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Research article

Epidemiology of coronavirus disease 2019 (COVID-19) in Japan during the first and second waves

Ryo Kinoshita[1,2], Sung-mok Jung[1,3], Tetsuro Kobayashi[1], Andrei R. Akhmetzhanov[4] and Hiroshi Nishiura[1,*]

[1] School of Public Health, Kyoto University, Kyoto, Japan
[2] National Institute of Infectious Diseases, Center of Surveillance Immunization and Epidemiologic Research, Tokyo, Japan
[3] Graduate School of Medicine, Hokkaido University, Sapporo, Japan
[4] College of Public Health, National Taiwan University, Taipei, Taiwan

* **Correspondence:** Email: nishiura.hiroshi.5r@kyoto-u.ac.jp; Tel: +810757534456; Fax: +810757534458.

Abstract: Following the emergence and worldwide spread of coronavirus disease 2019 (COVID-19), each country has attempted to control the disease in different ways. The first patient with COVID-19 in Japan was diagnosed on 15 January 2020, and until 31 October 2020, the epidemic was characterized by two large waves. To prevent the first wave, the Japanese government imposed several control measures such as advising the public to avoid the 3Cs (closed spaces with poor ventilation, crowded places with many people nearby, and close-contact settings such as close-range conversations) and implementation of "cluster buster" strategies. After a major epidemic occurred in April 2020 (the first wave), Japan asked its citizens to limit their numbers of physical contacts and announced a non-legally binding state of emergency. Following a drop in the number of diagnosed cases, the state of emergency was gradually relaxed and then lifted in all prefectures of Japan by 25 May 2020. However, the development of another major epidemic (the second wave) could not be prevented because of continued chains of transmission, especially in urban locations. The present study aimed to descriptively examine propagation of the COVID-19 epidemic in Japan with respect to time, age, space, and interventions implemented during the first and second waves. Using publicly available data, we calculated the effective reproduction number and its associations with the timing of measures imposed to suppress transmission. Finally, we crudely calculated the proportions of severe and fatal COVID-19 cases during the first and second waves. Our analysis identified key characteristics of COVID-19, including density dependence and also the age dependence in the risk of severe outcomes. We also identified that the effective reproduction number during the state of emergency was maintained below the value of 1 during the first wave.

Keywords: SARS-CoV-2; COVID-19; Japan; descriptive epidemiology

1. Introduction

At the end of December 2019, an outbreak of pneumonia of unknown etiology occurred in Wuhan, Hubei province, China [1]. Despite the geographic location of Japan over 2000 km away, it was not take long before infected individuals were detected in the country [2]. Because of the epidemic situation in Wuhan, the city entered a lockdown on 25 January 2020. Subsequently, Japan chartered five flights for evacuation of Japanese residents to their own country [3]. The country also faced additional obstacles in February 2020 because of the need to control an outbreak on the Diamond Princess cruise ship, which was owned by a United Kingdom-based company but docked in Yokohama, Japan [4].

Genomic epidemiology has revealed that the first 2 months of the pandemic centered in Asia until the epicenter shifted from China to the United States and Europe. The return of Japanese citizens from these countries led to clusters of secondary cases in March 2020 [5,6]. Japan implemented several control measures to mitigate the epidemic such as avoidance of the 3Cs (closed spaces with poor ventilation, crowded places with many people nearby, and close-contact settings such as close-range conversations) and "cluster buster" strategies [7]. Citizens were urged to avoid situations with high risks of initiating large clusters of infections [8]. The cluster buster strategy was implemented because only approximately 20% of infected individuals were believed to contribute to secondary transmission [9]. Promotion of preventive behaviors coupled with intense case finding, close contact tracing, and isolation of identified cases were among the key measures used to limit epidemic spread [9,10].

Despite these containment efforts, Japan entered a major epidemic phase by the end of March 2020. When the number of cases sharply increased, cluster buster strategies were difficult to sustain as demand for contact tracing increased and human resources in local health centers remained limited. The first epicenter of COVID-19 in Japan was in Hokkaido. To prevent further spread of the epidemic, the governor announced a prefectural-level state of emergency on 28 February 2020 and asked citizens to restrict their social contact and stay at home. While the epidemic situation in Hokkaido eventually eased, the reach of COVID-19 expanded to the whole nation. The country asked its citizens to restrict their physical contacts by announcing a non-legally binding state of emergency on 8 April 2020. The state of emergency was first implemented only in seven prefectures (Tokyo, Saitama, Chiba, Kanagawa, Osaka, Hyogo, and Fukuoka) but was later expanded to all of Japan. As the epidemic was mitigated, the country gradually relaxed the state of emergency in 39 prefectures starting on 7 April 2020 (excluding Hokkaido, Tokyo, Saitama, Chiba, Kanagawa, Osaka, Kyoto, and Hyogo). On 21 May 2020, the state of emergency was also lifted in Osaka and its neighboring prefectures Hyogo and Osaka. The state of emergency was completely lifted in all 47 prefectures by 25 May 2020.

To compensate for economic losses resulting from the state of emergency, the government conducted public support campaigns to encourage consumption, including the "Go To Travel" campaign starting on 22 July 2020 [11]. The campaign included a 35% discount on domestic travel costs, and starting in October 2020, vouchers were issued (worth 15% of the total travel cost) that could be used for travel within the prefecture. Because the epidemic situation in Tokyo was severe even after relaxing the state of emergency on 25 May 2020, and because of the reemergence of cases during a second wave, Tokyo was excluded from the campaign until 1 October 2020. Another nationwide "Go To Eat" campaign started on 1 October 2020 to encourage citizens to dine out by partially covering their expenses for meals.

In the present study, we aimed to quantitatively describe the propagation of the COVID-19 epidemic in Japan with respect to time, age, and space during the first two major waves in 2020 using simple mathematical models. By estimating the effective reproduction number (R_t) before and after the epidemic, we quantitated the impact of the announcement of a non-legally binding state of emergency during the first wave. We examined differences between the first and second waves by comparing the age-stratified proportions of severe and fatal cases.

