Waning COVID-19 vaccine effectiveness in Japan

Junko Kurita[1],*, Tamie Sugawara[2], Yasushi Ohkusa[2]

[1] Department of Nursing, Tokiwa University, Ibaraki, Japan;
[2] National Institute of Infectious Diseases, Tokyo, Japan.

SUMMARY   As of the end of November, 2021, the rate of completion for second-dose COVID-19 vaccine administration was almost 80% in Japan. We evaluated waning COVID-19 vaccine effectiveness in Japan, controlling for mutated strains, the Olympic Games, and countermeasures. The effective reproduction number R(t) was regressed on current vaccine coverage and data of a certain number of days prior, as well as shares of mutated strains, and an Olympic Games dummy variable along with data of temperature, humidity, mobility, and countermeasures. The study period was February, 2020 through November 4, as of November 25, 2021. Estimation results indicate that vaccine coverage of more than 90 days prior raises R(t) significantly. Especially, vaccine coverage with 90 or 120 days prior cancelled vaccine effectiveness completely. Results indicate significant waning of vaccine effectiveness from 90 days after the second dose.

Keywords   COVID-19, effective reproduction number, waning, vaccine coverage, vaccine effectiveness, variant strain

1. Introduction

Wide coverage of COVID-19 vaccination has altered outbreak situations in European countries and in the US. Unfortunately, vaccination in Japan started only in February, 2021 using BNT162b2 mRNA (Pfizer Inc., BioNTech) and mRNA-1273 (Moderna, Inc.) vaccines: among the latest of starting dates of vaccination programs in economically developed countries. Later, ChAdOx1 adenoviral vector (Oxford, AstraZeneca) also became available. By the end of November, 2021, the rate of completion for second dose vaccine administration had reached almost 80% in Japan (Figure 1) (*1,2*). The next challenge posed by vaccine issues in Japan might be waning of vaccine effectiveness.

In fact, waning vaccine effectiveness has been reported (*3,4*). One study revealed that the log of IgG antibody titer decreased by a factor of 18.3 when measured six months after second-dose vaccination. Another study revealed vaccine effectiveness as 77.5% at one month after the second vaccination, but it had decreased to about 20% when measured 5-7 months later. In the real world, vaccines of several types have been used. Moreover, vaccinated persons might change their behaviors. Therefore, this study assessed vaccine effectiveness and its waning capabilities against infectiousness in the real world, particularly in Japan.

By the time vaccinations started in Japan, the alpha variant strain had emerged and had expanded to dominate the recorded infections. Subsequently, a new mutant alpha variant strain appeared in May. Based mainly on data reported by the UK, its infectiousness and pathogenicity were estimated as 35-90% higher than those of the original strain circulating before the emerging variant strain (*5-8*). Therefore, we consider the prevalence of these mutated strains together when evaluating vaccine effects.

The object of this study was to estimate waning of vaccine effectiveness against SARS-CoV-2 infectiousness for the outbreak in Japan as a result of the vaccine effectiveness itself, the mutated strain, the Olympic Games, countermeasures, and other factors that might affect infectiousness.

2. Methods

2.1. Calculation procedure for R(t)

This study examined the numbers of symptomatic patients reported by the Ministry of Health, Labour and Welfare (MHLW) for February 1, 2020 – August 29, 2021 published (*9*) as of October 18, 2021. Some patients were excluded from data for Japan: patients presumed to be persons infected abroad or infected as Diamond Princess passengers. Those patients were presumed not to represent community-acquired infection in Japan. For some symptomatic patients with unknown onset dates, we estimated the onset dates from an empirical

distribution with duration extending from onset to the report date among patients for whom the onset date had been reported.

Onset dates among patients who did not report this information and a reporting delay were adjusted using the same procedures as those used for earlier studies (*10,11*). As described hereinafter, we estimated the onset dates of patients for whom onset dates had not been reported. Letting $f(k)$ represent this empirical distribution of the incubation period and letting N_t denote the number of patients for whom onset dates were not published and available at date t, then the number of patients for whom the onset date was known is t-1. The number of patients with onset date t-1 for whom onset dates were not available was estimated as $f(1)N_t$. Similarly, patients with onset date t-2 and for whom onset dates were not available were estimated as $f(2)N_t$. Therefore, the total number of patients for whom the onset date was not available, given an onset date of s, was estimated as $\Sigma_{k=1}f(k)N_s + k$ for the long duration extending from *s*.

