Workshop on the Mathematical Modelling of Variant Replacement of Infectious Diseases Pathogens

Prediction of Variant Replacement Using the Relative Instantaneous Reproduction Numbers

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Variant Replacement Model

The frequency of variant A_i at time t can be presented using R_{RI} of A_i w.r.t a as follows:

$$q_{A_i}(t) = \frac{k_i \sum_{j=1}^l g_{A_i}(j) q_{A_i}(t-j)}{\sum_{j=1}^l g_a(j) q_a(t-j) + \sum_i^n k_i \sum_{j=1}^l g_{A_i}(j) q_{A_i}(t-j)}$$
(6)

where $g_a(j), g_{A_1}(j), \dots, g_{A_n}(j)$ are the generation time distribution of a, A_1, \dots, A_n .

Note that the formula doesn't contain $R_a(t)$ or I(t)

K Ito, C Piantham, H Nishiura: *Eurosurveillance*, July 2021

Predicted dominance of variant Delta of SARS-CoV-2 before Tokyo Olympic Games, Japan, July 2021

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Citation style for this article:

Ito Kimihito, Piantham Chayada, Nishiura Hiroshi. Predicted dominance of variant Delta of SARS-CoV-2 before Tokyo Olympic Games, Japan, July 2021. Euro Surveill. 2021;26(27):pii=2100570. https://doi.org/10.2807/1560-7917.ES.2021.26.27.2100570

Article submitted on 15 Jun 2021 / accepted on 08 Jul 2021 / published on 08 Jul 2021

Using numbers of SARS-CoV-2 variants detected in Japan as at 13 June 2021, relative instantaneous reproduction numbers (R_{RI}) of the R.1, Alpha, and Delta variants with respect to other strains circulating in Japan were estimated at 1.25, 1.44, and 1.95. Depending on the assumed serial interval distributions, R_{RI} varies from 1.20–1.32 for R.1, 1.34–1.58 for Alpha, and 1.70–2.30 for Delta. The frequency of Delta is expected to take over Alpha in Japan before 23 July 2021.

on 25 April in 10 of the 47 prefectures in Japan. During the fourth wave in Japan, public health and social measures against COVID-19 included the closure of restaurants, cancellation of mass gathering events and requests to 'stay home'. New cases decreased in early May and the emergency state in Tokyo was lifted on 20 June, but new cases in Tokyo started increasing again hereafter [3]. As at 20 June, the R.1 variant, Alpha and Delta VOC are circulating in Japan in addition.

Situation in June 2021

- The Delta variants showed high transmissibility in India and United Kingdom.
- Tokyo Olympic Games form July 23, 2021.
- The replacement of the Alpha by the Delta was posing a public health threat in Japan.

Important questions (as of June 2021)

- How transmissible the Delta is compared to Alpha.
- When the Alpha will be replaced by the Delta.

Application to Japanese data



Collaboration with Prof Nishiura under AMED grant JP20fk0108535

 R_{RI} w.r.t. viruses in December 2020

variant	R _{RI}	Range
R.1	1.25	1.19–1.31
Alpha	1.44	1.33–1.58
Delta	1.95	1.70-2.30

Data until April 25 were collected from GISAID, and data from April 26 to June 14 were taken by PCR tests in Tokyo.

The Delta was predicted to take over Alpha before Olympic Games

Ito, Piantham, Nishiura, *Eurosurveillance*, 2021

Increase in Transmissibility



The transmissibility of COVID-19 would increase around the end of June 2021 due to infections by Delta.

Delta would exceed 90% at August 12 and the population average of R_{RI} become 1.90 w.r.t. viruses in December.

Reports by News Media

The New York Times (2021-06-23)

The New York Times https://nyti.ms/2SnaRcE

A Month Before the Olympics, How Is Japan Faring With Covid?

By Lauren Leatherby June 23, 2021

With a month to go until the Tokyo Olympics and a state of emergency freshly lifted in most of the country, Japan is seeing relatively low coronavirus case counts after a surge last month. But the country's low vaccination rate, especially compared with other rich countries, and variants on the rise there have prompted some public health experts in recent weeks to express concerns about the Games or call for them to be canceled.

As athletes and coaches from almost every country in the world prepare to descend on Japan, where tens of thousands of residents will work at or attend the Games, just 7 percent of the country's residents are fully vaccinated, compared with around a quarter of the population or more in most other rich countries. About 18 percent have received at least one shot, ranking Japan's vaccination rate among the lowest of its peers and leaving the population vulnerable at a time when the Delta variant is on the rise and predicted to become dominant.