2. Materials and methods

2.1. Epidemiological data

We retrieved incidence data for confirmed COVID-19 cases from the websites of municipal prefectures of Japan and complemented this dataset using national report data when needed by creating a line-list [12]. In Japan, all cases of COVID-19 confirmed by reverse transcription polymerase chain reaction were mandated to be notified to the government. When the date of reporting was missing in prefectural data, it was determined using national reporting data. All confirmed COVID-19 cases were categorized into two types: imported and domestic cases. Imported cases were defined as cases occurring in individuals with a history of international travel or who were passengers on the Diamond Princess cruise ship. All others were classified as domestic cases. Reported cases from chartered flights were excluded as they did not play a role in domestic transmission dynamics in Japan. Numbers of confirmed deaths and the outcome of each case (asymptomatic infection; mild or moderate disease; severe or critical disease; or death) were collected from the database by the Ministry of Health Labour and Welfare of Japan. These datasets are partially publicly available [12]. The outcome of infection was determined for all cases who tested positive by asking hospitals treating patients with COVID-19 to update the prognosis of COVID-19 cases after diagnosis. As the number of cases expanded, it is possible that recording may have become burdensome, potentially leading to under-reporting.

2.2. Statistical analysis

Pearson's correlation coefficients were calculated between the cumulative number of cases until 31 October 2020 and population size and population density per km^2. The risk of severe disease and the case fatality risk (*CFR*) were calculated using the total number of confirmed cases as the denominator (*cCFR*) [13]. The risk of severe disease and the *cCFR* were defined as follows:

$$Risk\ of\ severe\ disease = \frac{I_{severe\ or\ critical} + I_{death}}{I_{asymptomatic} + I_{mild\ or\ moderate} + I_{severe\ or\ critical} + c_{\ death}}$$

$$cCFR = \frac{I_{death}}{I_{asymptomatic} + I_{mild\ or\ moderate} + I_{severe\ or\ critical} + I_{death}},$$

where I is the number of infected individuals with a particular disease outcome (i.e., asymptomatic infection, mild or moderate disease, severe or critical disease, or death). We assumed that all individuals who died from COVID-19 experienced severe or critical symptoms. Following diagnosis, each case I was followed up and the date when the case experienced the worst outcome of disease was used as the input in the analysis. Because the prognosis of each infected individual was determined, right-censoring was adequately addressed in this analysis. The first epidemic wave covered the period between January and May 2020, whereas the second epidemic wave covered the period between June to October 2020. 95% confidence intervals (95% CIs) were calculated using the Wilson score interval. The risk of severe disease and the *cCFR* were also calculated by excluding asymptomatic cases from the denominator (Figure S1).

2.3. Evaluation of interventions

We assessed transmission dynamics by estimating the time-varying effective reproduction number (Rt), which is the average number of secondary cases generated by a primary case in the presence of partial immunity or implemented control measures. The mathematical model evaluating the impacts of COVID-19 interventions (i.e., the declaration of a state of emergency by the Japanese government and the Hokkaido prefectural government) was made up of two parts: (i) back-projection of the epidemic curve, and (ii) estimation of impact of interventions on R_t. First, reported cases whose date of illness onset was missing were back-projected to presumptive dates of illness onset using the reporting delay distribution. Then, we back-projected the epidemic curve from the date of illness onset to the date of infection. The time-varying R_t was estimated using the back-projected epidemic curve based on date on date of infection and by applying the renewal process to quantify the effects of interventions.

2.3.1. Back-projection

To accurately quantitate the impact of interventions on COVID-19 transmission dynamics, we reconstructed the epidemic curve as a function of infection time through non-parametric back-projection [14]. First, for reported cases with unknown illness onset dates, we back-projected from the date of laboratory confirmation to the date of illness onset using the probability mass function (PMF) of the empirically estimated time delay from illness onset to laboratory confirmation during the first wave (until 31 May 2020). The reporting delay was estimated as 6.7 days with a standard deviation of 4.5 days by fitting to the Weibull distribution. Non-parametric back-projection based on the Expectation-Maximization-Smoothing algorithm was conducted using the R package '*surveillance*' [15]. We then back-projected the epidemiological curve once again from the date of illness onset to the time of infection using the PMF of the incubation period [16] and applying the same method.

2.3.2. Estimation of the effective reproduction number

Let $C_{domestic}(t)$ represent the number of domestic cases on day t. Then, the expected number of domestic cases ($\mathrm{E}(C_{domestic}(t))$) can be modelled as:

$$\mathrm{E}\big(C_{domestic}(t)\big) = R_k \sum_{\tau=1}^{t-1} C_{total}(t-\tau)g(\tau) \quad (1)$$

where $C_{total}(t)$ is the total number of confirmed COVID-19 cases, including both imported and domestic cases, on day t, $g(\tau)$ is the PMF of the generation time distribution [17], and R_k is the effective reproduction number for period k (four periods with intervals of 20 and 30 days for Hokkaido and all of Japan, respectively). The periods of analysis were specifically selected considering the durations of interventions: the state of emergency in Hokkaido was lifted after 21 days, while the national state of emergency continued for 49 days. All infected individuals in the first wave were assumed to be reported in the data because enough time has passed to account for any reporting delay. To estimate R_k, we assumed that $C_{domestic}(t)$ followed a Poisson distribution. The likelihood function and the 95% CI of each estimate was derived using the profile likelihood,

$$\mathrm{L}\big(R_k; C_{domestic}(t)\big) = \prod_{t=1}^{T} \frac{\exp(-E(C_{domestic}(t)))(E(C_{domestic}(t)))^{C_{domestic}(t)}}{C_{domestic}(t)!} \quad (2)$$

3. Results

Figure 1 shows reported COVID-19 cases in Japan according to age and reported deaths as well as the chronology of major events. During the first wave, there were 18,946 reported cases, while during the second wave, there were 87,866 reported cases (Figure 1A). Age was recorded as NA for cases where age was not reported or when age was reported in categories larger than decades. The proportion of reported cases over 60 years old in the first wave (January to May 2020) was 28.0% but decreased to 17.1% during the second wave (June to October 2020). Conversely, the proportion of cases occurring among younger individuals (under 60 years old) increased from 59.1 to 76.2% from the first to the second wave (Table S1). A similar change in the age distribution of cases has been observed in the United States [18]. The peak of COVID-19 deaths was delayed by approximately 1 month compared with the peak number of reported cases (Figure 1B). The total number of deaths was 892 in the first wave and 873 in the second wave. Figure 1C shows the chronology of events during the early COVID-19 epidemic in Japan from January to October 2020.

