Infectivity of omicron BQ.1.1 comparison with other strains of SARS-Cov-2 in Japan

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Conflict of Interest:
No author has any conflict of interest, financial or otherwise, to declare in relation to this study.

ICMJE Statement

Contributors JK was responsible for the coordination of the study and responsible for the data setting. YO developed the model and TS illustrated the results. All authors contributed to the writing of the final manuscript.

Abstract

Background: After decline of BA.5 sublineage of omicron variant strain of SARS-CoV-2, BQ.1.1. sublineage had been emerging.

Object: The object of this study was to estimate infectivity of BQ.1.1. sublineage controlling other factors that might affect BQ.1.1's infectivity including vaccine effectiveness and waning, the mutated strain other than BQ.1.1, and countermeasuresBQ.1.1.

Method: The effective reproduction number(R(*t*)) was regressed on shares of BQ.1.1. as well as vaccine coverage, vaccine coverage with some delay, temperature, humidity, mobility, share of the other mutated strains, counter measures including Go To Travel Campaign and an Olympic Games. The study period was February, 2020 through the end of year 2022, as of January 31, 2023.

Results : We selected the specification with 90 days lag of waning. In this specification, Goto Travel Campaign and Olympic games were significantly negative and thus these event reduced infectivity. The estimated coefficient of BQ.1.1 sublineage of omicron variant strain was positive but insignificant.

Discussion: The obtained estimated results showed that BQ.1.1 may not have higher infectivity than BA.1, BA.2, BA.5 or other minor sublineage of omicron variant strains. It might be consistent with slower and gradually replacement from BA.5 to BQ.1.1.

Keywords: SARS-CoV-2, effective reproduction number, BQ.1.1., omicron variant strain, vaccine coverage, waning in vaccine effectiveness,

1. Introduction

Since September, 2022, BA.5sublineage of omicron variant strain of SARS-CoV-2 had declined and BQ.1.1.sublineage emerged in Japan (Figure 1). However, its speed of replacement might be slower than the past replacement. Though

ECDC reported infectivity of BA.5. was higher than BA.2 by 12-13% in Portugal and South Africa [1] or it was estimated to be increased by 27% point as of July 13, 2022 in Japan[2], infectivity of BQ.1.1 have not been reported yet. Moreover, , because these studies about BA.5 estimated infectivity through growth rate of patients and thus they ignored difference in other situation such as vaccination, mobility and/or climate condition, their estimated infectivity of BA.5 might not be precise. Therefore, this study examined to estimate infectivity of BQ.1.1. controlling other factors that might affect BQ.1.1's infectivity including vaccine effectiveness and waning, the mutated strain other than BQ.1.1, the Olympic Games, countermeasures, and other factors that might affect BQ.1.1's infectivity.

2. Methods

This study examined the numbers of symptomatic patients reported by the Ministry of Health, Labour and Welfare (MHLW) for February 1, 2020 – the end of year 2022 published

[3] as of January 31, 2023.

Estimation procedure for effective reproduction number was the same as previous study [4]. In short, let f(t) was the empirical distribution of incubation period and g(t) was the empirical distribution of the period from onset to be reported in public. Both were indicated in the previous study [4]. Then, $\Sigma_{s=1}g(s)x(t+s)$ should be estimated the number of patients whose onset date was t where x(t) was newly confirmed symptomatic patients on date t. x(t) was assumed to be constant proportion of total of newly confirmed symptomatic patients including asymptomatic cases, which were reported in public. Now, $\Sigma_{k=1}\Sigma_{s=1}f(k)g(s)x(t+s+k)$ should be estimated the number of patients who were infected on date t. On the other hand, let h(t) was distribution of infectivity power defined in the previous study [4]. Then $\Sigma_{k=1}\Sigma_{s=1}h(k)g(s)x(t+s+k)$ was sum of infectivity on date t. Therefore $R(t)= \Sigma_{k=1}\Sigma_{s=1}f(k)g(s)x(t+s+k) / \Sigma_{k=1}\Sigma_{s=1}h(k)g(s)x(t+s+k)$. Note that proportion of asymptomatic cases does not affect R(t) if it was constant.

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 four measures for the mutant strain shares in Tokyo, Japan: alpha, delta, BA.1, BA.2, BA.5 and BQ.1.1 sublineage of omicron variant strains [5].

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 Campaign (GTTC)” started on July 22, 2020. It was halted at the end of December 2020.

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.