Moreover, the reporting delay for published data from MHLW might be considerable. In other words, if *s+k* is larger than in the current period *t*, then *s+k* represents the future for period *t*. For that reason, N_{s+k} is not observable. Such a reporting delay engenders underestimation of the number of patients. For that reason, it must be adjusted as $\Sigma_{k=1}^{t-s}f(k)N_s+k /\Sigma_{k=1}^{t-s}f(k)$. Similarly, patients for whom the onset dates were available are expected to be affected by the reporting delay. Therefore, we have $M_{s|t} /\Sigma_{k=1}^{t-s}f(k)$, where $M_{s|t}$ represents the reported number of patients for whom onset dates were period *s* as of the current period *t*.

We defined R(*t*) as the number of infected patients on day *t* divided by the number of patients who were presumed to be infectious. The number of infected patients was calculated from the epidemic curve by the onset date using an empirical distribution of the incubation period, which is $\Sigma_{k=1}f(k)E_{t+k}$, where E_t denotes the number of patients for whom the onset date was period *t*. The distribution of infectiousness in symptomatic and asymptomatic cases $g(k)$ was assumed to be 30% on the onset day, 20% on the following day, and 10% for the subsequent five days (*12*). Then the number of infectious patients was $\Sigma_{k=1}g(k)E_{t-k}$. Therefore, R(*t*) was defined as $\Sigma_{k=1}f(k)E_{t+k}/\Sigma_{k=1}g(k)E_{t-k}$.

2.2. Data of other factors

Data indicating the shares of mutated variants among all cases were published by the Tokyo Metropolitan Government. Unfortunately, detailed information about mutated strains has not been published for the entirety of Japan. We used two measures for the mutant strain shares in Tokyo, Japan: alpha and delta variant strains (*13*).

We use average temperature and relative humidity data for Tokyo during the day as climate data because national average data are not available. We obtained data from the Japan Meteorological Agency (*https://www.*

data.jma.go.jp/gmd/risk/obsdl/index.php). Additionally, we identified several remarkable countermeasures in Japan: four state-of-emergency declarations, a travel campaign, and school closure and voluntary event cancellation (SCVEC). The latter, SCVEC, extended from February 27 through March in 2020: this countermeasure required school closure and cancellation of voluntary events, and even cancellation of private meetings. The first state of emergency was declared on April 7, 2020. It ceased at the end of May. It required school closures, shutting down of some businesses, and voluntary restriction against going out. To subsidize travel and shopping at tourist destinations, the "Go To Travel Campagn (GTTC)" started on July 22, 2020. It was halted temporarily at the end of December.

The second state of emergency was declared on January 7, 2021 for the 11 most-affected prefectures. This countermeasure required restaurant closure at 8:00 p.m., with voluntary restrictions against going out, but it did not require school closure. It continued until March 21, 2021. The third state of emergency was declared on April 25, 2021 for four prefectures: Tokyo, Osaka, Hyogo, and Kyoto. Later, the application areas were extended gradually. They never covered the entirety of Japan.

2.3. Estimation model for R(*t*)

To clarify associations among R(*t*) and current and the past vaccine coverage in addition to the mutant strains, climate, mobility, the Olympic Games, and countermeasures, we used ordinary least squares regression to regress the daily R(*t*) on daily current vaccine coverage and daily past vaccine coverage as well as dummy variables for the Games, weekly shares of alpha and delta variant strains, daily climate, mobility, and dummy variables for countermeasures. Temperatures were measured in degrees Celsius, with humidity and mobility as percentages in regression, not as standardized. Variables found to be not significant were excluded from explanatory variables. Then the equation was estimated again.

