

## Numerical Analysis of the Fifth Wave of COVID-19 epidemic in Tokyo, Japan

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### Abstract

**Background:** A mathematical investigation of the reasons for the fifth wave's quick expansion and reduction in Tokyo, Japan, is required to avoid the spread of subsequent COVID-19 infections.

**Methods:** Using the simple IR theory underlying the susceptible-infectious-removed (SIR) hypothesis of infectious disease epidemics, infected persons (I), infection rate, and testing/isolation rate are determined from accessible data of daily positive cases (R) and testing numbers.

**Results:** The rapid spread of illness from late July to mid-August was owing to a drop in the number of people tested to half that of weekdays during the Olympic Games' four and three-day vacations. The maximum number of daily positives would have been lowered to two-fifths of the actual positives in early August if the number of weekday tests had been maintained during these holidays and would have fallen monotonically thereafter. The infection rates mean value fell steadily from 0.65 in late August to around 0.25 by the end of September. The significant increase in vaccination rates is mostly to blame for the fall in infection rates. In Tokyo, the impact of mRNA-based vaccines on infection prevention and increased vaccination rates could reduce the infection rate to 1/2 on September 10 and 1/3 by the end of October.

**Conclusion:** According to the findings, a new infection like the delta variant can be suppressed to less than the fifth wave by increasing vaccination rates, eliminating three consecutive holidays, and implementing a precautionary testing system that maintains the same number of tests on weekends as on weekdays in the event of a rapid spread of infection in an emergency.

**Keywords:** Epidemiological model, Public health, SIR model, COVID-19, Vaccination, Japan

### Introduction

There have been five waves of COVID-19 infection in Japan, from the commencement of the first wave in early February 2020, with an outbreak on a cruise ship anchored at the Port of Yokohama, until the convergence of the fifth wave towards the end of November 2021. At the end of November, Japan's seven-day average of daily positive cases had dropped to 104, while Tokyo's had dropped to 14. There has been much discussion regarding why the fifth wave, which resulted in the biggest number of illnesses in

history, expanded and contracted so swiftly, to prevent the advent of a sixth wave in the future, but no opinion based on theoretical analysis has been identified.

Since March 2020, the author and Kikuchi have been studying the COVID-19 infectious pandemic in Tokyo utilizing the Susceptible-Infectious-Removed (SIR) hypothesis (1, 2) and its underlying Infectious-Removed (IR) theory. This is because infectious disease epidemic theory experts have only predicted the effective reproduction number and the proportion of socioeconomic activities that should be lowered in order to restrict infection spread (3). The number of

infected people in a city and the number of daily positive cases rise or fall based on the sign and magnitude of the difference between the infection rate and the testing/isolation rate, according to the SIR theory of infectious disease epidemics (3). It is critical to raise of the testing and isolation rate  $\gamma$  as well as to decrease the infection rate  $\beta$  by minimizing social interaction. The reason for this is that by increasing  $\gamma$ , infectious diseases should be considerably suppressed at a cost that is much lower than the economic loss to the country resulting from the reduced socioeconomic activity.

However, in comparison to those in China, Taiwan, Korea, and elsewhere, Japanese infectious disease specialists stuck to the conventional knowledge that only symptomatic patients should be tested and treated and did not realize the need of testing and isolation of asymptomatic patients. Furthermore, the infectious potential of Covid-19 is so great that even asymptomatic patients are very infectious, and several people fell severely ill at home and died because of the testing and isolation system's inadequacies.

Figure 1 depicts the daily number of positive cases in Tokyo from the first to fifth waves. During each wave, the table in the figure shows the total number of positive cases, the total number of deaths, and the fatality rate. It shows that during the initial wave, the number of tests was low, and the focus was on avoiding the 3Cs (closed, crowded, and close contact), wearing masks, washing hands, and cleaning, which resulted in a low number of positive cases but a high death rate.

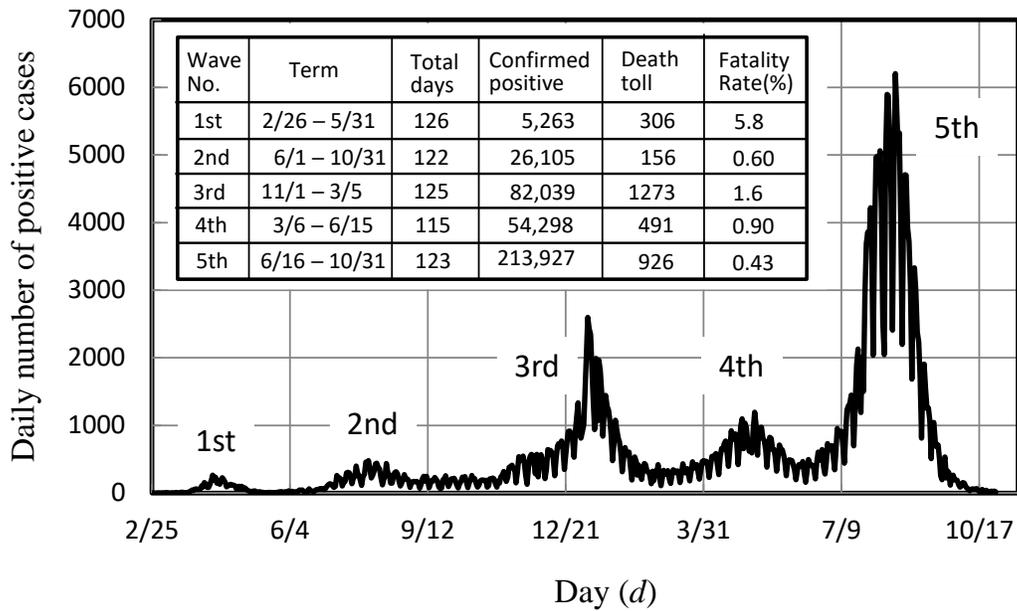
Some infectious disease experts claim that the low number of tests in Japan did not result in a tightening of the medical care system (4). However, when compared to the fatality rates after the first wave, in which the importance of the number of tests was gradually recognized and the number of tests successively expanded, the first wave showed a self-contradiction in that the fatality rate was remarkably high due to a lack of medical care, even though the medical care system did not collapse. Furthermore, when the situation in which schools were forced to close for an extended period to prevent infection, is considered, the importance of maintaining basic social and economic activities such as welfare, education, and various essential productive activities is clear, as is the importance of preventing cluster infections through early detection and isolation of positive cases through an enhanced inspection system.