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 variant strains, daily climate, mobility, and dummy variables for countermeasures.

Temperatures were measured in degrees Celsius. Because mobility data provided by Apple Inc. or Google Inc. had been ceased to provide to public in March 13, 2022 and October 15, 2022, we could not use mobility data. Thus we discard mobility to estimate for the effective reproduction number in this study even before date of ceased to release, though the previous studies used these information [4].

Information about vaccine coverage was provided Prime Minister's office [6]. We examined the current vaccine coverage of the second to fifth dose without delay. As of the end of year 2022, fifth dose of vaccination had been started. However, its coverage was not high o the end of study period as shown in Figure 1. 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 0.01. If the estimated coefficient of vaccine coverage were larger 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 might be supposed 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 150 days prior. Note that the waning of the fifth vaccination may not be identified with longer lag because it had started recently. 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 infectivity eventually. We supposed waning of vaccine effectiveness in the second and third vaccination because the fourth vaccination had just started in the study period. We also estimate it without any vaccine coverage in the past which implies to be no waning of vaccine effectiveness. We selected length of lag in vaccine coverage in the past trough adjusted coefficient of determinant which was a measure of goodness of fit when the number of explanatory variables were not the same.

We specified major variant strains as alpha and delta, and BA.1, BA.2 and BA.5

sublineage of omicron variant strain and minor sublineages of omicron variant strain of omicron such as BF.7, BA2.75 or XBB. The minor sublineages of omicron variant strain was represented by dummy variables for November 2021 and after period. Because the original Wuhan strain had disappeared until October 2021, we added this dummy variables for November, 2021. Its estimated coefficients might represent average infectivity among minor sublineages of omicron variant strain comparison with the original Wuhan strain. On the other hand, constant term represents infectivity of the original Wuhan strain.

We expected the sign of the explanatory variables as follows: vaccine coverage in any time reduced infectivity, however, its lag was supposed to be raise infectivity due to waning. The mutated strains were supposed to raise infectivity. Counter measure as the emergency status or SCVEC were supposed to decline the infectivity. Conversely, Olympic Games and/or GTTC which enhanced to mover persons might raise infectivity. We adopted 5% as the significance level.

3. **Results**

Figure 1 depicts vaccine coverage second and third dose with a 14-day delay. It showed the alpha variant strain emerged in March, 2021 and reached peak on May, 2021. The delta variant strain emerged April, 2021 and reached peak on November, 2021. The micron BA.1, 2, and 5 emerged in December, 2021, February and May, 20211, respectively. The former two variant strains reached peak on February and May, 2022. The latest proportion of BQ.1.1. in Figure 1 was higher than 80%.

The complete for the second vaccination had started in increasing since April, 2021 and it surpassed 80% in November, 2021 but it changed to b almost flat. The third vaccination had started in December, 2021, and it reached 65% in July, 2022.

Figure 2 depicts R(*t*) during the study period. The highest was around 9 in December, 2021 when the Delta variant strain dominated. The second highest was around in March, 2020 before the first emergency state declared. In other period, it fluctuated around one and less than three at highest.

Table 1 presents estimation results. We selected the specification with 90 days lag of waning of the second and third dose vaccination. In this specification, the first to third state of emergency, vaccine coverage except for the fifth dose and those with lag, and proportion of alpha and delta, and BA.2 and BA.5 sublineage of omicron variant strain, the first to third emergency status were significant with the expected sign. Conversely, SCVEC and the fourth emergency status were significant but with unexpected sign. GTTC and Olympic games were significantly negative and thus these events reduced infectivity. The estimated coefficient of BQ.1.1 sublineage of omicron variant strain was positive but insignificant. Minor sublineages of omicron variant strain comparison represented by dummy variable for November, 2021 and after was significantly negative and thus these minor sublineages had lower infectivity than the original Wuhan strain. This result might be consistent with these sublineage could not be major sublineage.

Discussion

The obtained estimated results showed that BQ.1.1 may not have higher infectivity than BA.1, BA.2, BA.5 or other minor sublineage of omicron variant strains. Note that basic reproduction number, R, for the mutated strain was probably impossible because vaccination was prevailed and other counter measures was activated and we cannot exclude these effect completely. Conversely, R(t) can always calculated as described above because it depends these several factors affected infectivity as well as R. Therefore, this study focused R(t) instead of R and then examined how several factors affected it. Therefore, the obtained result in this study might be more reliable than the previous study. Actually, in Figure 2, the last peak caused by BQ.1.1 was not much higher than other peak such as the high peak around the end of 2021 caused by BA.1 or peaks in 2020 caused by the original strain.

