Infectivity of omicron BA.5 comparison with original strain and other mutated strain 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: Pervious studies indicated that BA.5 sublineage of Omicron variant strain of SARS-CoV-2 has more infective than BA.2.

Object: The object of this study was to estimate infectivity of BA.5 controlling other factors that might affect BA.5's infectively including vaccine effectiveness and waning, the mutated strain other than , the Olympic Games, countermeasures, and other factors that might affect BA.5's infectively.

Method: The effective reproduction number R(*t*) was regressed on shares of BA.5 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 and countermeasures. The study period was February, 2020 through July 22, 2022, as of August 12, 2022.

Results : We selected the specification with 120 days lag of waning. In this specification, mobility, some state of emergency, vaccine coverage and those with lag, and proportion of delta and omicron BA.2 were significant with the expected sign. Conversely, proportion of omicron BA.1 were significant but with the unexpected sign. The estimated coefficient of BA.5 was negative but insignificant. Goto Travel Campaign was significantly negative and thus it reduced infectively. The Olympic games was negative but in significant and thus it did not raise infectively.

Discussion: The obtained estimated results showed that BA.5 did not have higher infectivity than the original strain and lower than delta or omicron BA.2 variant strains. Though it might be inconsistent the previous research, this study might be more reliable than the previous studies. Because BA.5. outbreak had not cease yet and we cannot predict its dynamics, the estimated BA.5 infectivity will change over time.

Keywords: SARS-CoV-2, effective reproduction number, BA.5, omicron, vaccine coverage, waning in vaccine effectiveness,

1. Introduction

Since BA.5 sublineage of Omicron variant strain of SARS-CoV-2 emerged, ECDC reported infectivity of BA.5 was higher than BA.2 by 12-13% in Portugal and South Africa [1]. Even in Japan, it was estimated to be increased by 27% point as of July 13, 2022 [2]. However, these studies estimated infectively through growth rate of patients and thus they ignored difference in other situation such as vaccination, mobility and/or climate condition. Therefore, this study examined to estimate infectivity of BA.5 controlling other factors that might affect BA.5's infectively including vaccine effectiveness and waning, the mutated strain other than BA.5, the Olympic Games, countermeasures, and other factors that might affect BA.5's infectively.

2. Methods

This study examined the numbers of symptomatic patients reported by the Ministry of Health, Labour and Welfare (MHLW) for February 1, 2020 – July 22, 2022 published [3]as of April 12, 2022.

Estimation procedure for effective reproduction number was the same as previous study [4] 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, omicron BA.1, BA.2 and BA.5 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. had been ceased to provide to public in March 13, 2022, we used the prediction by Google provided mobility data (https://www.google.com/covid19/mobility/) for Apple data through

$$(A_{1t}+A_{2t}+A_{3t})/3=a+b_1G_{1t}+ b_2G_{2t}+ b_3G_{3t}+ b_4G_{4t}+ b_5G_{5t}+ b_6G_{6t}+e_t$$

where A_{it} (i=1-3) were three types of mobility data provided by Apple and G_{it} (i=1-6) were six types of mobility data provided by Google. Because Google had started to provide February 15, 2020 though it was started in January 13, 2020 for Apple data, the period for the estimation was since February 15, 2020 until March 13, 2022. We used its prediction value as measure for mobility even before March 13, 2022. It means hybrid measure for mobility both of Apple data and Google data. After March 14, 2022, we can use the mobility data defined as above until that Google will cease to provide the data.

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 150 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

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

3. **Results**

Figure 1 depicts vaccine coverage second and third dose with a 14-day delay. 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 shows both of Apple provided mobility data and its prediction by Google provided mobility data. Of course, both variables fluctuate very similarly, though volatility of the predicted value was much smaller than the observed mobility data provided by Apple.

