would occur. Over the course of the outbreak, the delay from onset to isolation or quarantine had declined at a rate of 0.06 days (95% CI = 0.05, 0.08) per day (Figure 6).

Over the course of the outbreak, the posterior mean number of the secondary cases generated was 0.64 cases (95% CI = 0.63, 0.65) with a dispersion parameter of 0.40 (95% CI = 0.31, 0.51). As of April 1, 2020, we estimate that the mean unobserved cases per infectee was 0.1 arising from data truncation.

DISCUSSION

We presented the strategy that Singapore used to contain the spread of COVID-19 to date and estimated its effectiveness through statistical modeling of the temporal effective reproduction number (R_t). Since the start of the local outbreak, the estimated R_t has remained mostly below one for 2 months, suggesting that containment measures have been effective in reducing spread. This containment strategy is based on a comprehensive surveillance system to detect as many cases as possible, together with active case finding and containment of spread at the individual level, coupled with community-based measures calibrated to local transmission risk. This has thus far allowed the population to generally continue daily activities including school and work with some precautions such as physical distancing, and is less disruptive than broad-based community containment strategies involving widespread physical distancing, school or business closures, or lock-downs. More importantly, it helps to slow the spread and

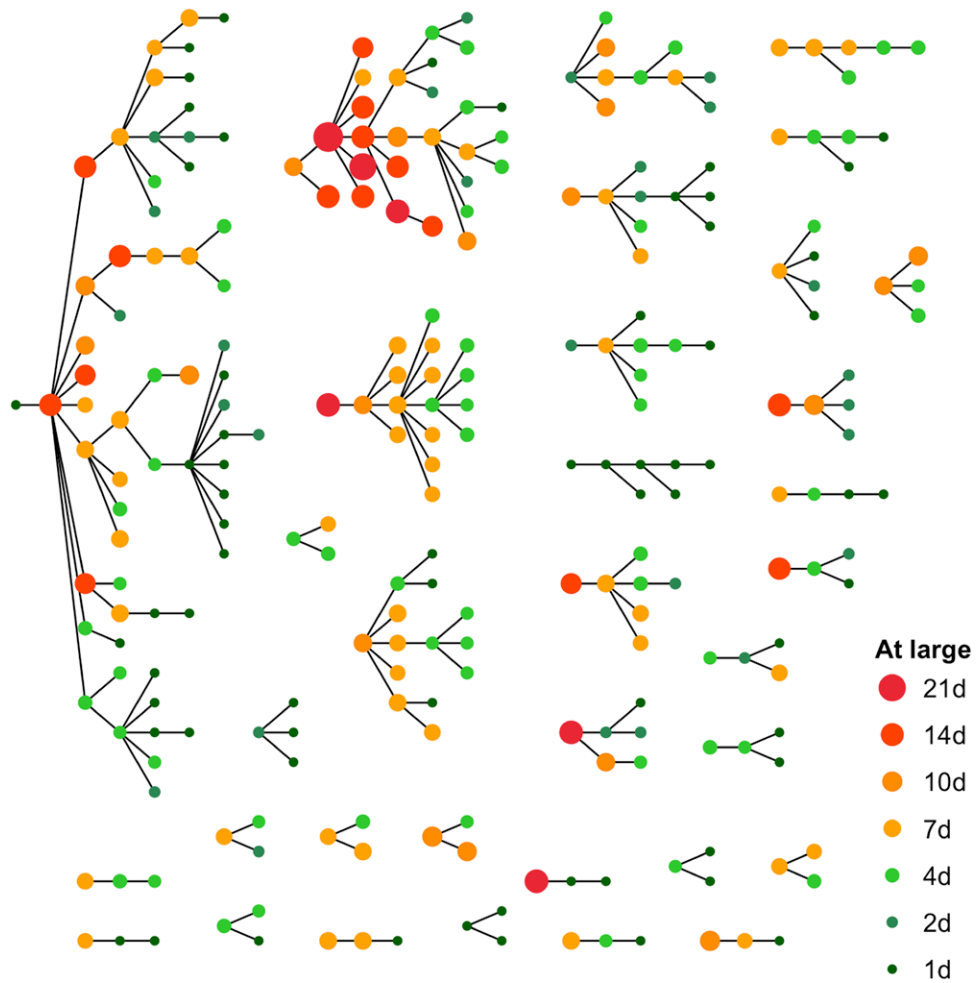


FIGURE 2. Inferred clusters of three or more cases. Nodes are coloured and sized by the duration at-large from symptom onset to isolation or quarantine. Vertices connect each case to his or her maximum a posteriori source of infection.