PCR testing, epidemiological surveys of infected persons' behavior and close contacts, hospitalization referrals, and health observation are all handled by public health centers in Tokyo's 23 wards and eight places in the western district. However, in the mid-

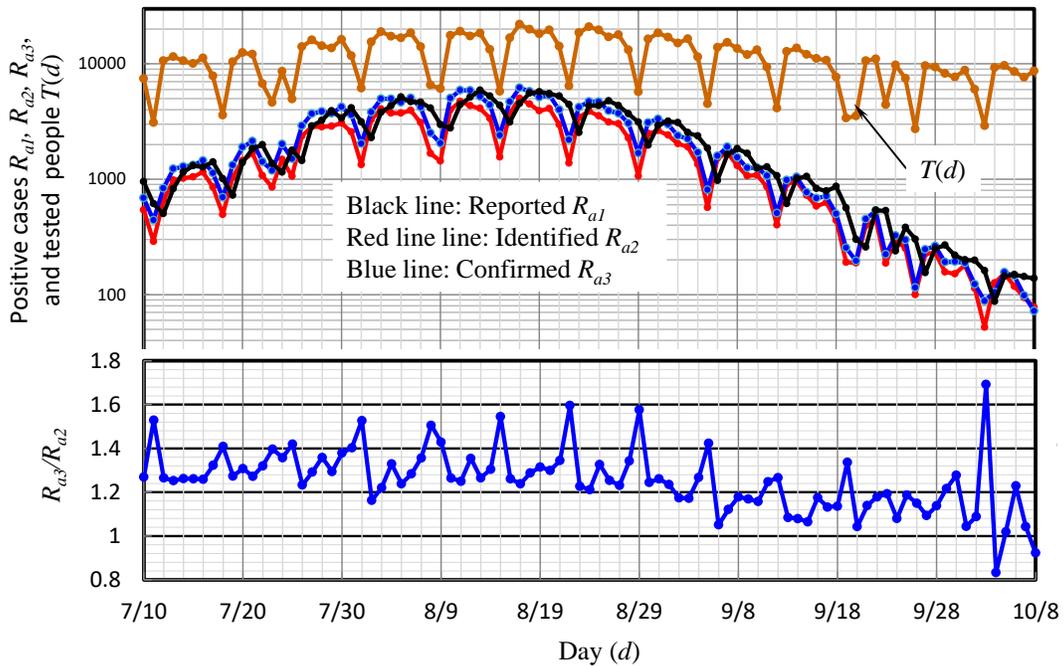
1990s, the number of public health facilities in charge of infectious disease control was halved, and they were unable to undertake epidemiological surveys of close contacts due to the increase in the number of patients after the first wave. The number of positive cases increased rapidly in the third wave from the end of last year to February this year, and in the fifth wave, which began in July this year and spread rapidly during the same period as the Olympic Games, as shown in figure 1, causing a tightening of medical care for infected people. As a result, more than 25,000 positive people with moderate or severe conditions were compelled to stay at home, and many died. Nonetheless, the fatality rate dropped from 5.8% in the first wave to 1.5 percent in the third wave, and then to 0.43 percent in the fifth wave, a drop of more than an order of magnitude.

The author and Kikuchi examined how infection rates and testing/isolation rates changed as the epidemic expanded and contracted from the first to the second wave, and they estimated how much the testing/isolation rate should be increased to lower the second wave (5). The third wave, which resulted in a large number of daily positive cases and deaths, was also studied, and it was discovered that the decrease in the number of people tested during the year-end and New Year holidays led to the epidemic's subsequent expansion, and that the only way to reduce the epidemic was to intensify the reduction and self-restraint of socioeconomic activities in accordance with the government's declaration of a state of emergency and keep the infection rate low (6).

The fifth wave, which resulted in the highest number of daily positive instances and tighter medical treatment (as shown in figure 1), was studied using the IR theory, and the main reasons that caused its expansion and contraction were elucidated. The results of the mathematical study based on the IR theory may provide useful recommendations for future countermeasures, not only for Japan but for many other countries throughout the world. Although the total number of sick persons in Japan should certainly be considered, discussing causation based on correct data is difficult because the number of infected people in other metropolitan regions is considerably off the waveband. To better understand the relationship between the number of tests and the number of positive cases, researchers looked at the conditions that caused illness to spread and contract in Tokyo, Japan's largest metropolis with a population of 13.84 million people, or 12% of the country's total population.



**Figure 1.** Daily number of confirmed positive cases of Covid-19 infection from 2/25/2020 to 10/31/2021 in Tokyo, Japan. The inset table shows the period, the total number of days, the cumulative number of positive cases, the number of deaths, and the fatality rate for the first through fifth waves.



**Figure 2.** Number of positive cases for each of the three different kinds in Tokyo  $R_{a1}$  (reported date),  $R_{a2}$  (Identified date),  $R_{a3}$  (confirmed date),  $R_{a3}/R_{a2}$ , and daily number of people tested  $T(d)$

## Methods

### 1. Explanation of IR model

The infection rate and the testing/isolation rate are used to identify the number of infected people  $I(d)$  in the community and the number of daily positive cases  $R$  in the IR theory (1,2), which predicts the epidemic phenomenon of infectious diseases by using the infection rate and the testing/isolation rate to identify the number of infected people  $I(d)$  in the community and the number of daily positive cases  $R(d)$ . The number of susceptible persons ( $S$ ), infected people ( $I$ ), and daily removed positive cases ( $R$ ) are all expressed as three simultaneous differential equations in the SIR theory.  $S$  can be assumed constant when the number of infected persons is small enough in contrast to the number of susceptible people, and the change rate of  $S$  can be ignored. As a result, the three equations are split into two separate differential equations for  $I$  and  $R$ . As a result, during the period of infection expansion and contraction, IR theory is equivalent to SIR theory.

A simple integrated equation can be used to express the number of infected people  $I$  and the number of daily positive cases  $R$ . The integrated equations are used in the following mathematical analysis. The number of infected people  $I(d)$  in the city on day  $d$ , which is today, can be a recursive expression of the number of infected people on previous day  $I(d-1)$

$$I(d) = I(d-1)e^{(\beta-\gamma)} \quad \text{Equation 1}$$

where  $e$  is the natural logarithm bottom. The infection rate  $\beta$  is the proportion of new infections in one day from  $I(d)$ , and the testing/isolation rate  $\gamma$  is the proportion of new positive patients through testing and isolation in one day from  $I(d)$ .

If  $R(d)$  is the number of new positive cases found by PCR and antigen tests and isolated each day,  $R(d)$  is given by, using is the testing/isolation rate  $\gamma$ ,

$$R(d) = \gamma I(d-1) \quad \text{Equation 2}$$

The number of daily positive cases  $R(d)$  for today  $d$  is taken to be  $\gamma$  times the number of infected persons  $I(d-1)$  for the previous day in equation 2, taking into account the testing delay.

The number of infected people  $I(d)$  grows exponentially with respect to  $\beta-\gamma$ , and the rising rate grows with an increase in the infection rate  $\beta$  or decreases in the testing/isolation rate  $\gamma$ , with the same effect. In other words, in order to reduce the number of infected persons, it is necessary to refrain from social and economic activities and reduce the infection rate by vaccination or increase the number of tests and increase the testing/isolation rate.