The spatiotemporal distribution of COVID-19 cases in each prefecture is shown in Figure 2. The first case of COVID-19 in Japan was confirmed in Kanagawa Prefecture on 15 January 2020. Hokkaido Prefecture was one of the first prefectures to experience escalating growth in case numbers, with the presumptive index cases occurring among international visitors to the annual snow festival held between 31 January and 11 February 2020 [19]. Later, the two major urban prefectures, Tokyo and Osaka (accounting for 11% and 7% of the 127 million population of Japan, respectively), experienced notable surges in COVID-19 case numbers. Tokyo and adjacent prefectures (Kanagawa, Yokohama, Saitama, and Chiba) frequently reported daily numbers of 10 or more cases even after the state of emergency was lifted on 25 May. This was sufficient for a second wave to begin nationally soon after the first wave.

Figure 3 shows heat-maps of COVID-19 cases reported in Japan during the first and second waves. During the first wave, the focal areas were prefectures with urban cities such as Hokkaido, Tokyo, Aichi, Osaka, and Fukuoka. Kanagawa, Saitama, and Chiba also experienced substantial numbers of cases as suburbs of Tokyo, the capital city of Japan. Similarly, Hyogo and Kyoto experienced a diffusion of cases from Osaka, the second largest city in Japan. During the second wave, similar focal areas were observed, although cases were increasingly observed in suburban and rural prefectures as the numbers of cases in prefectures with urban cities increased.

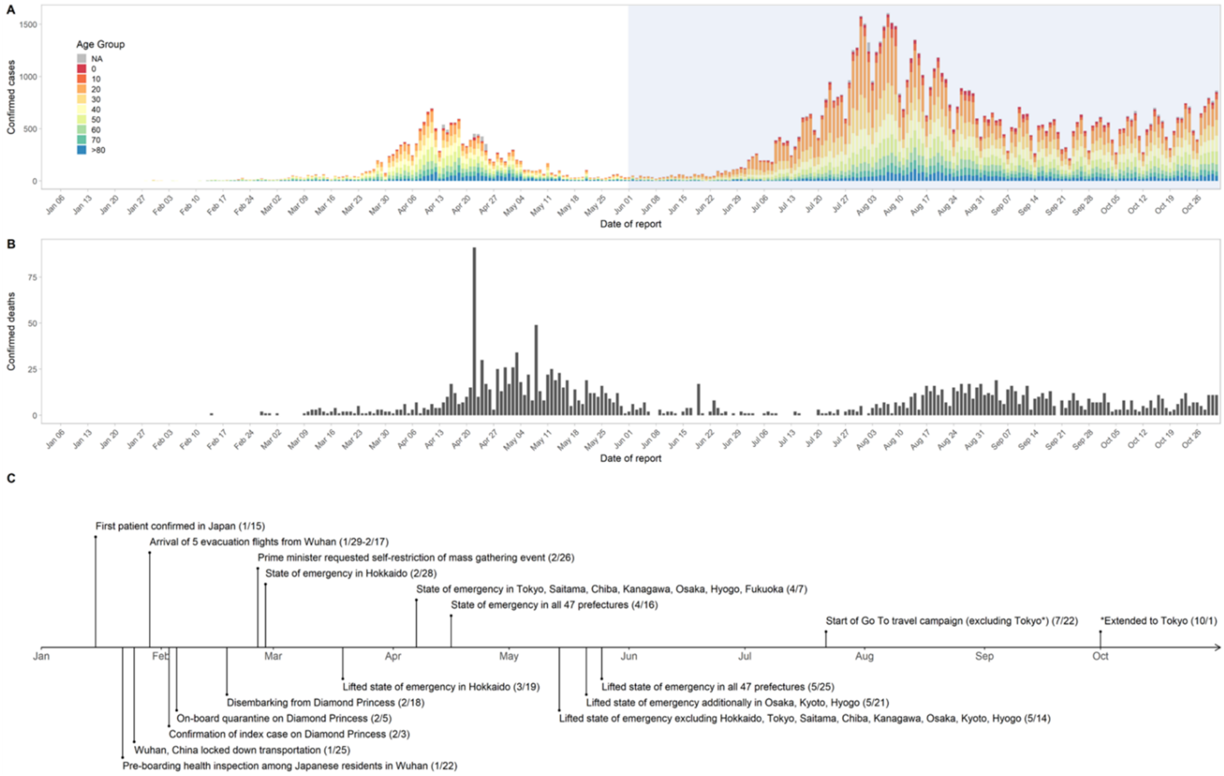

Figure 1. Confirmed cases of COVID-19 by age group and reported deaths in Japan from January to October 2020. (A) The number of confirmed cases by age is shown according to the date of reporting at the prefectural or national level. NA indicates cases with missing age information. We defined the unshaded area as the first wave (January to May 2020) and the shaded area as the second wave (June to October 2020) (B) The number of confirmed deaths is shown according to the date of reporting. (C) Chronology of events related to the COVID-19 epidemic in Japan.

The population density and absolute population size were strongly correlated with the cumulative number of reported cases (Figure 4). Hokkaido Prefecture has a large population (5.3 million) but a low population density (67/km^2). However, its capital, Sapporo, is the fifth most populous city in Japan and has a population density of 1750/km^2, thus contributing to additional spatially diffuse cases within the prefecture. In order that the risk of infection is compared against population density and population size, we also examined the cumulative incidence rate per population. The Pearson's correlation coefficient was estimated at 0.73 for population density (/km^2) ($p < 0.001$) and 0.69 for population size ($p < 0.001$), indicating the presence of density dependence in the mechanism of transmission.