We define vaccine coverage as the completion rate of the second dose without delay. If a vaccine perfectly protects the recipient from infection, then the estimated coefficient of vaccine coverage would be 0.01 if one assumes an average of R(*t*) with no vaccination in the study period. That would indicate that vaccine coverage increased by one percentage point could be expected to reduce R(*t*) by one percentage point. If the estimated coefficient of vaccine coverage were smaller than -0.01, then it might reflect imperfect personal prevention. Conversely, if the estimated coefficients of vaccine coverage were smaller than -0.01, then herd immunity can be inferred to have contributed to prevention of infection among non-recipients.

Waning of vaccine effectiveness was measured by the estimated coefficient of vaccine coverage in the past. Particularly, we examined every 30 days prior until

180 days prior. We expected the estimated coefficient to be positive if waning was occurring. If its estimated coefficient was positive but smaller than the absolute value of the estimated coefficient of current vaccine coverage, then waning was presumed to be partially occurring. Vaccination was presumed to be effective even if a part of effectiveness was waning. If the estimated coefficient of vaccine coverage in the past was positive and almost equal to the absolute value of the estimated coefficient of current vaccine coverage, then waning was presumed to be complete. We might not expect vaccine effectiveness until that time. Conversely, if the estimated coefficient of vaccine coverage in the past was positive and larger than the absolute value of the estimated coefficient of current vaccine coverage, then the vaccine might raise infectiousness eventually. We adopted 5% as the level at which we inferred significance of the results.
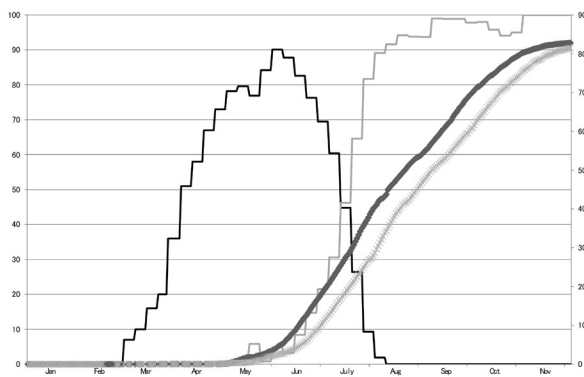
3. Results and Discussion

3.1. Data

Figure 1 depicts vaccine coverage for the first dose with a 12-day delay and depicts the second dose as scatter diagrams. It also shows the shares of alpha and delta variant strains as bars. These are increasing almost monotonically during the period. Adjustments were made for double counting for the number of vaccine recipients. Therefore, the vaccine coverage was sometimes less than it was earlier. Figure 2 depicts $R(t)$ during the study period.

Figure 3 presents an empirical distribution of the duration of onset to reporting in Japan. The maximum delay was 31 days. Figure 4 presents an empirical distribution of incubation periods among 91 cases for

Figure 1. Vaccine coverage and shares of alpha and delta variant strains in 2021. The black line represents shares of the alpha variant strain in Tokyo, as measured at the left-hand side. The gray line represents shares of the delta variant strain. Black scattered points denote vaccine coverage as defined by the first dose with a 12-day delay. Gray scattered points denote vaccine coverage defined by the second dose. The vaccine coverage data are measured at the right-hand side scale. Because the daily vaccine coverage was not reported on weekends or national holidays, data of vaccine coverage are missing for these days. Moreover, there were adjustments for double counting for the number of vaccine recipients. Therefore, the vaccine coverage was sometimes less than it was earlier.
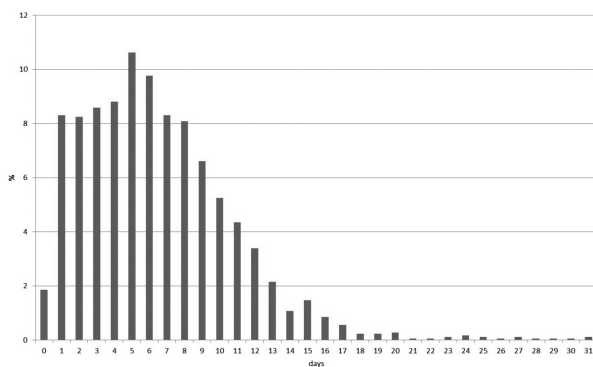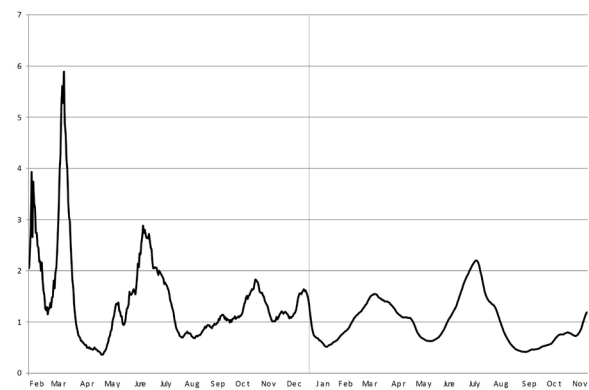