Table 1 presents estimation results. Based on the estimated adjusted R^2, we selected the specification with 120 days lag of waning of the second and third dose vaccination. In this specification, mobility, the 2nd and 3rd state of emergency, vaccine coverage of the second and third dose and those with lag, vaccine coverage of the fourth dose and proportion of delta and omicron BA.2 were significant with the expected sign. Conversely, SCVEC, the 4th state of emergency and proportion of omicron BA.1 were significant but with the unexpected sign. The estimated coefficient of BA.5 was negative but insignificant. Concerning about GTTC, it was significantly negative and thus it reduced infectively. Concerning about the Olympic games, it was negative but in significant and thus it did not raise infectively.

Discussion

The obtained estimated results showed that BA.5 did not have higher infectivity than the original strain and lower than delta or omicron BA.2 variant strains which has higher infectively than the original strain. It might be inconsistent the previous research [1,2]. However, though this study examine until July 22, 2022, the previous studies considered

it very earlier period. Moreover, these studies ignored difference in other situation such as vaccination, mobility and/or climate condition. For the above reasons, the previous studies were not precise estimation comparison with this study.

Therefore, the obtained result in this study might be more reliable than the previous study. Actually, in Figure 2, the last peak caused by BA.5 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 e with 120 days prior was the most appropriate specification. This duration may be comparable with earlier studies of waning [6,7], 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 infectively. 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 omicron

variant strains. However, results of one study indicated that the delta variant strain has a shorter incubation period than either original strain [15].

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

Conclusion

We found that BA.5 did not have higher infectivity than the original strain and lower than delta or omicron BA.2 variant strains. Though it might be inconsistent the previous research [1,2], this study might be more reliable than the previous studies. Because BA.5. outbreak had not cease yet and we cannot predict its dynamics, the estimated BA.5 infectivity will change over time.

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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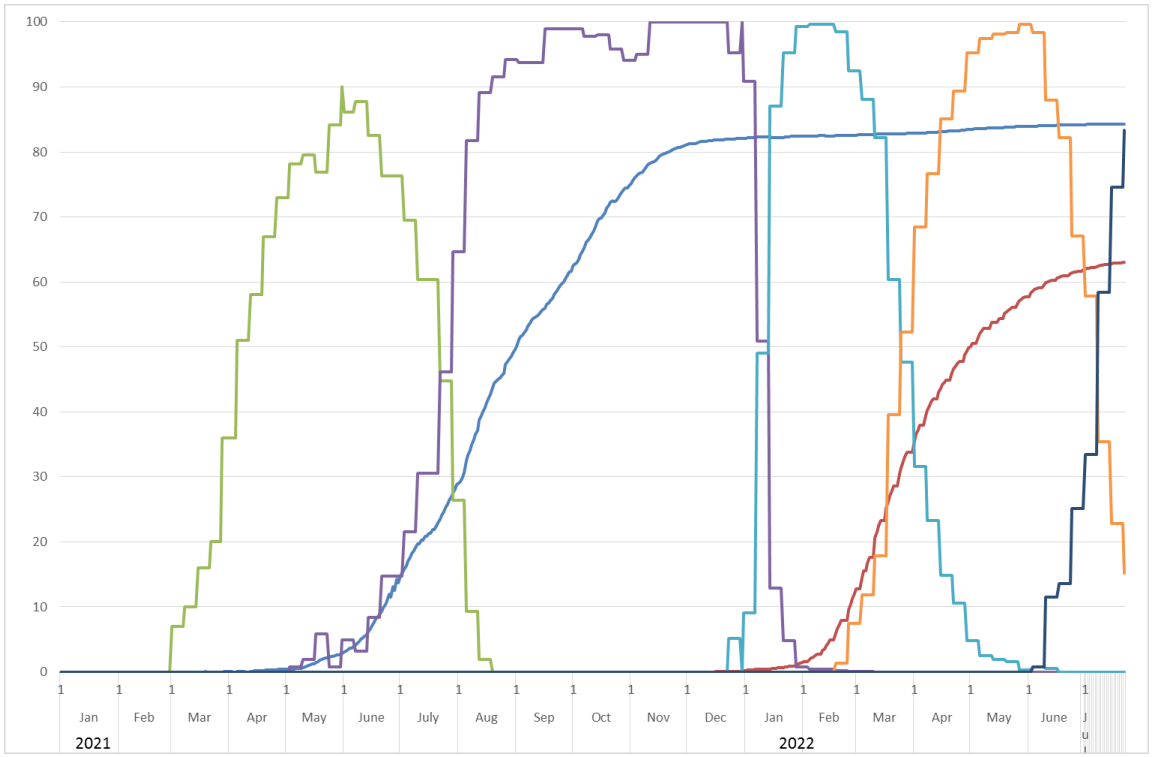
Figure 1: Vaccine coverage and shares of alpha and delta variant strains in 2021 until July 22, 2022.