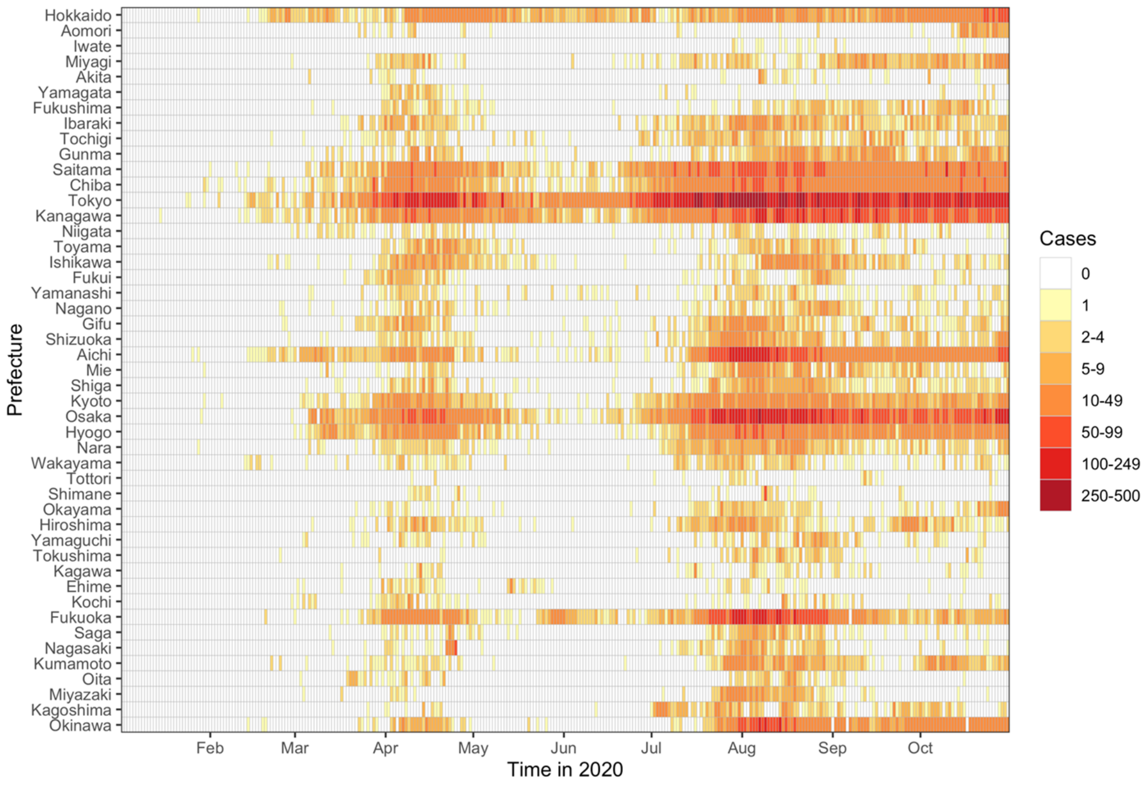

Figure 2. Spatiotemporal distribution of COVID-19 cases in Japan. The number of cases by date of reporting at the prefectural or national level is shown for all 47 prefectures of Japan. Prefectures are ordered from north to south.

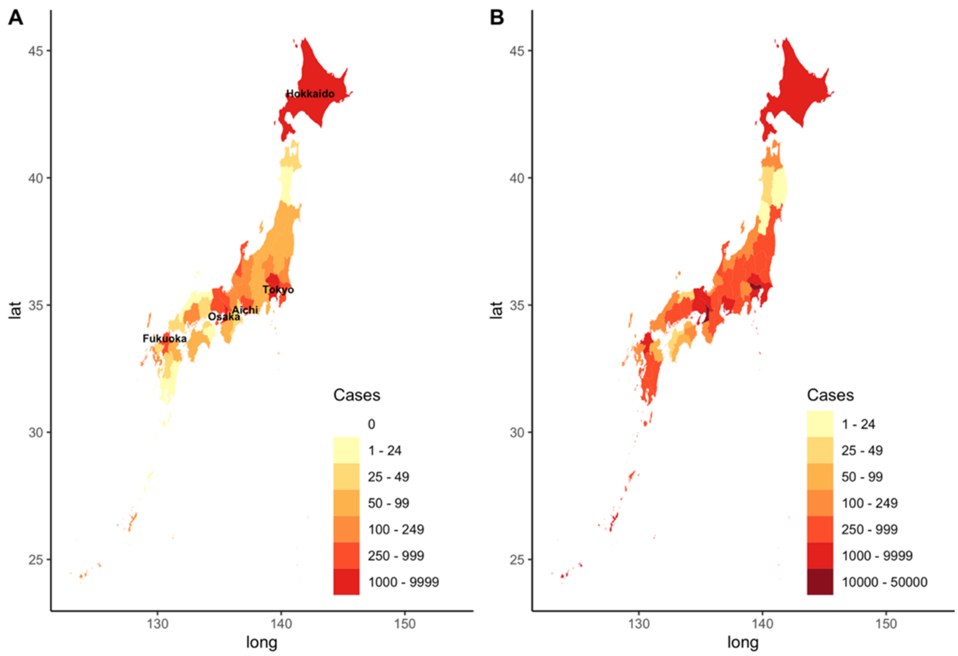

Figure 3. Spatial distribution of cumulative reported COVID-19 cases in Japan during the first wave (A) and the second wave (B). The x-axis corresponds to latitude and the y axis corresponds to longitude.