According to equation 2, increasing the testing/isolation rate  $\gamma$  increases the number of new

positive cases on that day; however, because the number of infected people decreases according to equation 1, decreasing  $I(d)$  has a stronger effect than increasing in  $\gamma$ , and  $R(d)$  can be reduced after a few days. On the other hand, because the number of tests is lower on Saturdays and Sundays due to holidays and  $\gamma$  decreases, the number of new positive cases recorded on Mondays is always lower, according to equation 2. However, as the value of  $\beta-\gamma$  grows in equation 1, the number of infected people who are not tested and isolated rises, and the number of new positive people who develop the disease quickly and are discovered at the same testing/isolation rate rises.

### 2. Tokyo Metropolitan Government's data on the number of daily positives and the number of people tested

The daily number of new positive cases  $R_a(d)$  (subscript  $a$  means actual data) of the latest infection trend in Tokyo on the Tokyo Metropolitan Government's website (7) for new coronary infections has three different kinds of data: by reported date ( $R_{a1}$ ), by identified date ( $R_{a2}$ ), and by confirmed date ( $R_{a3}$ ). The number of positive cases ( $R_{a1}$ ,  $R_{a2}$ , and  $R_{a3}$ ) and the number of people tested  $T(d)$ , which is the sum of the number of positive cases  $R_{a2}$  and the number of negative cases, are shown in the upper part of figure 2 as black, red, blue, and brown lines, respectively.  $R_{a1}$  is the number of positive cases based on the day when the outbreak was reported by the public health center including the results of tests conducted by medical institutions on their own. It is the number of positive cases reported immediately on TV. In general, it is the number of positive cases revealed because of tests conducted one to two days ago, and thus lags the fluctuation cycle of the number of people tested  $T(d)$  in figure 2 by more than one day.

$R_{a2}$  is the sum of 1. the results of administrative testing at the Tokyo Metropolitan Institute of Public Health, 2. PCR centers (regional outpatient and testing centers), and 3. tests covered by insurance at medical institutions.  $R_{a2}$  is the number of positive cases based on the date when the test results were known, including the epidemiological survey of people in close contact performed by the public health center. Together with  $R_{a2}$ , the number of persons tested  $T(d)$ , which is the sum of  $R_{a2}$  and the number of negative cases according to the test results, and the positivity rate ( $= R_{a2}/T(d)$ ) are shown.

On the other hand, the number of confirmed cases by date ( $R_{a3}$ ) is the number of cases reported by public health centers and private medical institutions, organized by the date when the physician confirmed the positive test result. The cumulative number of new

positive cases by date of detection ( $R_{a2}$ ) and by date of confirmation ( $R_{a3}$ ) is almost in sync with the change in the number of people tested  $T(d)$ .

$R_{a3}/R_{a2}$  is shown in the lower panel of figure 2. As can be seen, the  $R_{a3}$  of the week are 30% larger than  $R_{a2}$  on weekdays and 40-60% larger than  $R_{a2}$  on Saturdays and Sundays when the number of people tested by the public health center decreases. This means that on weekends and holidays, the number of governmental tests at public health centers decreases and the number of positive cases reported through private tests and medical institutions increases. The mean value of  $R_{a3}/R_{a2}$  was about 1.3 during August but declined from September to about 1.1 in October. This implies that the administrative inspection of public health centers was tight when the number of daily positive cases increased rapidly and reached its maximum, but the tightness eased in the contraction period. In this analysis,  $R_{a2}$  is used because it is considered that the testing/isolation rate is almost proportional to the total number of people tested related to  $R_{a2}$ .

### 3. Numerical method to estimate infection persons and infected rate from daily data of positive cases

To investigate the main factors of the expansion and contraction of the fifth wave of Covid-19 infection in Tokyo, equations 1 and 2 were used to analyze the change in the infection rate  $\beta$  and the testing/isolation rate  $\gamma$ , which can predict the change in the measured daily positive cases from July 12, when the state of emergency was declared in Tokyo, to the end of September. In the analysis of the third wave, it has already been clarified that the testing/isolation rate is almost proportional to the number of people tested (6). Therefore, using the data for each decision day and assuming relationship between the testing/isolation rate  $\gamma$  and tested people  $T(d)$ , it will be identified the changes in the infection rate  $\beta$  and the number of infected persons  $I(d)$  such that the 7-day average of the daily positive cases  $R(d)$  in equation 2 matches that of the measured daily positive cases  $R_{a2}(d)$ , and the history and main causes of the expansion and contraction of infection will be clarified.

For better understanding, the analysis method is explained using the figures of the analysis results. The upper panel of figure 3 shows the change in the actual value of  $R_a(d)$  ( $R_{a2}$  is expressed as  $R_a$  below for simplicity) for each day of positive cases (red line), and the number of PCR/antigen testers  $T(d)$  (brown line) as a function of the corresponding day. The red and brown dotted lines are the changes in the moving average of  $R_a(d)$  and  $T(d)$  over the past week, respectively. The solid black line in figure 3 is  $R(d)$  in equation 2, and the unknown  $\beta$  is determined so that the 7-day average value shown by the dotted black line

corresponds to the 7-day average value of the actual value  $R_a(d)$ . The dashed line connecting the black dots is the estimated infected persons  $I(d)$ . The only measured value is  $R_a(d)$ , from which the two parameters  $\beta$  and  $\gamma$  are to be identified. To do so, the case of analysis model 1 was compared, which is based on the hypothesis that  $\gamma$  is proportional to the number of people tested,  $T(d)$ , and the case of analysis model 2, which assumes that the proportionality constant of  $\gamma$  varies slightly with the positivity rate. Figure 3 shows the results of the analysis model 1, so the physical quantities are marked with subscript 1. First, the initial values of the unknown parameters in equations 1 and 2 on July 12 must be estimated as follows.

### 4. Setting the initial values of $\beta$ , $\gamma$ , and $I$

First, the exponents  $\beta-\gamma$  of the exponential function in equations 1 and 2 were estimated from the actual data  $R_a(d)$  of daily positive cases. As shown in figure 3, when  $R_a(d)$  is drawn in semilogarithmic graph, the average values of the days change linearly as shown by the red dotted line. If  $\beta-\gamma$  is constant for  $n$  days, then  $I(d) = I(d-n-1) e^{(\beta-\gamma)n}$ . Substituting this into equation 2 and taking the natural logarithm of equation 2,  $\ln R(d) = \ln \gamma(d) + \ln I(d-n-1) + (\beta-\gamma)n$  were obtained. On the other hand, equation 2 at  $d-n$  becomes  $\ln R(d-n) = \ln \gamma(d-n) + \ln I(d-n-1)$ . Taking the difference between the two equations,  $\ln\{R(d)/R(d-n)\} = \ln\{\gamma(d)/\gamma(d-n)\} + (\beta-\gamma)n$  were obtained. Here, the  $\gamma(d)$  also changes from day to day, but if the change is small, the first term on the right-hand side can be ignored. Then, using the measured value of  $R_a(d)$ , the ratio of  $R_a(d)/R_a(d-n)/n$  is obtained. From the natural logarithm of the ratio of  $R_a$  over  $n$  days, which varies linearly on a semilogarithmic graph, the exponent  $\beta-\gamma$  can be obtained.