We found that waning of the second and third dose vaccine with 90 days prior was the most appropriate specification. This duration may be comparable with earlier studies of waning [7,8], 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 infectivity. 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 important for management of public health.

Limitations

First, we assumed implicitly that epidemiological characteristics including incubation period or delay in reports were the same among the original strain, alpha, delta, and lineages of omicron variant strains. However, results of one study indicated that the delta variant strain has a shorter incubation period than either original strain [9].

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 infectivity. That finding does not necessarily mean that the vaccine coverage reduced infectivity. The lower infectivity might have caused or might have even simply coincided with higher vaccine coverage.

Conclusion

We found that BQ.1.1 did not have higher infectivity than alpha and delta or omicron

BA.2 or BA.5 sublineage of omicron variant strains. It probably the reason for slowly replacement from BA.5 to BQ.1.1. BQ.1.1 may be replaced other emerging sublineasge before it will dominant other sublineages.

The present study is based on the authors’ opinions: it does not reflect any stance or policy of their professionally affiliated bodies.

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Ethical considerations

All information used for this study was from official data published on the internet. There is therefore no ethical issue related to this study.

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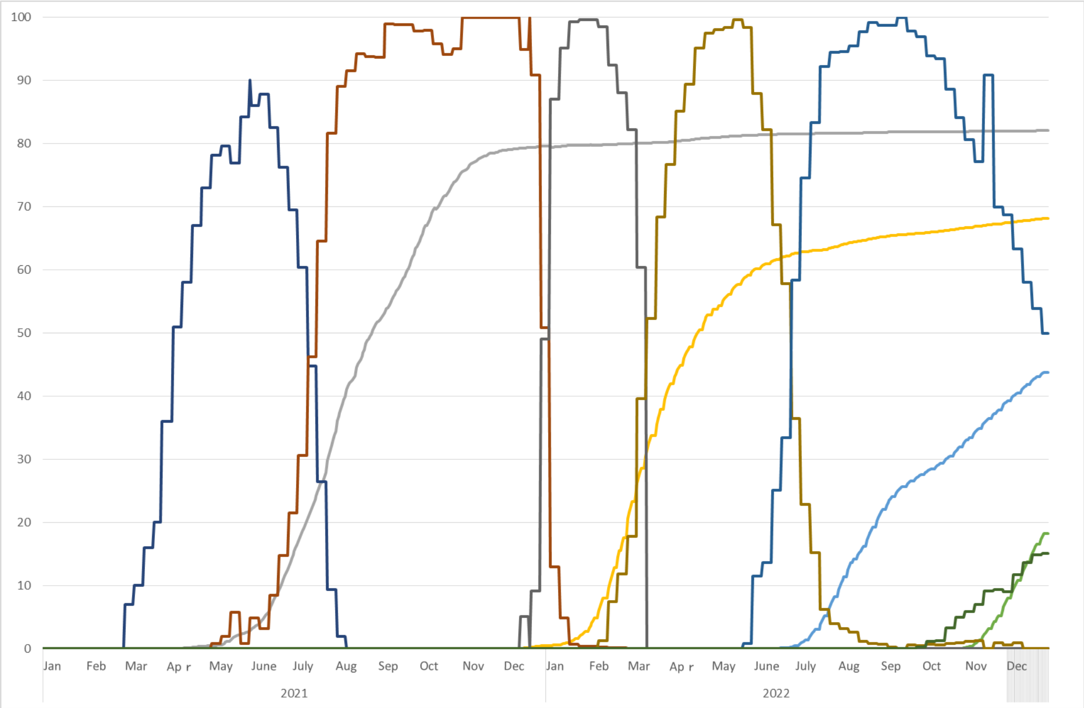
Figure 1: Vaccine coverage and shares of alpha and delta variant strains in 2021 until end of the year 2022.