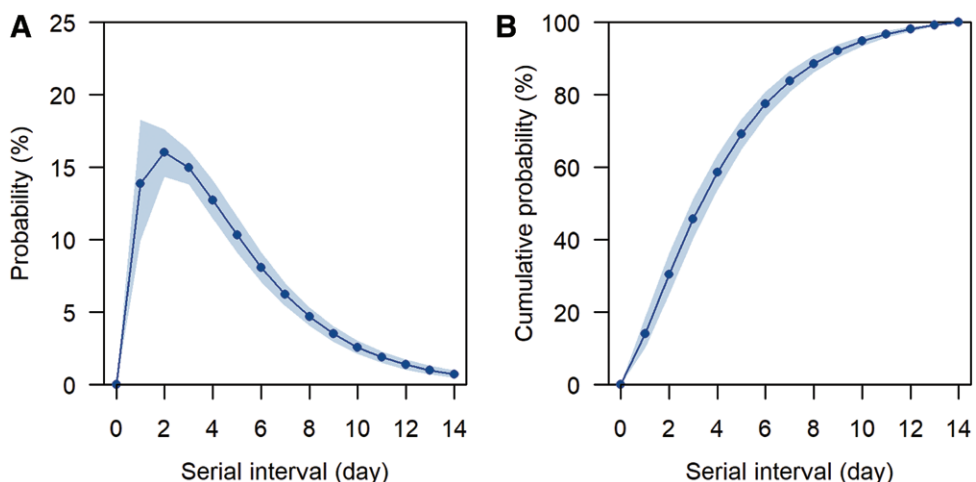


FIGURE 3. Serial interval (A) probability density and (B) cumulative density.

minimize the strain on healthcare resources, thereby ensuring that critical care to the vulnerable population is sustainable and reducing the case fatality.

The effectiveness of the Singapore containment strategy is dependent on several factors. First, it is founded on the ability to detect a sufficient proportion of cases in the

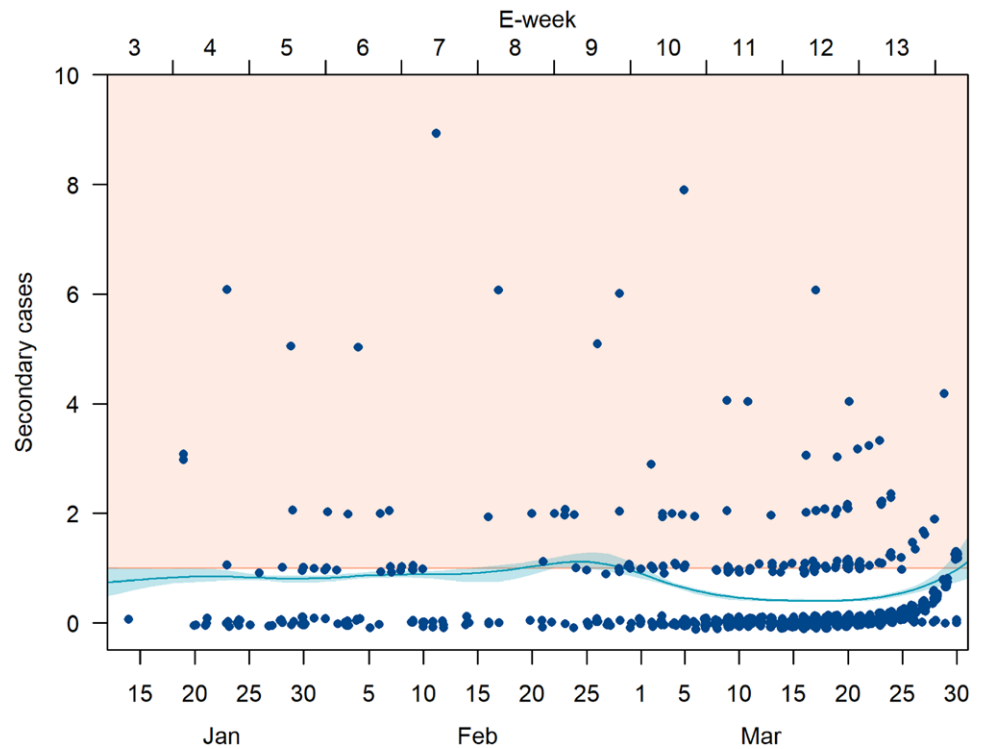


FIGURE 4. Effective reproduction number over time, R_t . Posterior mean number of secondary cases generated by each case (dot) is plotted against the symptom onset date in the respective case. Posterior estimates of R_t (line) is derived via spline interpolation from the dots in each iteration.