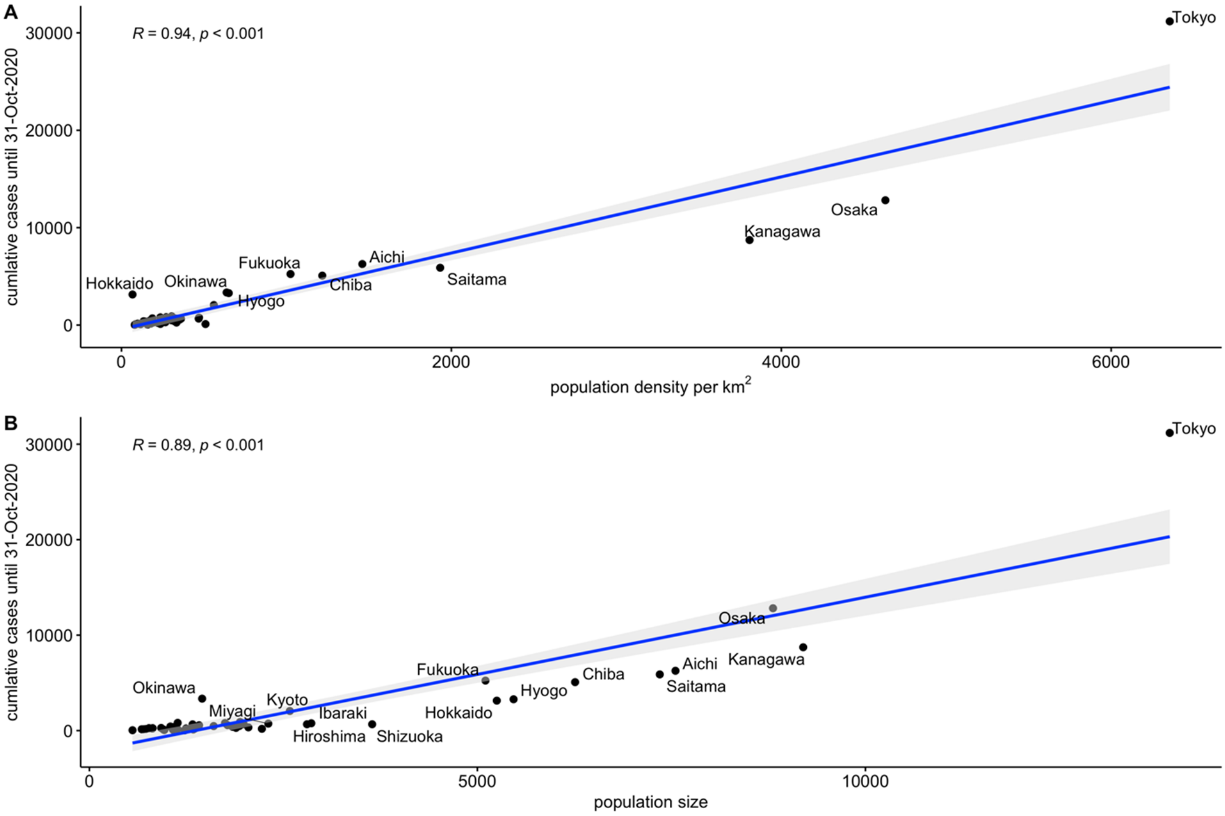

Figure 4. Correlations between cumulative COVID-19 cases in Japan and population size/density by prefecture. (A) Scatter plot of population density per km^2 and cumulative COVID-19 cases until the end of October 2020. (B) Scatter plot of population size and cumulative COVID-19 cases until the end of October 2020. *R* is the Pearson's correlation coefficient and *p* is the p-value.

To calculate the impact of the declaration of a state of emergency on the effective reproduction number (R_t), R_t was calculated in Hokkaido and for all of Japan (Figure 5). R_t in Hokkaido during two periods before the declaration of the first prefectural-level state of emergency, from 19 January 2020 to 7 February 2020 and from 8 February 2020 to 27 February 2020, was estimated as 1.65 (95% CI: 0.84–2.86) and 1.23 (95% CI: 1.02–1.46), respectively. During the state of emergency in Hokkaido (28 February to 18 March 2020), R_t was estimated as 0.70 (95% CI: 0.52–0.91). After lifting of the state of emergency, R_t increased to 1.86 (95% CI: 1.66–2.13). The R_t for all of Japan before declaration of the state of emergency (8 March to 6 April 2020) was estimated as 1.29 (95% CI: 1.26–1.31), while the R_t for all of Japan during two periods after declaration of the state of emergency (7 April to 6 May 2020 and 7 May to 5 June 2020) was estimated as 0.68 (95% CI: 0.66–0.70) and 0.95 (95% CI: 0.90–1.00), respectively. The R_t from 6 June to 5 July 2020 was estimated as 1.36 (95% CI: 1.31–1.38). The state of emergency contributed to reducing R_t below the value of 1, shifting the epidemic to a declining trend.