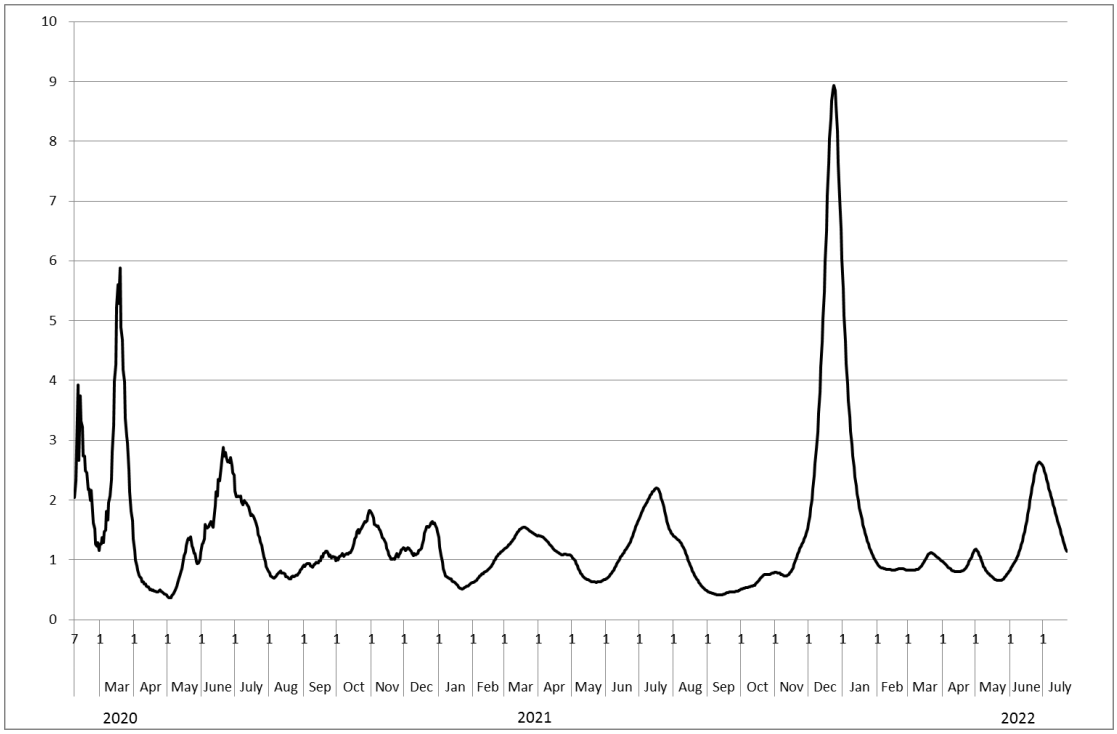
(%)



(date)