Figure 2. Effective reproduction number from February, 2020 through November 4, 2021. The line represents the effective reproduction number in Japan from February, 2020 through November 4, 2021, as of November 25, 2021. Calculation procedures are explained in the main text.
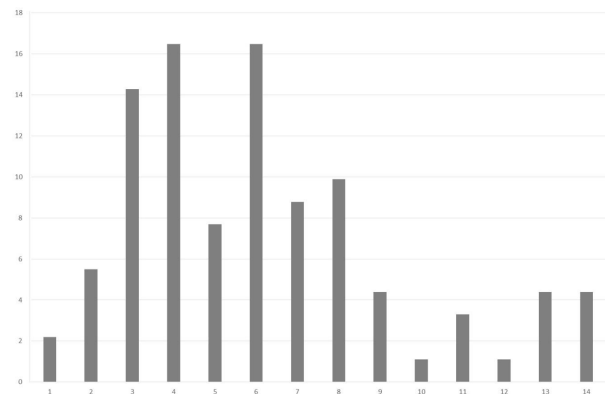

Figure 3. Empirical distribution of duration from onset to report by MHLW, Japan. Bars represent the probability of duration from onset to report based on 657 patients in Japan for whom the onset date was available. Data were obtained from MHLW, Japan.

Figure 4. Empirical distribution of the incubation period published by MHLW, Japan. Bars show the distribution of incubation periods for 91 cases for which the exposure date and onset date were published by MHLW, Japan. Patients for whom incubation was longer than 14 days are included in the bar shown for day 14.

which the exposed date and onset date were published by MHLW in Japan. The mode was six days; the average was 6.6 days.

3.2. Estimation results

Table 1 presents estimation results. The Olympic Games, climate conditions, and the fourth state of emergency were not found to have a significant effect. Therefore, we excluded these variables from the explanatory variables. All remaining variables in the specification were found to be significant in the final specification.

Current vaccine coverage reduced infectiousness significantly when vaccine coverage in the past was defined as 90 days prior. The estimated coefficients increased along with their duration of time into the past: from -0.0549 for vaccination coverage of 90 days prior to -0.0241 for vaccination coverage of 180 days prior.

The estimated coefficients of vaccine coverage in the past were significant and positive when vaccine coverage in the past was defined as 90 days prior. The estimated coefficients also increased with time into the past: from 0.0550 to 18.49.

The sums of the estimated coefficients of current and past vaccine coverage were not significantly different from zero for 90 or 120 days prior assumed for the past vaccine coverage. When assuming coverage as 150 or 180 days prior, the estimated coefficients of the past vaccine coverage were significantly larger in absolute terms than the current vaccine coverage.

The estimated coefficients of the share of the variant strain were negative. These findings were inconsistent with the expected effects of the variant strain. Especially, shares of the alpha variant strain were significant and negative consistently, although the shares of the delta variant strain were not significant, except when assuming past vaccine coverage as 30 or 60 days prior.

Mobility was found to be positive and significant. The first three state-of-emergency periods and GTTC were found to be negative and significant. However, SCVEC was found to be significant and positive. The fourth state-of-emergency period was significant but positive only when assuming past vaccine coverage as 60 or 180 days prior. Effects of the Olympic Games were not significant.