The testing/isolation rate  $\gamma$  can be considered to be proportional to the number of people tested from the mathematical model. The average value of  $T(d)$ , shown by the brown dotted line in figure 3, is almost constant between 7/4 and 7/18, so it can be assumed that  $\gamma$  is also constant during this period. Therefore, the rate of increase of the average value of  $R_a(d)$  during the period from 7/4 to 7/10 and 7/11 to 7/17 is  $857.4/595.4 = 1.44$ . From this natural logarithm,  $\beta-\gamma$  at the midpoint 7/12 is obtained as  $\beta-\gamma = \ln(1.44)/7 = 0.052 [\text{d}^{-1}]$ .

Next, it was assumed the initial values of  $\beta$  and  $\gamma$  to be 0.45 and 0.4, respectively. This is because the delta strain, which is said to be 1.5 to 2 times more

infectious than the conventional strains, has increased to 75% in Tokyo as of July 27, and the infection rate in the third wave was about 0.45, when the number of infected people and the number of severely infected people were the largest (6). In equations 1 and 2, the initial value  $I_0$  of the number of infected persons in the city on 7/11 is necessary. Since the average value of  $R_a$  for the week before and after the initial date of 7/12 is 753,  $R(7/12) = 750$  people is set, and from equation 2,  $I_0 = R/\gamma = 1850$  people. The cases where the initial value of  $I_0$  were changed to be 1500 and 2000 people for comparison were also analyzed. Then, it has been found that  $\beta$  becomes large in the initial region when  $I_0$  is small, and  $\beta$  becomes small when  $I_0$  is large, and, after the initial process of determining  $\beta$  to make  $R(d)$  equal to  $R_a(d)$ ,  $I(d)$  and  $\beta$  tend to converge to similar values, respectively.

## Results

### 1. Analysis results of the case where the testing/isolation rate $\gamma$ is proportional to the number of people tested $T(d)$ (Analysis model 1)

It is reasonable to assume that the testing/isolation rate  $\gamma$  is proportional to the number of people tested  $T$ , because  $\gamma$  is the rate at which positive cases  $R$  are found by testing and protected from the number of infected persons  $I$ . The average number of people tested within one week of the median initial date of 7/12 is 9146. Therefore, the initial value of the number of people tested was considered as 9150 and corresponding to the testing/isolation rate  $\gamma = 0.4$ . Accordingly, the testing and isolation rate  $\gamma(d)$  when the number of people tested is  $T(d)$  is given by

$$\gamma(d) = 0.4 \times T(d)/9150 \quad \text{Equation 3}$$

The case where  $\gamma$  is determined using equation 3 is referred to as analysis model 1, and is denoted by the subscript 1 for  $R(d)$ ,  $I(d)$ ,  $\beta$ , and  $\gamma$ .

The actual value of  $T(d)$  is shown by the brown line in the upper panel of figure 3, and the value of  $\gamma_1$  using equation 3 is shown by the blue line in the lower panel of the figure. The proportionality constant of  $\gamma_1$  to  $T(d)$  according to equation 3 is  $4.37 \times 10^{-5}$ , which is 1.4 times larger than the value obtained when the third wave was analyzed (6). This is thought to be due to the increase in the number of tests conducted by private institutions and the free distribution of antigen test kits to schools by the government, which started in July, improving the efficiency of testing and isolation at public health centers.

$\gamma_1$  after July 12 was determined by equation 3, and  $\beta_1$  was determined so that the 7-day average value of  $R_1(d)$ , shown by the black dotted line in figure 3, was equal to the 7-day average value of  $R_a(d)$ , shown by the red dotted line. The 7-day moving average curves

of  $R_a(d)$  and  $R_1(d)$  were almost identical from 17 July to 10 October, as indicated by the red and black dotted lines overwritten. The number of infected people  $I_1(d)$  in the city in equation 1, which can be calculated by  $\beta_1$  and  $\gamma_1$ , is shown by the black dashed line in the upper panel.

The features of the quantities observed from figure 3 are as follows:

1. The predicted value of  $R_1(d)$  of daily positive cases in the upper panel is generally consistent with the actual value of  $R_a(d)$ , but  $R_1(d)$  is usually larger than  $R_a(d)$  immediately after weekends and consecutive holidays. This is because the number of infected persons  $I_1(d)$  increases due to the decrease in  $T(d)$  during holidays, and  $R_1(d)$  assumes that all exposed and infectious persons are tested and isolated immediately after infection. In contrast, in the actual value  $R_a(d)$ , some of asymptomatic persons may be isolated by the close contact examination at the public health center, but most of them are examined and isolated after the onset of infection, which may cause a time delay. The IR theory, which assumes zero latency period, has the advantage of predicting  $I_1(d)$  and  $R_1(d)$  including exposed and infected persons immediately.

2. In general, the number of  $T(d)$  changes within a week, so all the quantities change with a cycle of one week. The lower panel shows that  $\gamma_1$  decreases on weekend and holidays, in accordance with the variation in  $T(d)$ , so  $\beta_1 - \gamma_1$  increases to a positive value of about 0.2–0.3. Since  $T(d)$  increases after the holiday,  $\gamma_1$  increases, but  $\beta_1$  also increases when the infection rate  $\beta_1$  is determined so that the daily positive  $R_1(d)$  is equal to the actual value  $R_a(d)$ . However, since  $\beta_1 - \gamma_1 < 0$ ,  $I_1(d)$  decreases from Monday to Friday, and  $R_1(d)$  and  $R_a(d)$  decrease accordingly. However, since  $T(d)$  on Wednesday and Thursday decreases slightly,  $\beta_1 - \gamma_1 > 0$  and  $I_1(d)$  and  $R_1(d)$  increase slightly on Friday. In the end, when the weekly mean of  $\beta_1 - \gamma_1$  is positive, the weekly mean  $I_1(d)$  and  $R_1(d)$  increase, and when it is negative, they decrease. It should be noted that if the decrease in  $T(d)$  on Saturdays and Sundays during the period of spread of infection is eliminated,  $\beta_1 - \gamma_1 < 0$  throughout the week can be set, and  $I_1(d)$  and  $R_1(d)$  can easily be changed to a decreasing trend.