(%)

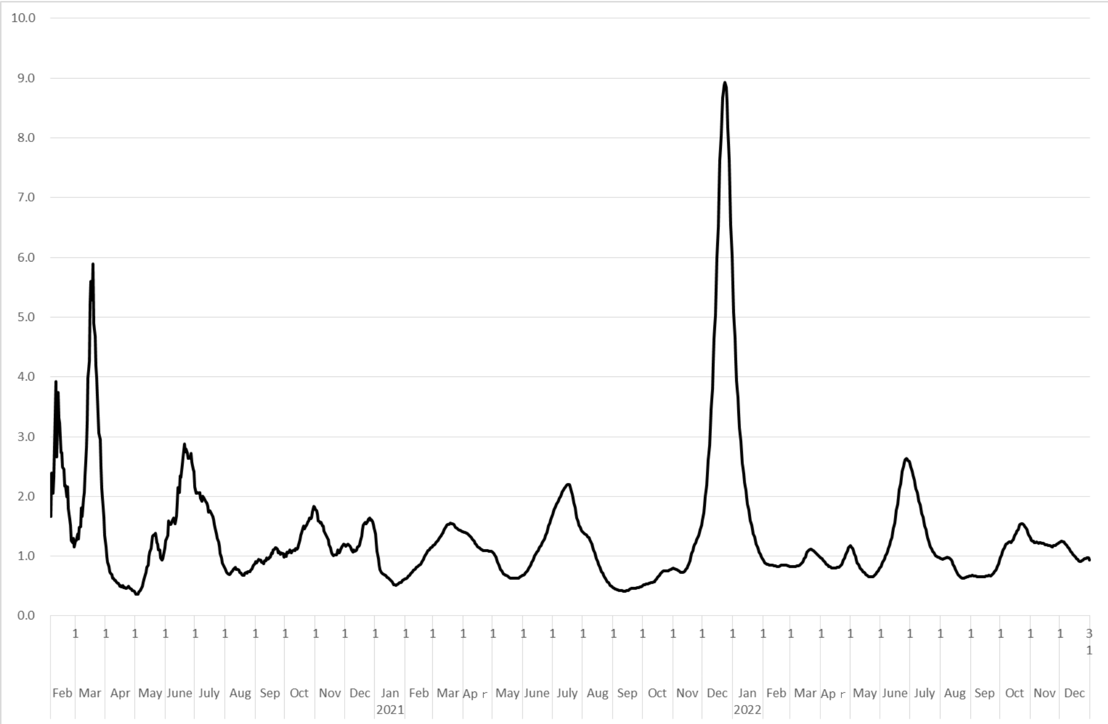


(date)

Note: Five lines with chevron shape and dark green increasing line started since September, 2022 indicates proportion of variant strains. The most left dark blue line with chevron shape indicates alpha variant strain, and orange line was delta variant strain. Following three lines were BA.1, BA.2 and BQ.1.1.sublineage of omicron variant strain. Dark green increasing line started since September, 2022 indicates BQ.1.1 sublineage of omicron variant strain. Monotonically increasing four line except for dark green increasing line started since September, 2022 indicates vaccine coverage rate. Gray increasing line indicates vaccine coverage of second dose, yellow increasing line was the third dose, and blue increasing line was the fourth dose. Light green increasing line started since November, 2022 indicates vaccine coverage of the fifth doze.

Figure 2: Effective reproduction number from February, 2020 through the end of year 2022.

R(t)



(date)

Note: The line represents the effective reproduction number in Japan from February, 2020 through the end of year 2022, as of the January 31, 2023. Calculation procedures are explained in the main text.

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

Lag of waning	Without waning		30		60	
Explanatory variable	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value
Temperature	-0.02002	0.001	-0.01164	0.051	-0.00133	0.803
Humidity	-0.00243	0.232	-0.00147	0.452	0.000961	0.584
SCVEC	0.812011	0.000	0.882405	0.000	0.981677	0.000
1st State of emergency	-1.11112	0.000	-1.10009	0.000	-1.08367	0.000
GTTC	-0.64247	0.000	-0.65377	0.000	-0.66723	0.000
2nd State of emergency	-1.10221	0.000	-1.0282	0.000	-0.90518	0.000
3rd State of emergency	-0.80738	0.000	-1.22172	0.000	-1.49801	0.000
4th State of emergency	-0.14292	0.476	0.723344	0.001	2.066863	0.000

Olympic Games	0.416441	0.094	1.006643	0.000	0.557323	0.010
Vaccine coverage of the second dose(%)	-0.0245	0.002	-0.09368	0.000	-0.21406	0.000
Vaccine coverage of the second dose with lag (%)			0.099257	0.000	0.223002	0.000
Vaccine coverage of the third dose(%)	-0.00419	0.779	-0.0817	0.000	-0.07114	0.000
Vaccine coverage of the third dose with lag (%)			0.064156	0.000	0.037988	0.000