3.3. Brief history of countermeasures

The Olympic Games and Paralympic Games of 2020 began on July 23, 2021. A subject of great concern for COVID-19 outbreak effects in Japan was whether audiences would be allowed to attend game events, or not. As part of this controversy, some experts asserted that the Games should be abandoned because they would expand the outbreak explosively (*14*). As a result, the game events were held with no live audience. Under the state of emergency declared in Tokyo, effects of the 2020 Tokyo Games must be included to evaluate vaccine effectiveness.

As countermeasures against the COVID-19 outbreak in Japan, school closure and voluntary event cancellation were adopted from February 27, 2020 through the end of March. Large commercial events were cancelled. Subsequently, a state of emergency was declared for April 7 through 25 May, stipulating voluntary restrictions against leaving home. Consumer businesses such as retail shops and restaurants were shuttered. During this period, the first peak of infection was reached on April 3. Infections subsequently decreased through July 29. The so-called "Go To Travel Campaign" (GTTC) was launched on July 22 as a 50% subsidized travel program aimed at supporting sightseeing and tourism businesses with government-issued coupons for use in shopping at tourist destinations. It was expected that the campaign might expand the outbreak. Thereafter, GTTC continued to the end of December, by which time a third wave of infection had emerged. The third wave in December, which was larger than either of the preceding two waves, reached its highest peak at the end of December. Therefore, GTTC was inferred as the main reason underlying the third wave (*15*).

To suppress that third wave of infection, a second state of emergency was declared from January 8, 2021 through March 15, 2021. However, a fourth wave emerged at the end of February, probably because of the spread of variant strains. To support hosting of the Olympics and Paralympics games in Tokyo in July, a third state of emergency was declared on April 25, 2021. It had ceased on June 20, 2021 in Tokyo. Nevertheless, the outbreak commenced again before the Tokyo Games 2020 started. Therefore, a fourth state of emergency was declared on July 13, 2021. It continued thereafter until the Tokyo Games 2020 had closed.

Although results have been mixed, some findings from earlier studies suggest that COVID-19 is associated with climate conditions (*16-19*). If that were true for Japan, then GTTC might not have been the main factor contributing to the third wave. In fact, mobility was inferred as the main cause of the outbreak dynamics for the first wave in Japan (*20*) and throughout the world (*21-24*).

3.4. Implications of estimation results

Results showed complete waning by 90 days after the second dose of vaccine was administered. This duration is remarkably shorter than those reported from earlier studies of waning (*3,4*), which reached their conclusions based on antibody titer or test negative design. Readers must be reminded that waning estimated for the present study might include behavioral changes among the vaccinated persons to adoption of more risky behavior that is prone to exacerbating infectiousness. Such behaviors and the vaccine itself affect waning results, but they are not separately discernible based on results of this study. Weakening of immunoreaction and behavioral change are separate factors, but their mutual effects might be the most

Table 1. Estimation results of R(*t*) with vaccine coverage, prevalence of the variant strains, and Olympic Games with the climate condition, mobility, and countermeasures