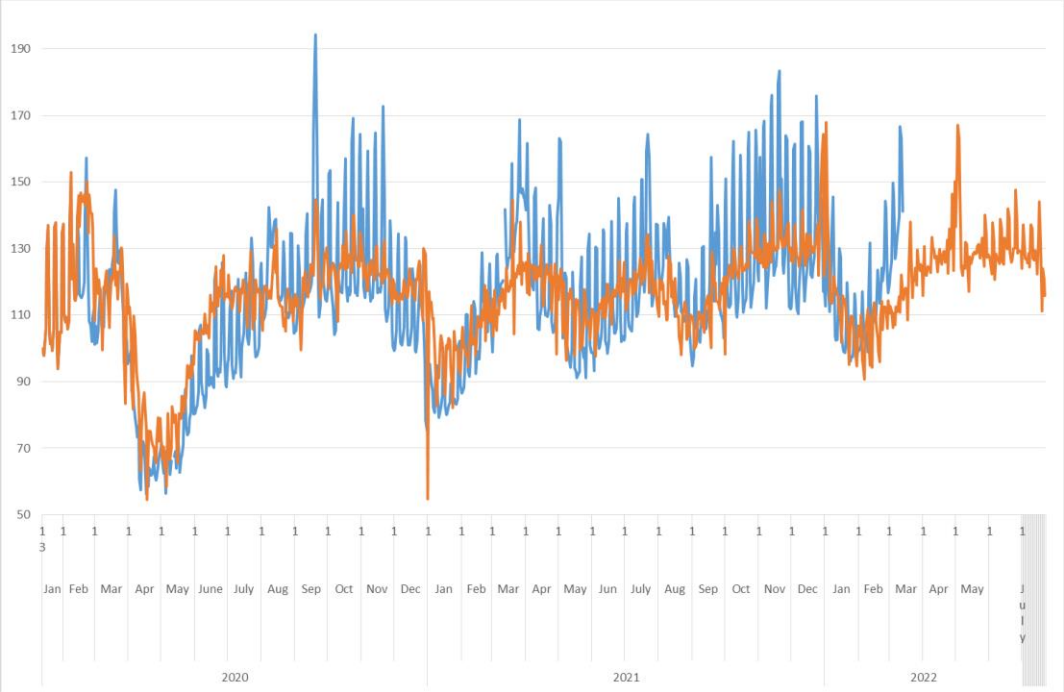
Note: The gray line represents shares of the alpha variant strain, the yellow line represents shares of the delta variant strain, and light blue line indicates the omicron variant strain BA.1 before BA.2 emerging in Tokyo. Green line indicates share of BA.2 variant strain and small dark blue line on June 2022 indicates share of BA.5 only. Blue line denotes completed vaccine coverage as defined by the second dose with a 14-day delay. Red line denotes coverage defined by the third dose. 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 sometimes slightly decreases from before.

Figure 2: Effective reproduction number from February, 2020 through July 22, 2022.



Note: The line represents the effective reproduction number in Japan from February, 2020 through July 22, 2022, as of the August 12, 2022. Calculation procedures are explained in the main text.

Figure 3: Mobility from Apple data and its prediction by Google data until July 22, 2022



Note: Blue line represents mobility data from Apple data. Orange line indicates its prediction by Google data. Apple data had been ceased to provide to public in March 13, 2022.

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	Without lag for waning		30		60	
Explanatory variable	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value	Estimated coefficient	*p*-value
Temperature	-0.0237394	0.000	-0. 0123548	0.057	-0. 0007603	0. 896
Humidity	0.00015	0. 948	0. 0024559	0.271	0.0044559	0. 026
Mobility	0.0275738	0.000	0. 025193	0.000	0. 0212749	0.000
SCVEC	0.7632658	0.000	0. 9261383	0.000	1.05439	0.000
1st State of emergency	-0.0437312	0. 835	-0. 0652778	0.747	-0. 1827503	0. 312
GTTC	-0. 7460926	0.000	-0. 6987047	0.000	-0. 6810992	0.000
2nd State of emergency	-0. 769198	0.000	-0.6377812	0.000	-0. 5415689	0.000
3rd State of emergency	-0. 416374	0. 039	-1. 240444	0.000	-1. 712866	0.000
4th State of emergency	1.326348	0. 000	0. 7027006	0.036	1. 399634	0.000

Olympic Games	1.475286	0. 000	0.9966634	0.000	0. 451078	0.074
Vaccine coverage of the second dose(%)	0. 1026886	0.000	-0. 119773	0.000	-0. 2190181	0.000
Vaccine coverage of the second dose with lag (%)			0.41414609	0.000	0. 2012076	0.000
Vaccine coverage of the third dose(%)	-0.0697996	0.000	-0.0809565	0. 000	-0.0913966	0.000
Vaccine coverage of the third dose with lag (%)			0.0293575	0.007	0.0277316	0.000