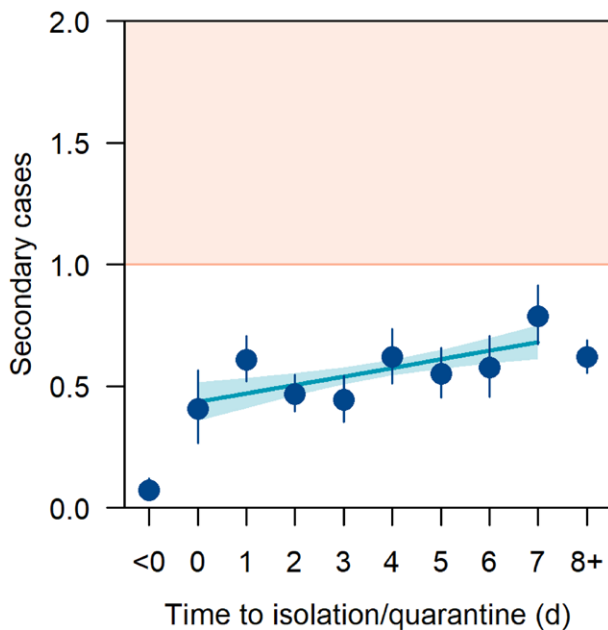


FIGURE 5. Secondary cases generated by time from onset to isolation/quarantine. For cases with the same duration from symptoms onset to isolation or quarantine, the posterior mean number of secondary cases (dot) and the 95% credible interval (vertical line) is plotted. Linear regression of the mean secondary cases against time from onset to isolation/quarantine is performed at each iteration to derive the posterior incremental number of cases for each day of delay from onset to isolation (turquoise inclined line).

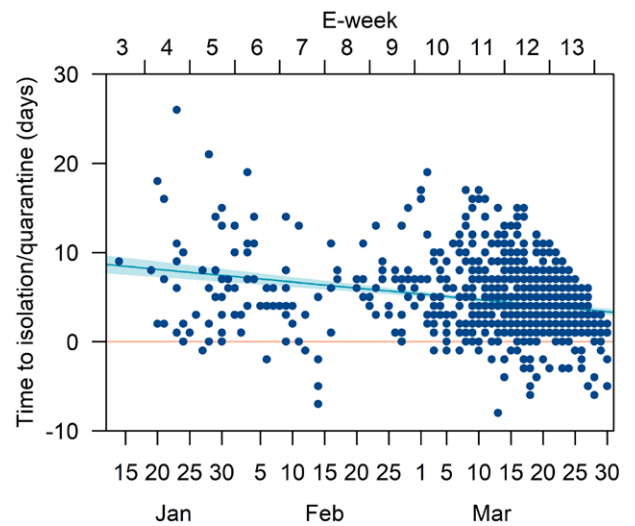


FIGURE 6. Time from onset to isolation/quarantine over the course of the outbreak. Duration from onset to isolation/quarantine for each case (dot) is plotted against the respective case's symptom onset date. Linear regression (turquoise line) of the data points shows the trend over the course of the outbreak.

community. Nearly half of the cases were detected through active case finding rather than cases spontaneously appearing, unlinked, in the health system, indicating the importance of having layers of surveillance to identify as many cases as possible. Most cases (83%) infected less than one person while a

few spreading events resulted in clusters of community transmission. These findings suggest an overdispersed offspring distribution and corroborates with Endo et al (2020).²⁴ This may mean that even if some milder COVID-19 cases are missed in the community, containment could still work as long as the more severe cases, and most of the cases associated with each cluster, that appears are identified and contained together with active case finding. Only 15.0% of the cases had no known infector and were not associated with any clusters. It is easier to identify clusters than individual cases because there is a high probability that some cases in the cluster will develop more severe illness and are identified, and active case finding will then detect the milder cases and contain further spread. Active case finding, coupled with greater awareness by medical practitioners and the public on COVID-19, has also likely reduced the delay from onset to isolation or quarantine at a rate of 0.06 days per day since the start of the outbreak. Our analyses suggest that these efforts can keep R_t below one.