NHK (2021-06-24)



Evaluation of Predictions



Evaluation of Predictions



Dec 01 Dec 01 Jan 09 Jan 22 Jun 27 Jun 27 Jun 27 Jun 27 Jun 27 Aug 28 Aug 28 Aug 23 Aug 27 Aug 28 Aug 27 Aug 28 Aug 27 Aug 27 Aug 28 Aug 27 Aug 28 Aug 27 Aug 28 Au Prediction using data up to 6/14 and Observation after 6/14

The three-month predictions reported to the Japanese Government were matched with later observations almost perfectly.

Situation in December 2021

- The Omicron variants showed high transmissibility in South Africa.
- The replacement of the Delta by the Omircon was posing a public health threat worldwide.

Important questions (as of December 2021)

- How transmissible the Omicron is compared to Delta.
- When the Delta will be replaced by the Omicron.

Omicron in Denmark



Relative Reproduction Number (R_{RI}) w.r.t Delta

Variant	R _{RI}	95%CI
Omicron	3.19	2.82-3.61

Data source:

58,669 sequences submitted GISAID Database from Denmark from November 1 to December 9, 2021

It is suggested that Omicron had exceeded 50 % in Denmark on December 16, 2021

Work was conducted under an AMED grant (JP20fk0108535) with Prof H. Nishiura in Kyoto U

Ito, K., Piantham, C., & Nishiura, H. (2022). Journal of Medical Virology (IF=20.7)

Contributions to Risk Management

- The results are used by the CDC and worldwide media.
- Real-time analyses of variant replacements were reported to the COVID-19 advisory board meeting in the Ministry of Health Labour and Welfare, Japan 20 times since 2021.

CDC (2022-01-04)



CNN (2022-01-04



Prediction made on 2021-12-18



Actual Data Observed Later



Generation time of Omicron is shorter than Delta



Mathematical Biosciences and Engineering MBE, 19 (9): 9005–9017. DOI: 10.3934/mbe.2022418 Received: 22 April 2022 Revised: 08 June 2022 Accepted: 16 June 2022 Published: 21 June 2022

http://www.aimspress.com/journal/MBE

Research article

Estimating relative generation times and reproduction numbers of Omicron BA.1 and BA.2 with respect to Delta variant in Denmark

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Generation time of Omicron

- The mean generation time of Omicron BA.1 is 0.44–0.46 times that of Delta.
- The mean generation time of Omicron BA.2 is 0.76–0.80 times that of BA.1.
- The *R_{RI}* of BA.1 and BA.2 w.r.t Delta is 1.88–2.19 and 1.25– 1.27, respectively.



Retrospective Prediction Tests

- 399,530 nucleotide sequences of Alpha and Delta variants of SARS-CoV-2 viruses collected from England from 1 January to 31 July 2021.
- Predictions were made using relative reproduction numbers when the relative frequency of Delta was 5%, 10%, 15%, ..., 90%.



Prediction at 5% (on April 21)



Prediction at 10% (on April 26)



Prediction at 15% (on April 30)



Prediction at 20, 25, ..., 45%



Prediction of the date when the relative frequency become 90%



Once a new variant's relative frequency reached 0.15, the date when the relative frequency of the new variant would reach 0.90 was predicted with maximum absolute prediction errors of three days.

Collaboration with Fiocruz

nature communications

Article

https://doi.org/10.1038/s41467-023-37541-6

Comparative epidemic expansion of SARS-CoV-2 variants Delta and Omicron in the Brazilian State of Amazonas

Received: 21 September 2022	Ighor Arantes ^{1,2,16} , Gonzalo Bello $\mathbf{O}^{1,16}$, Valdinete Nascimento ³ , Victor Souza ³ ,	
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Arantes, I., Bello, G.,..., Naveca, F. G. (2023). Nature Communications

Relative Re of SARS-CoV-2 VOCs in Amazonas



The relative Re of Gamma and Omicron BA.1 w.r.t. Delta was estimated to be 0.76 (95% CI: 0.74–0.77) and 3.25 (95% CI: 2.88–3.29), respectively.

Summary

- The future trajectory of variant replacement can be predicted.
- Accurate predictions were expected after the new variant reached around 15% in frequency.
- Public health policymakers may have only a short time to prepare control measures for the increase in viral transmissibility.
- A quick decision-making process is needed to take advantage of the prediction.