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Limited capacity of SARS-CoV-2 variants testing in Japan: A secondary analysis using publicly available data

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Dear Editor

As of early 2021, the widespread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to the emergence of more virulent genetic variants globally, which is more infectious with a high mortality rate [1,2]. Hence, a rapid elucidation of the details of SARS-CoV-2 genetic variants, their infectious capacity, and regional surveys to assess the incidence are crucial to controlling the spread of the virus. In Japan, a country early affected in the pandemic [3,4], a variant of concern 202012/01 was first identified in the airport quarantine station on December 25, 2020. Concerned about the further spread of SARS-CoV-2, the Japanese government declared a second state of emergency from January 8 to March 21, 2021.

Under these circumstances, it is imperative to establish a system for variant testing and identify the actual spread of infection accurately. The Japanese government temporarily set a goal of increasing the variant testing ratio for RT-PCR-positive cases to 40 % to strengthen the variant surveillance system. Consequently, the various mass media have also reported anecdotal trends in variant testing, especially the ups and downs of variant testing ratio. However, this has not been rigorously evaluated in academic literature. Furthermore, it has not been verified whether the variant testing ratios were arranged based on the actual spread of infection or whether Japan's policy in variant testing was appropriate. Therefore, to summarize the trend of variant testing ratios against the number of positive RT-PCR cases and the number of variant positive cases in Japan, we conducted a secondary analysis of publicly available but piecemeal data, firstly published by several governmental agencies scattered way (https://www.mhlw.go.jp).

We retrieved and examined open data on RT-PCR testing and N501Y variant tests in Japan both on a national and prefectural basis (https://www.mhlw.go.jp). The 47 prefectures of Japan were categorized according to the population densities; the three most populated prefectures (the capital city Tokyo, Osaka, and Kanagawa) were shown individually, and the remaining 44 prefectures were divided into quartiles equally. We investigated the information on the number of RT-PCR cases, positive cases, RT-PCR positive ratio, variant cases, and the variant test ratios (the number of variant tests divided by the number of SARS-CoV-2 positive cases) on the whole country from February 22 to April 11, 2021. For the data per prefecture, only the variant test ratios were shown due to data availability.

In Japan as a whole, the proportion of RT-PCR positive cases among the total number of RT-PCR tests increased from 2.3 % (February 22 to 28, 2021) to 5.6 % (April 5 to 118, 2021) (Table 1). The variant test ratios among total RT-PCR positive cases were consistently less than 40 % throughout the study period, although they were upward from 17.4 % (February 22 to 288, 2021) to 36.3 % (April 5 to 118, 2021) (Table 1). Additionally, the proportions of variant positive cases among total variant tests steadily increased from 4.5% (56/1234) to 46.0% (3489/7581) during the study period. Concerning comparing the RT-PCR test positive cases receiving the variant testing in each region by the population densities, high-density prefectures had fewer proportions than in the low-density prefectures throughout the entire study period (Table 1).

This study found that the variant test ratio among RT-PCR positive cases increased to just below 40 % in early April 2021. That means that the Japanese government has almost achieved its original goal set for variant testing. However, a worrying fact is that both the proportions of RT-PCR positive cases per RT-PCR testing and variant-positive cases per variant testing have been continuously rising. As such, the Japanese government was forced to declare a state of emergency on April 25, 2021, for the third time (https://www.mhlw.go.jp). That poses a question for variant testing strategy by the Japanese government so far and needs further scrutiny for improvement.

We also compared the results by prefectures and found that the proportions of RT-PCR-positive cases who underwent the variant test were lower in prefectures with higher population densities than those with lower population densities throughout the entire period. The primary reason might be the limited capacity of variant testing in densely populated prefectures.

Under the current testing system in Japan, a certain number of

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Table 1
Number of RT-PCR tests, RT-PCR positive cases, variant tests, and N501Y variant positive cases in Japan, 2021.