3. The 7-day median moving average of  $R_a(d)$  at the initial value on 7/12 was 753, and the averages for the next 10 days (7/22, 8/1, 8/11) were 1233, 2991, and 3377, respectively, rapidly increasing 1.64, 3.97, and 4.48 times. The maximum value of  $R_a(d)$  was 5011 on August 17 (The number of confirmed positive  $R_{a3}$  reached its maximum value of 6205 on the same day). The reason for the 2.42 times increases in  $R_a(d)$  and the rapid increase in  $\beta_1$  from July 22 to August 1 is that

$T(d)$  decreased during the four consecutive holidays from July 22 to 25 for Olympic opening ceremony, and as shown in the lower panel,  $\beta_1 = \sim 0.45$ , while  $\gamma_1$  decreased significantly, resulting in  $\beta_1 - \gamma_1 \cong 0.2$ . The Tokyo metropolitan government declared a state of emergency on July 12, and the Olympics were held in a bubble fashion without spectators, so it is unlikely that the flow of people increased during the holidays of the Olympics opening. In addition, the citizens of Tokyo were watching the Olympics ceremony and games on TV, so it is not considered that they relaxed their self-restraint. The moving average value of  $\gamma_1$  became close to  $\beta_1$  around August 1, but the state  $\beta_1 - \gamma_1 \geq 0$  continued thereafter.  $\beta_1 - \gamma_1$  became positive during the three consecutive holidays on the closing ceremony of the Olympics from August 7 to 9, and its average value also increased slightly with positive values.

4. Figure 4 shows the trend of the number of consultations on fever and other illness received at the Tokyo Metropolitan Fever Consultation Center. In general, the inspection activities of public health centers are reduced during the two consecutive weekends, and many medical institutions are closed. For this reason, even those with fever or other symptoms of coronary infection cannot be responded immediately and can be examined and isolated on Monday or later, increasing the probability of the spread of infection during this period. Figure 4 shows that a particularly large number of consultations occurred during the four consecutive holidays from July 22 to 25, including the day of the Olympic Games ceremony. From the lower panel of figure 3, since  $\beta_1 - \gamma_1 \approx 0.2$  during this period, if this situation continues for four days, the number of people infected in the city increases by a factor of  $e^{0.2 \times 4} = 2.2$  according to equation 1. The explosion of infection in the fifth wave was mainly caused by this four-day holiday. After that, the number of consultations during the two consecutive weekends from July 31 to August 1 and the three consecutive weekends from August 7 to 9 were also contributing to the increase in  $I_1(d)$ ,  $R_1(d)$ , and  $\beta_1$  successively, as seen in figure 3.

5. What is the main reason for the decrease in  $R_a(d)$  after 8/17? It is noteworthy that although the moving average of  $\beta_1$  increased from 8/15 to 8/26, the moving average of  $T(d)$  and  $\gamma_1$  increased during the same period, resulting in  $\beta_1 - \gamma_1 < 0$ . In other words,  $\beta_1$  is increasing, but  $\gamma_1$  is increasing more than  $\beta_1$ . This is the reason why  $R_a(d)$  is decreasing. However, after August 27, although  $T(d)$  and  $\gamma_1$  began to decrease,  $\beta_1$  itself decreased at a faster rate than  $T(d)$ , and  $\beta_1 - \gamma_1$  became relatively large negative values. Therefore, the weekly median of  $R_a(d)$  decreased by 0.49, 0.23, and 0.073 times on 9/6, 9/16, and 9/26, respectively,

compared to 2774 on 8/27, and decreased to 151 on 9/30. During this period, the mean value of  $\beta_1$  decreased from 0.7 to about 0.25, with a decreasing rate of about 0.1 per week. The main reason for this rapid decrease in  $\beta_1$  can be speculated as an increase in the vaccination rate. Especially after September, when vaccination of young people with high infection rates increased. The effect of the increase in vaccination rate on the reduction of infection rate will be discussed in detail later. Furthermore, it should be noted that the decrease of  $T(d)$  in September was slower than that of  $\beta_1$ , and the mean decrease rate of  $\gamma_1$  was smaller than that of  $\beta_1$ , indicating that  $\beta_1 - \gamma_1 < 0$  was maintained, which also contributed to the reduction of  $R_a(d)$ . The maximum  $R_a(d)$  was observed on August 17, and the maximum number of patients treated at home was 26409 on August 21, and the maximum number of daily deaths was 30. It is possible that the fear of this horrible fact may have contributed to the reduction of  $\beta_1$  to some extent.

6. There is a fear that the decrease in the number of inspections during the 3 consecutive holidays of Respect-for-Senior-Citizens Day on 9/18~20 would cause an increase in  $\beta_1$ . However, the increase in the number of consultations in figure 4 is not so large because  $I_1(d)$ , shown by the black dashed line, has decreased markedly compared to  $I_1(d)$  around 7/22~25. The mean value of  $\beta_1$  in this period is small compared to that of  $\gamma_1$ , and  $\beta_1 - \gamma_1 < 0$  is maintained.

7. In the lower panel of figure 3,  $\beta_1$  decreased sharply on 9/13-14, increased sharply on 9/16-17, and then decreased sharply again on 9/18-20. The similar large fluctuation behavior of  $\beta_1$  was observed from 8/31 to 9/4. Although the change in  $\beta_1$  relative to the change in  $\gamma_1$  is similar to that in other weeks, it is significantly larger than that in other weeks, and the reason for this is currently unknown. Incidentally, if  $R_1 = 0.15$  (9/13) and 0.16 (9/14) to  $R_1 = 0.3$ , and  $R_1 = 0.76$  (9/16) and 0.74 (9/17) to  $R_1 = 0.5$  are changed, the 7-day moving average of  $R_1$  shifts upward, but the daily number of  $R_1(d)$  becomes close to  $R_a$ , and the change in the average of  $\beta_1$  becomes smooth. On the contrary, when there is trying to make the moving average of  $R_1$  match that of  $R_a$ , the tendency for  $R_1$  on Monday to be higher than  $R_a$  and  $R_1$  on Thursday to be lower than  $R_a$  becomes more pronounced with a rapid change in  $\beta_1$ , as shown in figure 3.

8. The public data of  $R_a(d)$  and  $T(d)$  of Tokyo Metropolitan Government (7) are often changed later for the past two months at most. The data values used in this paper are as of November 30, and the data after the end of September may be changed only slightly, if any.

## 2. Analysis results of calculating the testing/isolation rate $\gamma$ based on $T(d)$ , taking into account the change in the positivity rate (Analysis model 2)

In the above analysis model 1,  $\gamma$  was assumed to be proportional to  $T(d)$ . However, as the number of daily positive persons  $R_a(d)$  increases, the administrative inspection and isolation work of the public health center will become tighter, and the positivity rate  $PR$  ( $= R_a(d)/T(d)$ ) will increase because the public health center will not be able to sufficiently investigate the close contacts.