Lag for waning	30		60		90		120		150		180	
Explanatory variable	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value
Temperature	-0.0053	0.158	-0.0042	0.277	-0.0034	0.373	-0.0034	0.383	-0.0034	0.385	-0.0034	0.380
Humidity	-0.0007	0.582	0.0004	0.772	0.0006	0.686	0.0005	0.689	0.0006	0.686	0.0006	0.677
Mobility	0.0085	0.000	0.0082	0.000	0.0080	0.000	0.0080	0.000	0.0080	0.000	0.0081	0.000
SCVEC	0.7430	0.000	0.7909	0.000	0.8064	0.000	0.8055	0.000	0.8048	0.000	0.8036	0.000
1st State of emergency	-0.8875	0.000	-0.8692	0.000	-0.8671	0.000	-0.8687	0.000	-0.8677	0.000	-0.8645	0.000
GTTC	-0.9088	0.000	-0.8801	0.000	-0.8720	0.000	-0.8735	0.000	-0.8745	0.000	-0.8762	0.000
2nd State of emergency	-1.0461	0.000	-1.0071	0.000	-0.9933	0.000	-0.9936	0.000	-0.9935	0.000	-0.9931	0.000
3rd State of emergency	-0.3107	0.017	-0.6941	0.000	-0.7406	0.000	-0.7309	0.000	-0.7287	0.000	-0.7292	0.000
4th State of emergency	0.2832	0.290	0.7525	0.007	0.4292	0.134	0.4929	0.079	0.5163	0.064	0.5479	0.048
Olympic Games	0.2927	0.049	0.4532	0.022	-0.0487	0.802	0.0576	0.739	0.0915	0.585	0.1370	0.398
Vaccine coverage (%)	0.1486	0.000	0.0337	0.243	-0.0539	0.001	-0.0355	0.001	-0.0298	0.000	-0.0241	0.000
Vaccine coverage with lag (%)	-0.1416	0.000	-0.0406	0.095	0.0550	0.012	0.0928	0.016	0.3399	0.017	1.8498	0.026
Share of alpha variant strain (%)	-0.0107	0.000	-0.0041	0.008	-0.0031	0.033	-0.0033	0.022	-0.0033	0.020	-0.0034	0.020
Share of delta variant strain (%)	-0.0447	0.000	-0.0313	0.010	0.0074	0.411	-0.0006	0.916	-0.0033	0.565	-0.0063	0.228
Constant	1.1571	0.000	1.0542	0.000	1.0384	0.000	1.0395	0.000	1.0353	0.000	1.0251	0.000
Adjusted *R*²	0.6042		0.5714		0.5740		0.5737		0.5736		0.5730	
Number of observations							604					

Notes: The dependent variable was R(*t*); GTTC stands for "Go To Travel Campaign"; SCVEC denotes school closure and voluntary event cancellation. The sample period was February 1, 2021 through November 4, 2021, as of November 25, 2021.

important for management of public health.

However, when we assumed the past vaccine coverage as greater than 90 days prior, the current vaccine coverage was found to be significant and to have absolute value greater than 0.01.

Vaccine efficacy was estimated as 95% through clinical trials (*25*). In the real world, it was also estimated as 46-80% for the first dose and 86-90% for the second dose (*26-31*) through case-control studies or test-negative design. However, even in the real world, such studies specifically examine protection for vaccine recipients only and ignore herd immunity, representing vaccine effects on non-vaccine recipients. The latter was not able to be estimated through clinical trials, case-control studies, or test negative design. In this sense, these earlier studies have been incapable of evaluating the overall effects of vaccination on the community. Instead of those methods, we evaluated vaccine effectiveness on the entire community, of course including herd immunity, through its effects on SARS-CoV-2 infectiousness.

Results indicated no significant result of momentary effects from the current vaccine coverage or waning from past vaccine coverage when the past vaccine coverage was defined as less than 60 days prior. Particularly, these estimated coefficients had unexpected signs but were significant. These results were probably caused by multicollinearity among the current and past vaccine coverage. Because of smaller time differences among these variables, correlation among them can be expected to be higher. Therefore, the smaller time differences distorted estimation results.

Conversely, when the past vaccine coverage was defined as more than 120 days prior, the estimated coefficients of the past vaccine coverages were much larger than the estimated coefficients of the current vaccine coverage in absolute terms. Statistically, the result probably reflected that the past vaccine coverage occurring longer ago should be a very small number, as shown in Figure 1. Therefore, the estimated coefficients should be larger than the correspondence when the past vaccine coverage was defined as 60 or 90 days prior. Expressed semantically, because that waning might not reduce the immunization level to less than before the vaccination was administered, these results imply that behavioral changes to adopt more risky behaviors prone to infection among vaccinated persons raise infectiousness considerably. No evidence exists to indicate that the Tokyo Games 2020 exacerbated the outbreak of COVID-19. Expectations by some experts before the Olympic Games might have been wrong. It seems likely that most Japanese people watched TV at home and rooted for athletes. The no-audience policy might have contributed to reduction in infectiousness during the Games. Even though lower infectiousness prevailed during the Games, if it actually became higher than unity, then the number of newly infected or newly confirmed patients would be expected to grow during the period. Therefore, the number of patients

has not represented the outbreak situation accurately. Infectiousness must be specifically examined during that period to evaluate policies adequately.