Vaccine coverage of the fourth dose(%)	-0.0514	0.000	-0.13958	0.000	-0.08401	0.000
Vaccine coverage of the fourth dose with lag (%)			0.111633	0.000	0.127043	0.000
Vaccine coverage of the fifth dose(%)	-0.08168	0.011	-0.00866	0.869	0.068524	0.106
Vaccine coverage of the fifth dose with lag (%)			-0.07478	0.473	-1.47435	0.783

Share of alpha variant strain (%)	-0.00067	0.778	0.006349	0.016	0.012177	0.000
Share of delta variant strain (%)	0.005905	0.277	-0.00344	0.612	0.0422	0.000
Share of BA.1 sublineage of omicron variant strain (%)	-0.01069	0.048	-0.01928	0.002	-0.00208	0.698
Share of BA.2 sublineage of omicron variant strain (%)	-0.01299	0.179	-0.01305	0.192	0.018085	0.037

Share of BA.5 sublineage of omicron variant strain (%)	0.001097	0.917	-0.00127	0.915	0.021671	0.028
Share of BQ.1.1 sublineage of omicron variant strain (%)	0.146444	0.003	0.035983	0.483	-0.11306	0.114
Other minor sublineage of omicron variant strain	2.548303	0.000	1.655614	0.000	-0.16896	0.48
Constant	2.334156	0.000	2.114901	0.000	1.752487	0.000
Adjusted R^2	0.3367		0.3959		0.5117	

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 end of the year 2021, as of January 31, 2023. Number of observations was 1016. Yellow markers indicate significant except for constant term.

(cont.)

Lag of waning	90		120		150	
Explanatory variable	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value
Temperature	-0.00378	0.465	-0.00711	0.180	-0.00946	0.087
Humidity	-3.7E-05	0.983	-0.00135	0.442	-0.00235	0.199
SCVEC	0.948816	0.000	0.922494	0.000	0.907286	0.000
1st State of emergency	-1.09352	0.000	-1.089	0.000	-1.08175	0.000
GTTC	-0.66916	0.000	-0.65399	0.000	-0.63905	0.000
2nd State of emergency	-0.9325	0.000	-0.95978	0.000	-0.98541	0.000

3rd State of emergency	-1.12902	0.000	-0.84981	0.000	-0.79999	0.000
4th State of emergency	1.329025	0.000	-0.95056	0.000	-1.63496	0.000
Olympic Games	-0.51901	0.016	-0.54788	0.013	-0.46609	0.043
Vaccine coverage of the second dose(%)	-0.18953	0.000	-0.13324	0.000	-0.12117	0.000
Vaccine coverage of the second dose with lag (%)	0.255558	0.000	0.171784	0.000	0.179273	0.000
Vaccine coverage of the third dose(%)	-0.19267	0.000	-0.15894	0.000	-0.10172	0.000

Vaccine coverage of the third dose with lag (%)	0.136109	0.000	0.337271	0.000	-0.10895	0.060
Vaccine coverage of the fourth dose(%)	-0.07606	0.000	-0.36499	0.000	0.136426	0.180
Vaccine coverage of the fourth dose with lag (%)	0.050846	0.244	0.225215	0.085	0.061296	0.484
Vaccine coverage of the fifth dose(%)	-0.04038	0.136	-0.27287	0.044	-0.15232	0.029
Vaccine coverage of						

the fifth dose with lag (%)						
Share of alpha variant strain (%)	0.006081	0.003	0.000644	0.754	-0.00029	0.892
Share of delta variant strain (%)	0.062869	0.000	0.070881	0.000	0.074018	0.000
Share of BA.1 sublineage of omicron variant strain (%)	-0.00501	0.281	0.007692	0.107	-0.00487	0.317
Share of BA.2 sublineage of omicron	0.065219	0.000	0.059178	0.000	-0.00451	0.604

variant strain (%)						
Share of BA.5 sublineage of omicron variant strain (%)	0.027976	0.002	-0.03001	0.011	0.02564	0.011
Share of BQ.1.1 sublineage of omicron variant strain (%)	0.125446	0.160	0.239258	0.000	0.162172	0.002
Other minor sublineage of omicron variant strain	-2.91656	0.000	-1.09338	0.000	0.642061	0.005

Constant	1.874651	0.000	2.019275	0.000	2.123218	0.000
Adjusted R^2	0.5359		0.5100		0.4644	