Figure 5 shows the daily change in the positivity rate and the moving median average over the seven-day period. The moving average of the positivity rate on July 10 was 0.074, which rose to 0.10 on July 16, then rapidly increases to 0.2 on July 30, gradually increased to 0.24 on August 15, and then decreased almost monotonously. In general, when the positivity rate increases, the number of  $T(d)$  is insufficient for the number of infected persons  $I(d)$ , and if the number of  $T(d)$  were increased to keep the positivity rate lower value, more daily positive cases would be found. In other words, since the testing/isolation rate  $\gamma$  is the ratio of testing/isolation positives to infected persons  $I(d)$  in the community, the proportionality constant of the testing/isolation rate  $\gamma$  to  $T(d)$  should decrease as the positivity rate increases. Therefore, if the average positivity rate is denoted by  $PR$ , which increases from the median positivity rate of 0.1 on 7/16, the effective testing/isolation rate  $\gamma$  should be modified as  $\gamma = 0.4 \times T(d)/9150 \times (0.1/PR)$ . However, if this is done, the testing/isolation rate will be less than half during the period from July 30 to August 21, and  $R(d)$  will be extremely large. In other words, if it is assumed that the testing/isolation rate is inversely proportional to the positivity rate, it will probably overestimate the effect. The increase in the  $PR$  is also caused by an increase in the efficiency of testing and isolation by medical institutions. An increase in the number of infected persons  $I(d)$  also has the effect of increasing the testing/isolation rate, since persons with mild disease and their close contacts are more likely to undergo antibody/PCR testing. Therefore, the effect of a decrease in the testing/isolation rate due to an increase in the positivity rate is 20%, and 80% is proportional to  $T(d)$ . Thus, multiplying the testing/isolation rate by  $(0.8+0.2 \times 0.1/PR)$ , it can be obtained:

$$\gamma(d) = 0.4 \times T(d)/9150 \times (0.8 + 0.2 \times 0.1/PR) \quad (PR > 0.1)$$

Equation 4

Equation 4 is used to determine  $\gamma$ , but equation 3 is used before July 15 and after September 9, when the positivity rate  $PR$  is less than 0.1. The analysis method in which  $\gamma$  is determined using equations 3 and 4 is called analysis model 2 and calculated quantities are

expressed by using subscript 2.

Figure 6 shows the results of the analysis model 2 using equations 3 and 4 with an initial value of  $I_0 = 1875$  as in analysis model 1. The testing/isolation rate  $\gamma_2$  is shown by the solid blue line in the lower panel of figure 6. The average value of  $\gamma_2$ , which has a maximum value around August 24, is about 0.1 lower than that of  $\gamma_1$  in analysis model 1 in figure 3.

Using this  $\gamma_2$  value, by determining  $\beta_2$  so that the 7-day moving average of the theoretical daily positive persons  $R_2(d)$  matches that of the actual value of  $R_a(d)$  shown by the red line.  $R_2(d)$  is shown by the black line in the upper panel of figure 6, and  $\beta_2$  is shown by the black line in the lower panel of figure 6. The 7-day moving averages of  $R_a(d)$  and  $R_2(d)$  in the upper panel of figure 6 are shown by the red and black dotted lines, respectively, and they are in good agreement. The black dashed line in the upper panel of figure 6 is the calculated number of infected persons  $I_2(d)$ , corresponding to the daily positive cases  $R_2(d)$ . The brown line is  $T(d)$ , as the same as figure 1. The features of analysis model 2 are described below:

1.  $R_2(d)$  in figure 6 is almost the same as  $R_1(d)$  in analysis model 1 shown in figure 3, but  $I_2(d)$  is larger during August when the positivity ratio is larger than 0.1 because of the relationship  $I(d) = R(d)/\gamma$ .

2. Comparing the characteristics of  $\gamma_2$  and  $\beta_2$  in the lower panel of figure 6 with those of  $\gamma_1$  and  $\beta_1$  in the lower panel of figure 3, the weekly fluctuation amplitude and moving average of  $\gamma_2$  become smaller during August, with the maximum value of  $\gamma_2 = 0.83$  on August 24 compared to  $\gamma_1 = 0.92$ . Therefore, the weekly variation of  $\beta_2$  is smaller than that of  $\beta_1$ , and the moving average and the maximum value around 8/24 are also smaller by about 0.05, indicating smooth changes. In particular, the large fluctuations of  $\beta_1$  from 8/31 to 9/5 and 9/13 to 9/20 in figure 3 are not seen in  $\beta_2$  in figure 6. This corresponds to the fact that  $R_1(d)$  in the upper panel of figure 3 is significantly larger than  $R_a(d)$  on Mondays and deviates significantly smaller than  $R_a(d)$  on Thursdays, while the deviation of  $R_2(d)$  from  $R_a(d)$  in figure 6 is suppressed.

3. The moving average of  $\beta_2 - \gamma_2$ , which dominates the changes in  $I_2(d)$  and  $R_2(d)$ , changes from positive to negative after 8/15, as does  $\beta_1 - \gamma_1$  in the lower panel of figure 3. However, the positive mean value of  $\beta_2 - \gamma_2$  was larger than that of  $\beta_1 - \gamma_1$  before 7/30, when the infection spread rapidly, and the negative value of  $\beta_2 - \gamma_2$  increased more monotonously than that of  $\beta_1 - \gamma_1$  after 9/1, when the infection shrank rapidly.

Therefore, it can be said that the fifth wave of COVID-19 epidemic spread rapidly due to the decrease of  $\gamma_2$  caused by the decrease of  $T(d)$  during the consecutive holidays from July 22 to 25. Although  $\gamma_2$  catches up

with  $\beta_2$  after 7/29 due to the increase of  $T(d)$  after the holidays,  $\beta_2 - \gamma_2$  becomes a large positive value and  $R_a(d)$  continues to increase because  $T(d)$  decreases to about 1/3 of the weekday value on Sunday 8/1, holidays 8/8-9, and Sunday 8/15.

After 8/16, the moving average of  $\beta_2$  continued to slightly increase until 8/25, but  $T(d)$  and  $\gamma_2$  continued to increase more than  $\beta_2$ , so  $R_a(d)$  entered a period of decrease. However, since the end of August,  $\beta_2$  itself has clearly decreased. Moreover, the moving average of  $\beta_2 - \gamma_2$  is increasing in the negative direction because the rate of decrease of  $T(d)$  is small and the degree of decrease of  $\gamma_2$  is small. The positivity rate also decreases, and it becomes less than 0.1 after 9/10. Therefore,  $\gamma_2$  is assumed to be proportional to  $T(d)$  after 9/10.

Since  $\beta_2 - \gamma_2 \approx -0.1$  is maintained from around 9/20 to late October,  $I_2(d)$  and  $R_2(d)$  are halved ( $e^{(-0.1 \times 7)} \approx 0.5$ ) week by week. The monotonicity of the changes in the infection rate  $\beta_2$  and  $\beta_2 - \gamma_2$  suggests that analytical model 2 is a more reasonable representation of the process of infection expansion and contraction than analytical model 1.

### 3. Effect of vaccination on reduction of the fifth wave infection

The fact that the infection rate  $\beta$  decreased from September to October and remained in the range of  $R_a = 10 \sim 30$  in November, unlike previous waves, suggests that the infectivity of COVID-19 is relatively decreasing. The main reason for this is the increase in vaccination rate, especially among the younger generation, which was the main source of infection. The lifestyle of masking, handwashing, disinfection, and 3Cs avoidance has already become routine, and it is expected that the infection rate will not change much due to the interaction of people with or without the declaration of a state of emergency. In this study, the effect of increasing the vaccination rate on reducing the infection rate has been examined.