Alpha variant strain effects were significant and negative. Additionally, the share of delta variant strain was not found to be significant, with some exceptions. These results were not consistent with results reported from earlier studies (*5-8*).

3.5. Limitations

First, we assumed implicitly that epidemiological characteristics including incubation period or delay in reports were the same among the original strain, alpha and delta variant strains. However, results of one study indicated that the delta variant strain has a shorter incubation period than either original strain (*32*).

Secondly, readers must be reminded when interpreting the obtained results that they do not indicate causality. Results of this study demonstrated that a negative association exists between the vaccine coverage and infectiousness. That finding does not necessarily mean that the vaccine coverage reduced infectiousness. The lower infectiousness might have caused or might have even simply coincided with higher vaccine coverage.

4. Conclusion

The estimation results are evidence of significant waning in vaccine effectiveness from 90 days after the second dose. (The present study is based on the authors' opinions: it does not reflect any stance or policy of their professionally affiliated bodies.)

References

1. Prime Minister and his Cabinet. Novel Coronavirus Vaccines. *https://www.kantei.go.jp/jp/headline/kansensho/vaccine.html* (accessed Nov 30, 2021). (in Japanese)
2. Japan Ministry of Health, Labour and Welfare. Situation of vaccine coverage for COVID-19. *https://www.mhlw.*

go.jp/stf/seisakunitsuite/bunya/vaccine_sesshujisseki.html (accessed November 30, 2021).

3. Levin EG, Lustig Y, Cohen C, Fluss R, Indenbaum V, Amit S, Doolman R, Asraf K, Mendelson E, Ziv A, Rubin C, Freedman L, Kreiss Y, Regev-Yochay G. Waning immune humoral response to BNT162b2 Covid-19 vaccine over 6 months. N Engl J Med. 2021; 385:e84.

4. Chemaitelly H, Tang P, Hasan MR, *et al.* Waning of BNT162b2 vaccine protection against SARS-CoV-2 infection in Qatar. N Engl J Med. 2021; 385:e83.

5. Leung K, Shum MHH, Leung GM, Lam TTY, Wu JT. Early transmissibility assessment of the alpha variant strain of SARS-CoV-2 in the United Kingdom, October to November 2020. Euro Surveill. 2021; 26:2002106.

6. Graham MS, Sudre CH, May A, *et al.* Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. Lancet Public Health. 2021; 6:e335-e345.

7. Davies NG, Abbott S, Barnard RC, *et al.* Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. Science. 2021; 372:eabg3055.

8. Zhao S, Lou J, Cao L, Zheng H, Chong MKC, Chen Z, Chan RWY, Zee BCY, Chan PKS, Wang MH. Quantifying the transmission advantage associated with alpha variant strain substitution of SARS-CoV-2 in the UK: An early data-driven analysis. J Travel Med. 2021; 28:taab011.

9. Japan Ministry of Health, Labour and Welfare. Press Releases. *https://www.mhlw.go.jp/stf/newpage_10723.html* (accessed Jan18, 2022). (in Japanese)

10. Kurita J, Sugawara T, Ohkusa Y. Estimated effectiveness of school closure and voluntary event cancellation as COVID-19 countermeasures in Japan. J Infect Chemother. 2021; 27:62-64.

11. Sugishita Y, Kurita J, Sugawara T, Ohkusa Y. Effects of voluntary event cancellation and school closure as countermeasures against COVID-19 outbreak in Japan. PLoS One. 2020; 15:e0239455.

12. Kimball A, Hatfield KM, Arons M, *et al.* Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility – King County, Washington, March 2020. Morb Mortal Wkly Rep. 2020; 69:377-381.