Second, containment is possible if there is low continued importation of cases, as the pressure on containment will be substantial if large numbers of imported cases continue to seed transmission.²⁵ China has essentially prevented further exportation to Singapore and other countries by locking down Wuhan and other cities in Hubei, enacting massive community-based containment across other Chinese cities, and by suspending all outgoing tour groups. The restrictions imposed by China resulted in a sharp decrease in travel volume from China, and no imported cases to Singapore from China (excluding those from dedicated evacuation flights) was detected after January 31, 2020. However, Singapore has subsequently detected imported cases starting from March 3, 2020 from other countries in Europe, the Americas, and Asia. Without the same community containment measures that China has imposed to prevent transmission and exportations, this could result in continuous waves of imported cases leading to difficulties in containment. The impact of imported cases on containment is likely to depend on the resources available in the country to prevent secondary transmission from these cases. It is also not feasible for any country to totally shut its borders for a prolonged period of time to prevent importation from multiple sources, especially from returning residents. The alternative therefore is strengthening surveillance and containment measures, as these will be important both for countries that face early importations, and countries that have controlled their outbreaks but could face a second epidemic wave.

Third, sufficient human and infrastructural resources must be in place for contact tracing and quarantine, as these activities require substantial operational capacity and coordination. The capabilities in Singapore have been built over many years since the SARS outbreak in 2003,²⁶ and regularly exercised, leading to the prompt activation. This includes the building of the new National Centre for Infectious Diseases to incorporate clinical, laboratory, epidemiology, and research and training capabilities under one roof. Preparedness

exercises were held annually to determine their effectiveness and to strengthen areas for improvement. As such, about 51% of the cases were isolated within 4 days of their symptom onset or developed symptoms only after quarantine or isolation. However, these capabilities may not be sustainable if the numbers of imported and subsequent autochthonous cases continue to rise. One option would be self-isolation at home upon development of fever or respiratory symptoms, as this study showed that with each day's delay in isolating a symptomatic case, approximately 0.13 secondary cases would occur. This would effectively reduce the possibility of undetected COVID-19 cases from seeding further transmission in the community, and limit transmission if any to household contacts, who can be much more readily contact traced (as opposed to social or workplace contacts). In line with this strategy, Singapore introduced a recommendation for doctors to prescribe 5 days of sick leave for respiratory illnesses since February 14, 2020. Such a measure is likely to be feasible where a culture of social responsibility, and accessible and competent health systems, exist.

We extended the approach of Wallinga and Teunis to accommodate the case wherein epidemiologic links are known or suspected for some but not all cases. This approach obviated the need to separately estimate the serial interval from a secondary dataset and may be useful for other countries with contact tracing activities, especially if used as part of regular situation updates for policy formulation. Our estimates are markedly lower than the reproduction numbers estimated for the early phase of the Wuhan outbreak.⁸ We believe this may be due to the effect of isolation and quarantine, coupled with social responsibility, thus far experienced in Singapore. However, it is also possible that these estimates are due to underascertainment of infections. If that were so, we would expect it to surface through pneumonia and ILI surveillance streams, and we are monitoring these carefully for any signal that containment is losing its effectiveness.

This study had a limitation in that the algorithm assumes that all cases with unknown infector could only acquire infection from the observed cases, as in the original study by Wallinga and Teunis. Furthermore, active case finding facilitates prompt identification of secondary cases, thereby reducing their chances of recall bias of their onset dates and reduce their time spend in the community to generate tertiary infections. Consequently, as suggested in a study by Ali et al (2020),²⁷ for a cluster, the observed serial intervals would potentially shorten over time with the strengthening of public health interventions and such effects were not adjusted for in the current analysis.

CONCLUSIONS

Our findings suggest that a combination of a robust surveillance system, active case detection, prompt contact tracing and quarantine of contacts, coupled with community-based measures based on risk assessments, may help to reduce the

effective reproduction number below one and thereby limit the spread of COVID-19 outbreaks.

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