Figure 7 shows the population ratios of people who received the first and second doses of vaccine in Tokyo, as reported in the latest infection trend website of the Tokyo Metropolitan Government (7). The red and blue dotted lines indicate the first and second vaccination rates, respectively. The prophylactic efficacy of the mRNA-based vaccines manufactured by Pfizer and Moderna, which have been adopted in Japan, is relatively higher than that of other vaccines in preventing infection. According to some data, the first vaccination is 82% effective in preventing infection, and the second vaccination is 94% effective in preventing infection. If it is assumed that the infectivity of the first vaccination decreases to 1/4 and

that of the second vaccination decreases to 1/10, and if the percentage of the population vaccinated with the first vaccination is  $\alpha_1$  and that vaccinated with the second vaccination is  $\alpha_2$ , the reduction rate of infectivity  $RR$  is given by

$$RR = \alpha_2 \times 0.1 + (\alpha_1 - \alpha_2) \times 0.25 + (1 - \alpha_1) \quad \text{Equation 5}$$

Substituting the values of vaccination rate in figure 7 into equation 5, it can be drawn the reduction rate  $RR$  as shown in the black dotted line in figure 7. Because the infection rate  $\beta$  is considered to be given by the product of the probability of infection by human flow and the infectivity of the virus itself, the black dot in figure 7 can be regarded as the degree of reduction of the infection rate  $\beta$ . The black dotted line in equation 5 is the case where the above preventive effect is obtained immediately after inoculation, but the above effect is not actually obtained until about 2 or 3 weeks later.

Thus, in figure 7,  $RR = 0.5$  on August 23, but the infection rate  $\beta$  is thought to have been reduced to 1/2 around September 10. After that, the infection rate continued to decrease to 1/3 until October but did not decrease further due to saturation of the vaccination rate. Figure 6 shows that the infection rate  $\beta$  gradually decreased from the maximum value of 0.65 in mid-August to 0.25 at the end of September, about 1/3 of reduction rate, which is numerically consistent with figure 7.

To increase the effectiveness of vaccination in reducing the infection rate, it is important to increase the vaccination rate. Equation 5 shows that when the second vaccination rate increases to 80, 90, and 100%, the  $RR$ , namely the reduction rate of infection rate  $\beta$ , becomes 0.28, 0.19, and 0.1, respectively. Therefore, it is extremely important to aim for a vaccination rate of 100%.

Leading infectious disease control experts have suggested that the reasons for the rapid contraction of the fifth wave include 1. the strengthening of infection control measures by citizens, 2. a decrease in the number of people staying in the area, especially at night, 3. an increase in vaccination rates, 4. a decrease in the number of people infected in clusters at medical institutions and elderly care facilities, and 5. weather factors. In addition, the theory of self-destruction by viral mutation has been proposed as a possible explanation. The author's opinion, based on the results of the mathematical analysis in this paper, is that the first factor is the vaccine effect described in reason 3, and the second factor is the expansion of the number of tests, as described above, which has maintained the testing/isolation rate  $\gamma$  above the infection rate  $\beta$  since mid-August. The increase in  $\gamma$  is expected to be due to the spread of PCR and antigen testing and the introduction of free testing.

As for the effect of reasons 1 and 2, the probability of infection was reduced to some extent because people became fearful of the situation in which  $R_a$  exceeded 5,000 and the number of serious cases and deaths was increasing, and they tried to refrain from going out without necessity. However, citizens are already familiar with wearing masks, washing hands, disinfecting, and avoiding 3Cs environments, and efforts to reduce the flow of people are close to the limit. Therefore, the decrease in the probability of infection may be small.

Compared to other countries, the effect of vaccination on infectiousness reduction in Japan was well-timed, starting at the height of the fifth wave. The infection-preventing effect of vaccination shown in figure 7 can be maintained for 3 to 4 months, but it is said to decrease considerably after 6 months. Therefore, it is necessary to monitor whether  $\gamma > \beta$  is maintained during the period up to the third booster vaccination, and to conduct additional vaccinations while maintaining the testing/isolation rate  $\gamma$  higher than the infection rate  $\beta$  by making PCR and antibody testing free and immediate.

#### 4. Prediction of the infection spread and reduction status when $T(d)$ does not decrease during the four and three consecutive holidays associated with Olympic Games

It has already stated in the previous section that the main reason for the largest spread of infection in the fifth wave was that the number of people tested  $T(d)$  during the four and three consecutive holidays associated with the Olympic Games was reduced by about half compared to  $T(d)$  during the ordinary weekdays. Therefore, the simulation in analysis model 2 was performed, when  $T(d)$  on the previous day, July 21, is maintained during the four consecutive holidays 7/22~25. This case can be called hypothetical model A. It was also performed the simulation of hypothetical model B when  $T(d)$  on the previous day, August 6, is also maintained during the three consecutive holidays 8/7~9 in addition to the hypothetical model A. The change of  $R_2(d)$  for each day was simulated using equations 1, 2, 3 and 4 in these two cases. The subscripts A and B in the various quantities mean that they are the results of calculations under hypothetical models A and B, respectively.

The calculated results are shown in figure 8. In the upper panel of figure 8, the red and brown lines are the actual values of  $R_a(d)$  and  $T(d)$ , which are already shown in figures 3 and 6. Hypothetical model A is the case where  $T(d)$  between July 22 and 25 remains equal to  $T(d) = 12090$  on July 21, as shown by the black dots in the brown line. In this case, the estimated positive cases  $R_{2A}$  is shown by the green line. On the other hand, in hypothetical model B, in addition to the case of

model A,  $T(d)$  during the August 7 to 9 is maintained at the previous day's level of 18528, as shown by the black dots. In this case, the estimated positive cases  $R_{2B}$  is shown by the blue line. The green line is overlaid by the blue line because  $R_{2A}$  is the same as  $R_{2B}$  before August 6. The dotted lines of the same color are the moving averages of each quantity over the past seven days.

In hypothetical model A, the maximum value of  $R_{2A}$  on 8/17 (2432 people) is less than half of the maximum value of  $R_a(d)$  (5011 people), and  $R_{2A}$  has been shrinking while keeping the moving average value less than 40% of  $R_a(d)$  since then. Furthermore, in hypothetical model B, the maximum value of  $R_{2B}$  (1863 people) is obtained on August 3, and  $R_{2B}$  decreases monotonically until August 13 due to the high number of inspections during the three consecutive holidays. After that, the apparent decrease in  $R_{2B}$  due to the decrease in  $T(d)$  on Saturdays and Sundays is followed by an increase on Mondays, Tuesdays, and Wednesdays. However, the moving average of  $R_{2B}$  shows a decrease from 8/7 and a monotonous decrease at a level of 1/8 of  $R_a(d)$  after 8/17 and can be reduced to less than 100 on 9/15. Therefore, it can be estimated that the rapid spread of infection in the fifth wave would not have occurred if the number of examinees had been maintained at the same level as that of weekdays during the four consecutive holidays and the three consecutive holidays associated with the Olympic Games.