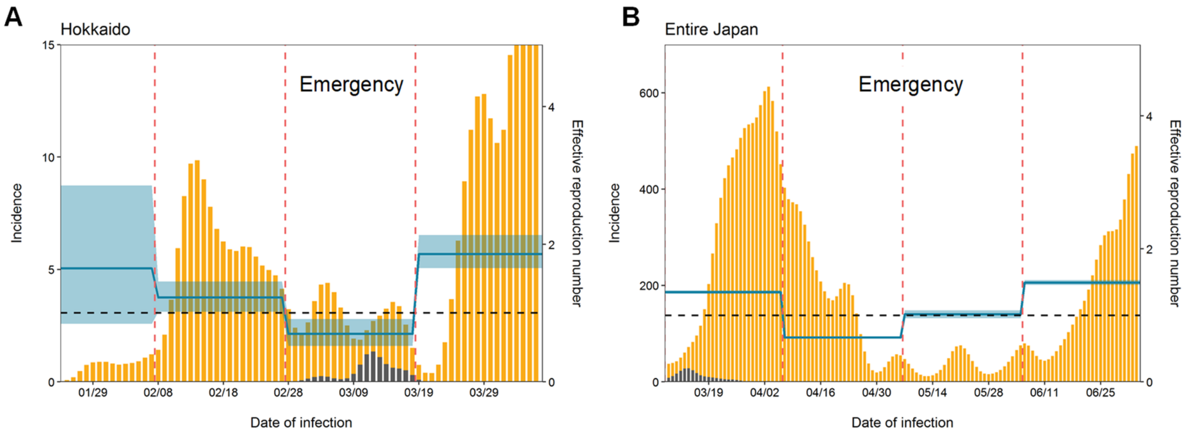

Figure 5. Effective reproduction number of COVID-19 before and after the declaration of emergency in Hokkaido (A) and in all of Japan (B). The yellow bars represent domestic cases and the navy bars represent imported cases. The effective reproduction number and its 95% CI are plotted in blue. (A) In Hokkaido, the state of emergency was declared on 28 February 2020 (second vertical dotted line in red) and periods of 20 days were analyzed (the first period had 15 days because there were no cases prior to 25 January 2020). (B) In Japan, a national state of emergency was declared on 7 April 2020 (second vertical dotted line in red) and periods of 30 days were analyzed. Estimated values by region in tabular format can be found in Table S2.

Interestingly, the number of cases appeared to decline before the implementation of the state of emergency. Our analysis included time-steps of a fixed number of days (20 days for Hokkaido and 30 days for all of Japan) to simplify comparisons between time-steps. However, changes between time-steps may be perceived as sudden changes in R_t. We caution that the impact on R_t was gradual and was substantially affected by the decline in population mobility (Figure S2). Among six mobility datasets provided by the Google Community Mobility Reports [20], retail and recreation, workplaces, and transit stations followed trends similar to that of R_t for all of Japan when a piecewise constant regression was fitted (Figure S3). To confirm that R_t dropped prior to declaration of the state of emergency, we analyzed R_t in Tokyo by events/alerts without fixing the number of days to be analyzed (Figure S4). Before the prime minister announced the state of emergency in Japan, the governor of Tokyo Metropolis made several strong alerts and requests for residents to restrict going out on the weekends and going out to bars, which may have contributed to the decline in mobility and risky contacts.

Finally, the proportion of severe COVID-19 cases and deaths was calculated (Figure 6). During both the first and the second wave, the risk of severe symptoms or death increased with advancing age, especially those over 60 years of age. In the first wave, the risk of severe symptoms or death by age decade were as follows: 60s, 15.0% (95% CI: 13.2–17.1%); 70s, 23.5% (95% CI: 21.1–26.0%); 80s, 31.1% (95% CI: 28.0–34.3%); and 90s, 36.1% (95% CI: 31.2–41.3%). During the second wave, the risk of severe symptoms or death decreased in all age groups. The rate of decrease of the point estimate was especially high among younger age groups. The reduction in the risks of severe symptoms or death by age decade as follows: 60s, 0.26-fold; 70s, 0.40-fold; 80s, 0.50-fold; and 90s, 0.53-fold compared with the first wave. During the second wave, the risks of severe symptoms or death by age decade were as follows: 60s, 4.0% (95% CI: 3.5–4.5%); 70s, 9.4% (95% CI: 8.6–10.2%); 80s, 15.7% (95% CI: 14.5–16.9%), and 90s, 19.0% (95% CI: 16.9–21.3%) (Table S3). Similarly, the risks of death (*cCFR*) during the first wave by age decade were as follows: 60s, 5.3% (95% CI: 4.2–6.6%); 70s, 14.9%

(95% CI: 12.9–17.0%); 80s, 27.4% (95% CI: 24.5–30.5%); and 90s, 34.9% (95% CI: 30.0–40.1%). These rates were 0.31-, 0.39-, 0.49-, and 0.530-fold lower in the respective age bands/decades in the second wave compared with the first wave. The *cCFRs* during the second wave by age decade were as follows: 60s, 1.7% (95% CI: 1.4–2.0%); 70s, 5.8% (95% CI: 5.2–6.5%); 80s, 13.5% (95% CI: 12.4–14.7%); and 90s, 18.5% (95% CI: 16.4–20.8%) (Table S4).