		During second state of emergency				After lifting state of emergency		
	Date (month/day):	2/22-28	3/1-7	3/8-14	3/15-21	3/22-28	3/29–4/4	4/5-11
Japan								
Number of RT-PCR tests		311,913	338,846	372,968	417,083	496,677	375,036	373,675
Number of RT-PCR positive cases		7,084	7,237	7,921	8,914	11,954	16,805	20,911
RT-PCR positive ratio*, %		2.3	2.1	2.1	2.1	2.4	4.5	5.6
Number of Variant tests		1,234	2,256	2,041	2,378	3,824	5,669	7,581
Variant test ratio**, %		17.4	31.2	25.8	26.7	32.0	33.7	36.3
Number of Variant positive case		56	141	195	369	767	2,031	3,489
Classification of 47 prefectures in Japan based on population density (Tokyo, Osaka, and Kanagawa were shown separately)								
	Population density (people/km^2)	Variant test ratio,** %						
Tokyo	6,306	3.1	2.7	3.4	4.1	22.6	24.9	35.7
Osaka	4,645	10.3	33.0	14.6	21.9	18.5	24.4	25.8
Kanagawa	3,811	3.1	9.3	9.6	5.8	25.6	21.1	28.5
Tokyo + Osaka + Kanagawa	4,969	4.2	9.7	6.9	8.6	21.5	24.2	29.4
Fourth quartile		18.3	24.2	23.7	24.5	31.6	37.2	35.5
Third quartile		65.2	108.4	54.5	25.7	41.5	35.2	54.2
Second quartile		87.2	86.0	97.9	80.3	50.3	64.5	54.0
First quartile		25.8	25.2	38.1	61.0	60.3	51.7	51.0

RT-PCR: polymerase chain reaction. We referred to open data from the Ministry of Health, Labor and Welfare. CR and variant tests are performed by the following institutions and organizations: National Institute of Infectious Diseases, prefectural health laboratories, medical institutions, health centres of medical associations, and private testing companies. The population density was calculated based on the 2020 Basic Resident Ledger. The 44 prefectures other than Tokyo, Osaka, and Kanagawa were shown divided into quartiles according to the population densities of each prefecture: first quartile (−173, people/sq km), second quartile (173–245, people/sq km), third quartile (245–357, people/sq km), and fourth quartile (357, people/sq km -). *RT-PCR positive ratio indices % against the number of RT-PCR tests. **Variant test ratio indices % against total RT-PCR positive cases. Modified and analyzed from Ministry of Health LaW. Ministry of Health, Labour and Welfare: COVID-19 Open Data. 2021 (https://www.mhlw.go.jp/english/).

individuals are selected for variant RT-PCR testing after they become positive by initial RT-PCR-testing (two-step testing), complicated logistics of variant checking with increased costs. It can be an alternative option to implement one-step testing of variant checking with a multiplex RT-PCR kit of SARS-CoV-2, which can detect representative variant such as N501Y. Further, as of April 2021, some regions, including Tokyo, have begun to test for other variants, including E484K variants, voluntarily [5]. According to recent data from the genomic surveillance reported to the GISAID platform (https://nextstrain.org/ncov/), the variants of concern alpha and delta are currently present in Japan, in addition to the clades 19A, 20C, and 20B (Fig. 1). In this context, genomic surveillance would be crucial for estimating the virulence to spread infection and predict the disease's severity [6]. Also, a prefecture-wise analysis will help us understand the actual geographical