13. Tokyo metropolitan Government. Data of COVID-19 monitoring meeting in metropolitan Tokyo. *https://www. bousai.metro.tokyo.lg.jp/taisaku/saigai/1013388/index.html* (accessed January 21, 2022). (in Japanese)

14. Hoang VT, Al-Tawfiq JA, Gautret P. The Tokyo olympic games and the risk of COVID-19. Curr Trop Med Rep. 2020; 7:126-132.

15. Anzai A. "Go To Travel" campaign and travel-associated Coronavirus Disease 2019 cases: A descriptive analysis, July-August 2020. J Clin Med. 2021; 10:398.

16. Shi P, Dong Y, Yan H, Zhao C, Li X, Liu W, He M, Tang S, Xi S. Impact of temperature on the dynamics of the COVID-19 outbreak in China. Sci Total Environ. 2020; 728:138890.

17. Tobias A, Molina T. Is temperature reducing the transmission of COVID-19? Environ Res. 2020; 186:109553.

18. Yao Y, Pan J, Liu Z, Meng X, Wang W, Kan H, Wang W. No association of COVID-19 transmission with temperature or UV radiation in Chinese cities. Eur Respir J. 2020; 55:2000517.

19. Walrand S. Autumn COVID-19 surge dates in Europe correlated to latitudes, not to temperature-humidity, pointing to vitamin D as contributing factor. Sci Rep. 2021; 11:1981.

20. Kurita J, Sugishita Y, Sugawara T, Ohkusa Y. Mobility data can reveal the entire COVID-19 outbreak course in Japan. JPHS. 2021; 7.

21. Bergman N, Fishman R. Mobility reduction and Covid-19 transmission rates. 2020; https://www.medrxiv.org/content/10.1101/2020.05.06.20093039v3

22. Flaxman S, Mishra S, Gandy A, *et al.* Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature. 2020; 584:257-261.

23. Li Y, Campbell H, Kulkarni D, Harpur A, Nundy M, Wang X, Nair H, for the Usher Network for COVID-19 Evidence Reviews (UNCOVER) group. The temporal association of introducing and lifting non-pharmaceutical interventions with the time-varying reproduction number (R) of SARS-CoV-2: A modelling study across 131 countries. Lancet Infect Dis. 2021; 21:193-202.

24. Larrosa JMC. SARS-CoV-2 in Argentina: Lockdown, mobility, and contagion. J Med Virol. 2020; 93:2252-2261.

25. Polack FP, Thomas SJ, Kitchin N, *et al.* Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020; 383:2603-2615.

26. Chung H, He S, Nasreen S, *et al.* Effectiveness of BNT162b2 and mRNA-1273 covid-19 vaccines against symptomatic SARS-CoV-2 infection and severe covid-19 outcomes in Ontario, Canada: test negative design study. BMJ. 2021; 374:n1943.

27. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, Hernan MA, Lipsitch M, Reis B, Balicer RD. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med. 2021; 384:1412-1423.

28. Vasileiou E, Simpson CR, Shi T, *et al.* Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet 2021; 397:1646-1657.

29. Bernal JL, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R, Cottrell S, Roberts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J, Ramsay M. Effectiveness of the Pfizer–BioNTech and Oxford–AstraZeneca vaccines on Covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ. 2021; 373:n1088.

30. Bjork J, Inghammar M, Moghaddassi M, Rasmussen M, Malmqvist U, Kahn F. Effectiveness of the BNT162b2 vaccine in preventing COVID-19 in the working age population: first results from a cohort study in southern Sweden. Infect Dis (Lond). 2021; 1-6.

31. Pawlowski C, Lenehan P, Puranik A, Agarwal V, Venkatakrishnan AJ, Niesen MJM, O'Horo JC, Virk A, Swift MD, Badley AD, Halamka J, Soundararajan V. FDA-authorized COVID-19 vaccines are effective per real-world evidence synthesized across a multi-state health system. Med (N Y) 2021; 2:979-92.e8.

32. Li B, Deng A, Li K, *et al.* Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant. Nat Commun. 2022; 13:460.

Address correspondence to:
Junko Kurita, Department of Nursing, Tokiwa University, 1-430-1 Miwa, Mito, Ibaraki 310-8585 Japan.
E-mail: kuritaj@tokiwa.ac.jp