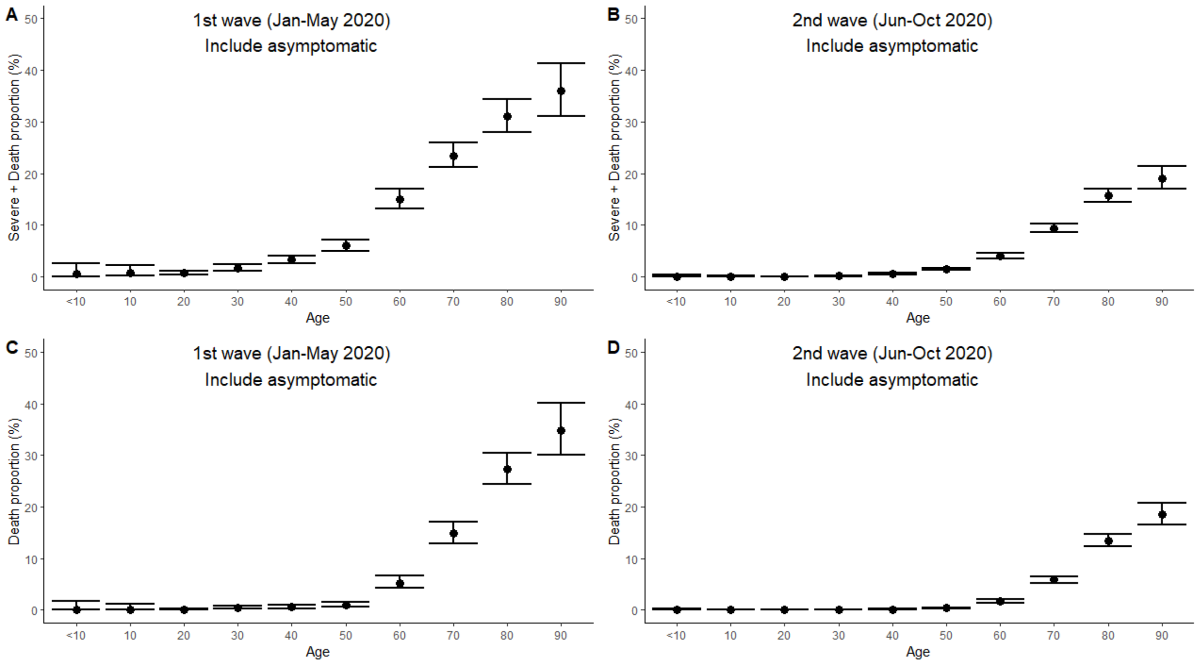

Figure 6. Proportions of severe disease and death by age group. (A, B) Risk of severe symptoms and death during the first wave (A) and the second wave (B). (C, D) Risk of death (*cCFR*) during the first wave (C) and the second wave (D). 95% CIs were calculated using the Wilson score intervals. Age was categorized in decades.

4. Discussion

The present study analyzed the propagation of COVID-19 in Japan from January to October 2020. Until February, the country had been successful in implementing cluster-focused intervention strategies to contain cases originating from Wuhan, China. Because of further importations from new epicenters in Europe and the United States, the first wave of the COVID-19 epidemic in Japan occurred in March 2020, and was controlled after declaration of a state of emergency along voluntary restrictions among citizens to restrict unnecessary physical contact. However, the state of emergency was eased before cutting chains of transmission, especially in urban locations. While the low numbers of cases in June allowed the country to resume cluster-focused intervention strategies and socio-economic activities, clusters were sporadically and continuously observed, leading to the emergence of a second wave in the country.

Our descriptive analysis allowed us to understand key characteristics of the COVID-19 epidemic in Japan. First, cases were concentrated in urban cities during the first wave, but during the larger second wave, more cases were observed in rural areas (Figures 2 and 3). Second, there were clear correlations between the cumulative numbers of cases, population density, and population size (Figure 4). Third, the declaration of a state of emergency contributed to maintaining R_t below a value of 1 during the first wave, showing that voluntary restrictions in Japan would be effective to mitigate and bring epidemics under control. Fourth, the risk of severe outcomes (*cCFR* or risk of severe symptoms) was age-dependent with higher risks observed among the elderly. The outcome of infection improved over the first and second waves, most likely owing to improvements in treatment and improved identification of mild and asymptomatic cases with increased testing and contact tracing. Finally, there was a reduction in the risk of severe outcomes between the first wave and the second wave, likely owing to increased case ascertainment and improved treatment. We believe that descriptive epidemiology in Japan demonstrating how the social, political, and scientific factors modulate the epidemic situation in Japan will contribute to pandemic preparedness against future emerging infectious diseases outbreaks.

Considering these findings, an important conclusion that policymakers should take from the present study is that, unless chains of transmission are cut, another epidemic will occur [21]. Even after the lifting of the state of emergency in Tokyo, there were continuous chains of transmissions that may have driven the emergence of the second wave. Moreover, during the second wave, the introduction of the “Go To Travel” campaign promoted intra-prefecture mixture of individuals, potentially contributing to increased case numbers in rural prefectures. Thus, before the country achieves sufficient COVID-19 vaccine coverage or effective anti-viral treatments become available, continuous containment efforts will be vital to bring the epidemic under control.

Several limitations of this study should be noted. First, analysis of COVID-19 cases was based on notification data, and thus the ascertainment rate was likely to have changed over time. Changes in the ascertainment rate may differ by age and disease severity, as has been demonstrated during the early phase of the first wave [22–24]. Specifically, analysis of the *cCFR* includes asymptomatic cases in the denominator, and the ascertainment of those individuals is likely to have changed over time. Second, R_t is estimated based on notifications in the prefecture where diagnosis occurred, and thus we were unable to account for inter-prefecture migration of individuals exhibiting “health seeking” behaviors. Third, our analysis is a case study of Japan, and our findings and their interpretations would be context-dependent and may not be applicable to the rest of the world. Fourth, while there were observable changes in the reproduction number after the declaration of the state of emergency and the start of “Go To Travel” or “Go To Eat” campaigns, causal relationships have yet to be determined and our analysis was not able to understand to what extent these interventions have contributed to the increase or decrease of the cases. Fifth, the factors that caused the second wave to peak in August without any stringent interventions were not identified in this study. Analysis of such features are important topics of future studies.

5. Conclusions

The present study comprehensively described how the COVID-19 epidemic started in Japan and how it has propagated by age, space, and time despite the countermeasures implemented to control disease spread. Sustained transmission of COVID-19 is still being observed in the country, and the size of the epidemic has become even larger in subsequent waves. Before sufficient vaccination coverage is reached or effective anti-viral treatments become widely available, the only practical strategy to mitigate the epidemic is to limit numbers of contacts. The economic burdens of such strategies may be high, but without strong leadership to implement such strategies, the epidemic may continue to grow.

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Conflict of interest

The authors declare no conflicts of interest.