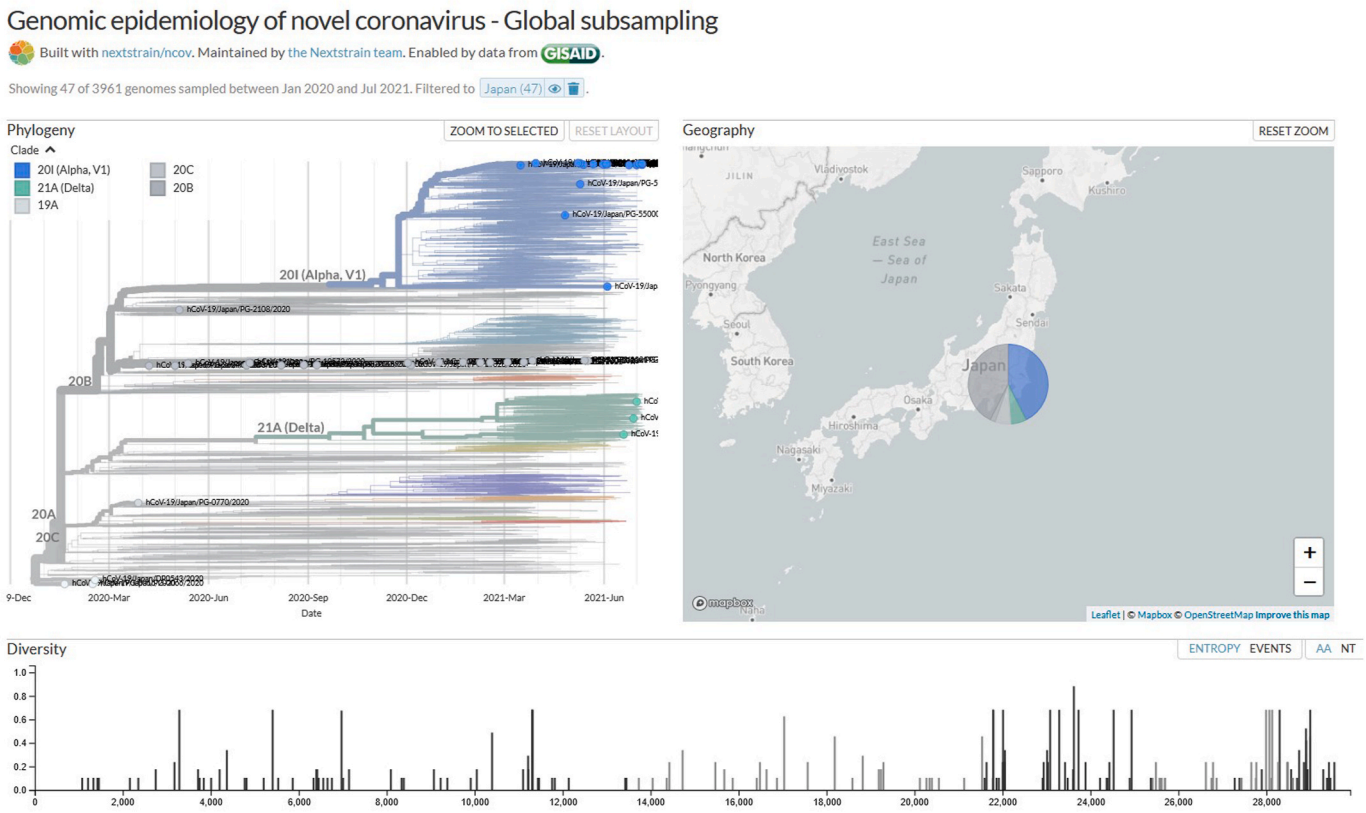

Fig. 1. Genomic sequences analyzed by GISAID from Japan, July 18, 2021 (https://nextstrain.org/ncov/gisaid/global?f_country=Japan).

and temporal distribution of the concern variants. By doing so, we can analyze their actual impact and learn about their transmission routes, infectivity, morbidity and mortality. In conclusion, to cope with the rapidly expanding and diversifying variants, we call for establishing a more sophisticated variant testing system, including genome analysis, as soon as possible in Japan (Fig. 1).

Author contributions

TH wrote the first draft of the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and approved the final manuscript.

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Declaration of competing interest

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References

[1] Sah R, Khatiwada AP, Shrestha S, Bhuvan KC, Tiwari R, Mohapatra RK, et al. COVID-19 vaccination campaign in Nepal, emerging UK variant and futuristic vaccination strategies to combat the ongoing pandemic. Trav Med Infect Dis 2021; 41:102037.
[2] Schlagenhauf P, Patel D, Rodriguez-Morales AJ, Gautret P, Grobusch MP, Leder K. Variants, vaccines and vaccination passports: challenges and chances for travel medicine in 2021. Trav Med Infect Dis 2021;40:101996.
[3] Gallego V, Nishiura H, Sah R, Rodriguez-Morales AJ. The COVID-19 outbreak and implications for the Tokyo 2020 summer olympic games. Trav Med Infect Dis 2020; 34:101604.
[4] Sawano T, Ozaki A, Rodriguez-Morales AJ, Tanimoto T, Sah R. Limiting spread of COVID-19 from cruise ships: lessons to be learnt from Japan. QJM 2020;113: 309–10.
[5] Tokyo bureau of social Welfare and public health. Tokyo Bureau of Social Welfare and Public Health; 2021.
[6] CDC. Centers for Disease Control and Prevention. Genomic surveillance for SARS-CoV-2 variants. 2021.

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