Vaccine coverage of the fourth dose(%)	-0. 5852429	0. 000	-0.6186315	0.002	-0. 69708	0. 000
Share of alpha variant strain (%)	-0.0044647	0. 057	0.0096099	0.001	0.016719	0.000
Share of delta variant strain (%)	-0.0812932	0. 000	-0.0046606	0. 758	0.0559342	0.000
Share of omicron BA.1 variant strain (%)	-0. 083355	0. 000	-0.01295339	0. 390	0.0225019	0. 079
Share of omicron BA.2 variant strain (%)	-0.0610412	0. 000	0.0022286	0. 898	0.0488046	0. 002

Share of omicron BA.5 variant strain (%)	-0.0218885	0.292	0.0367097	0.089	0.0821	0.000
Constant	-1. 001822	0.038	-1.150305	0.013	-1.062528	0.010
Adjusted R^2	0. 3515		0. 4009		0. 5210	
Number of observations	909					

Notes: The dependent variable was R(t); GTTC stands for “Go To Travel Campaign”; SCVEC denotes school closure and voluntary event cancellation. Mobility was defined as Apple data predicted by Google data. The sample period was February 1, 2021 through July 22, 2022, as of August 17, 2022.

Table 1 (cont.)

Lag for waning	90		120		150	
Explanatory variable	Estimated coefficient	p-value	Estimated coefficient	p-value	Estimated coefficient	p-value
Temperature	-0. 0027867	0. 629	-0. 0008797	0. 871	-0. 0013643	0. 803
Humidity	0.0029786	0. 134	0. 0024896	0. 181	0. 0024038	0. 204

Mobility	0. 0217272	0.000	0. 0221832	0.000	0. 0246376	0.000
SCVEC	0. 9677033	0.000	0. 9518523	0.000	0. 9230476	0.000
1st State of emergency	-0. 2271722	0. 210	-0. 232556	0. 171	-0.1585786	0. 358
GTTC	-0. 7370287	0.000	-0. 7655587	0.000	-0. 794833	0.000
2nd State of emergency	-0. 6071491	0.000	-0. 6011735	0.000	-0. 5903268	0.000
3rd State of emergency	-1. 119283	0. 000	-0. 8213824	0.000	-0. 6386243	0.007
4th State of emergency	0.8417915	0. 004	0.7821097	0.005	0. 7950988	0.005
Olympic Games	-0.1717013	0. 514	-0.1967271	0. 418	0. 2577879	0. 285
Vaccine coverage of the second dose(%)	-0. 1428801	0.000	-0. 0794882	0.000	-0. 0186331	0. 194

Vaccine coverage of the second dose with lag (%)	0.1496195	0.000	0. 1465854	0.000	0. 1870139	0.000
Vaccine coverage of the third dose(%)	-0. 1668994	0.000	-0. 1872556	0. 000	-0. 1916716	0.000
Vaccine coverage of the third dose with lag (%)	0. 0836138	0.000	0.3255188	0.000	0.0413105	0.000
Vaccine coverage of the fourth dose(%)	-0.6052721	0. 000	-1.1756647	0. 000	-0.9610531	0. 019

Share of alpha variant strain (%)	0..0065499	0. 002	0.0013991	0.464	-0.0017092	0.376
Share of delta variant strain (%)	0.0491084	0. 000	0.0235633	0. 0038	-0. 0090791	0. 407
Share of omicron BA.1 variant strain (%)	0. 0099012	0. 429	-0. 0267872	0.016	-0.0813209	0.000
Share of omicron BA.2 variant strain (%)	0. 0692801	0. 000	0.0329551	0.025	-0.0470264	0. 001
Share of omicron BA.5 variant strain (%)	0.0784126	0.000	-0.00178288	0.421	0.0115647	0.530
Constant	-0.9150806	0.027	-0.9419219	0.016	-1.192681	0.003

Adjusted R^2	0. 5201	0.5782	0. 5640
Number of observations		909	