References

1. Q. Li, X. Guan X, P. Wu, X. Wang, L. Zhou, Y. Tong, et al., Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia, *N. Engl. J. Med.*, **382** (2020), 1199–1207. https://doi.org/10.1056/NEJMoa2001316
2. I. I. Bogoch, A. Watts, A. Thomas-Bachli, C, Huber, M. U. Kraemer, K. Khan, Pneumonia of unknown aetiology in Wuhan, China: Potential for international spread via commercial air travel, *J. Travel Med.*, **27** (2020). https://doi.org/10.1093/jtm/taaa008
3. H. Nishiura, T. Kobayashi, Y. Yang, K. Hayashi, T. Miyama, R. Kinoshita, et al., The rate of underascertainment of novel coronavirus (2019-nCoV) infection: Estimation using Japanese passengers data on evacuation flights, *J. Clin. Med.*, **9** (2020), 419. https://doi.org/10.3390/jcm9020419
4. K. Mizumoto, K. Kagaya, A. Zarebski, G. Chowell, Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020, *Eurosurveillance*, **25** (2020), 2000180. https://doi.org/10.2807/1560-7917.ES.2020.25.10.2000180
5. T. Sekizuka, K. Itokawa, M. Hashino, T. Kawano-Sugaya, R. Tanaka, L. Yatsu, et al., A genome epidemiological study of SARS-CoV-2 introduction into Japan, *MSphere*, **5** (2020), e00786–20. https://doi.org/10.1128/mSphere.00786-20
6. Y. Furuse, Y. K. Ko, M. Saito, Y. Shobugawa, K. Jindai, T. Saito, et al., Epidemiology of COVID-19 outbreak in Japan, January–March 2020, *Jpn. J. Infect. Dis.*, **73** (2020), 391–393. https://doi.org/10.7883/yoken.JJID.2020.271
7. H. Oshitani, Cluster-based approach to coronavirus disease 2019 (COVID-19) response in Japan, from February to April 2020, *Jpn. J. Infect. Dis.*, **73** (2020), 491–493. https://doi.org/0.7883/yoken.JJID.2020.363

8. Y. Furuse, E. Sando, N. Tsuchiya, R. Miyahara, I. Yasuda, Y. K. Ko, et al., Clusters of coronavirus disease in communities, Japan, January–April 2020, *Emerg. Infect. Dis.*, **26** (2020), 2176–2179. https://doi.org/10.3201/eid2609.202272
9. H. Nishiura, H. Oshitani, T. Kobayashi, T. Saito, T. Sunagawa, T. Matsui, et al., Closed environments facilitate secondary transmission of coronavirus disease 2019 (COVID-19), *medRxiv*, 2020. https://doi.org/https://doi.org/10.1101/2020.02.28.20029272.
10. A. Endo, S. Abbott, A.J. Kucharski, S. Funk, Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China, *Wellcome Open Res.*, **5** (2020), 67. https://doi.org/10.12688/wellcomeopenres.15842.3
11. A. Anzai, H. Nishiura, "Go To Travel" campaign and travel-associated coronavirus disease 2019 cases: A descriptive analysis, July–August 2020, *J. Clin. Med.*, **10** (2021), 398. https://doi.org/10.3390/jcm10030398
12. *Open data (COVID-19)*, Ministry of Health Labour and Welfare of Japan, 2021. Available from: https://www.mhlw.go.jp/stf/covid-19/open-data.html.
13. S. M. Jung, A. R. Akhmetzhanov, K. Hayashi, N. M. Linton, Y. Yang, B. Yuan, et al., Real-time estimation of the risk of death from novel coronavirus (COVID-19) infection: Inference using exported cases, *J. Clin. Med.*, **9** (2020), 523. https://doi.org/10.3390/jcm9020523
14. S. M. Jung, A. Endo, A. R. Akhmetzhanov, H. Nishiura, Predicting the effective reproduction number of COVID-19: Inference using human mobility, temperature, and risk awareness, *Int. J. Infect. Dis.*, **113** (2020), 47–54. https://doi.org/10.1016/j.ijid.2021.10.007
15. M. Höhle, A. Riebler, *The R package 'surveillance'*, 2005. Available from: https://cran.r-project.org/web/packages/surveillance/index.html.
16. N. M. Linton, T. Kobayashi, Y. Yang, K. Hayashi, A. R. Akhmetzhanov, S. M. Jung, et al., Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: A statistical analysis of publicly available case data, *J. Clin. Med.*, **9** (2020), 538. https://doi.org/10.3390/jcm9020538.
17. H. Nishiura, N. M. Linton, A. R. Akhmetzhanov, Serial interval of novel coronavirus (COVID-19) infections, *Int. J. Infect. Dis.*, **93** (2020), 284–286. https://doi.org/10.1016/j.ijid.2020.02.060
18. T. K. Boehmer, J. DeVies, E. Caruso, K. L. van Santen, S. Tang, C. L. Black, et al., Changing Age Distribution of the COVID-19 Pandemic-United States, May–August 2020, *MMWR Morb. Mortal. Wkly. Rep.*, **69** (2020), 1404–1409. https://doi.org/10.15585/mmwr.mm6939e1
19. A. R. Akhmetzhanov, K. Mizumoto, S. M. Jung, N. M. Linton, R. Omori, H. Nishiura, Estimation of the actual incidence of coronavirus disease (COVID-19) in emergent hotspots: The example of Hokkaido, Japan during February–March 2020, *J. Clin. Med.*, **10** (2021), 2392. https://doi.org/10.3390/jcm10112392
20. *COVID-19 Google community mobility reports*, Google, Available from: https://www.google.com/covid19/mobility/.
21. P. Wilmes, J. Zimmer, J. Schulz, F. Glod, L. Veiber, L. Mombaerts, et al., SARS-CoV-2 transmission risk from asymptomatic carriers: Results from a mass screening programme in Luxembourg, *Lancet Reg. Health Eur.*, **4** (2021), 100056. https://doi.org/10.1016/j.lanepe.2021.100056
22. R. Omori, K. Mizumoto, H. Nishiura, Ascertainment rate of novel coronavirus disease (COVID-19) in Japan, *Int. J. Infect. Dis.*, **96** (2020), 673–675. https://doi.org/10.1016/j.ijid.2020.04.080

23. T. Kawashima, S. Nomura, Y. Tanoue, D. Yoneoka, A. Eguchi, C.F.S. Ng, et al., Excess all-cause deaths during coronavirus disease pandemic, Japan, January–May 2020, *Emerg. Infect. Dis.*, **27** (2021), 789–795. https://doi.org/10.3201/eid2703.203925.
24. T. Yoshiyama, Y. Saito, K. Masuda, Y. Nakanishi, Y. Kido, K. Uchimura, et al., Prevalence of SARS-CoV-2-specific antibodies, Japan, June 2020, *Emerg. Infect. Dis.*, **27** (2021), 628–631. https://doi.org/10.3201/eid2702.204088