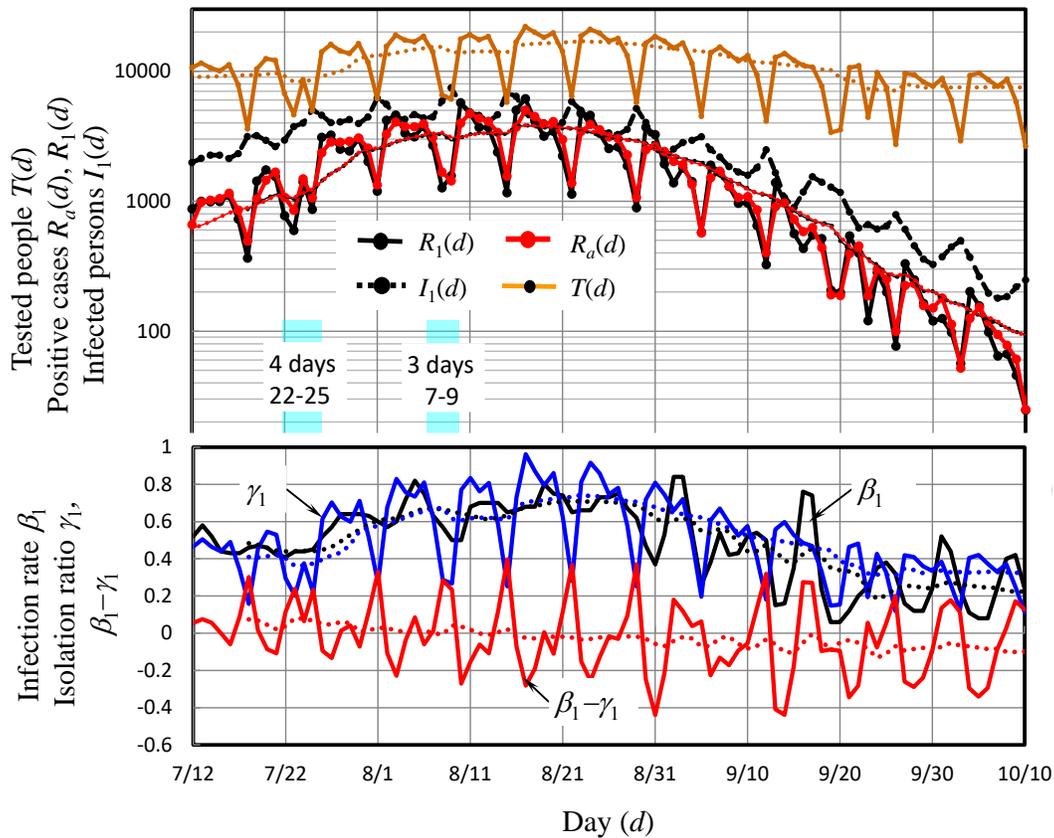
The lower panel of figure 8 shows the values of  $\beta_2$  and  $\gamma_2$  for which  $R_{2A}$  and  $R_{2B}$  in the upper row were calculated. The blue line  $\gamma_{2B}$  corresponds to the testing/isolation rate when  $T(d)$  in the upper row remains high as shown in the black line during four and three consecutive holidays, while the green line  $\gamma_{2A}$  is the inspection/isolation rate in model A when  $T(d)$  during three consecutive holidays is low. The green line,  $\gamma_{2A}$ , is the same as the blue line,  $\gamma_{2B}$ , except for the three-day holidays on 8/7 to 8/9. The infection rate  $\beta_2$  is assumed to be the same in both cases as in figure 6 when  $T(d)$  decreased on consecutive holidays. If hypothetical models A and B are implemented, the infection rate  $\beta_2$  should be lowered than that in figures 6 and 8, and  $R_{2A}$  and  $R_{2B}$  should be even lower than in figure 8. If one looks at the moving average of  $\beta_2 - \gamma_2$ , which determines the expansion and contraction of infection,  $\beta_{2A} - \gamma_{2A}$  and  $\beta_{2B} - \gamma_{2B}$  become negative between July 25 and 31 because  $\gamma_{2A}$  and  $\gamma_{2B}$  are kept a higher value during the four consecutive holidays from July 22 to 25. After that,  $\beta_{2A} - \gamma_{2A}$  shows positive values close to zero until Aug. 15, as shown by the purple dotted line. Therefore,  $R_{2A}$  is about half the maximum of  $R_a$  in this period.

On the other hand,  $\beta_{2B}-\gamma_{2B}$  showed a large negative value from the three-day holidays of August 7~9 to August 16, and this is the reason why  $R_{2B}$  decreased more markedly than  $R_{2A}$ .

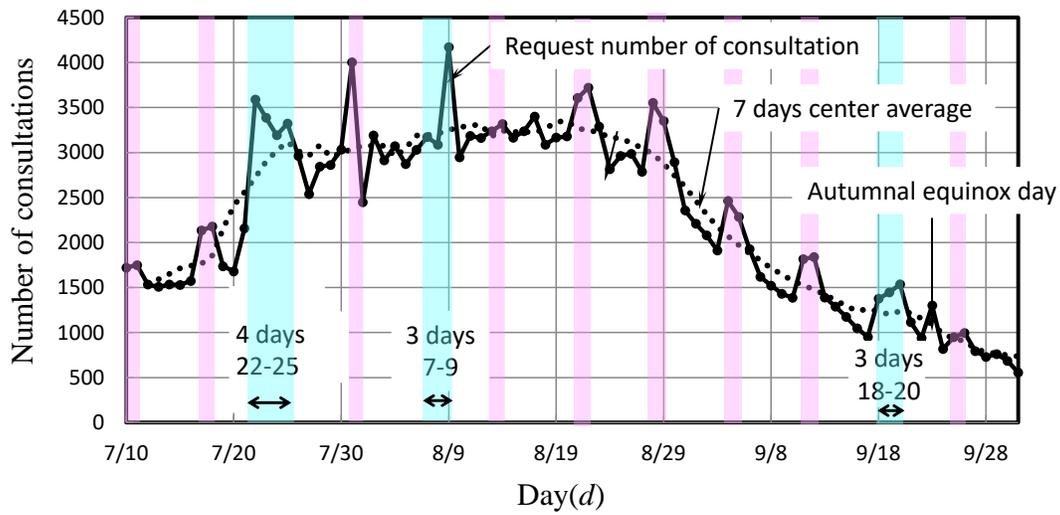
In analysis model 1, in which the testing/isolation rate  $\gamma$  is proportional to the number of people tested  $T(d)$ , the  $\gamma$  is evaluated larger than in analysis model 2, so the maximum values of  $R_{1A}(d)$  and  $R_{1B}(d)$  are smaller than those of  $R_{2A}(d)$  and  $R_{2B}(d)$  shown in figure 8, and the tendency of infection reduction is stronger.

Considering the above, if experts in infectious disease medicine and epidemic theory, as well as government officials, had recognized that the halving of the number of people tested over three consecutive holidays would be a major factor in the spread of

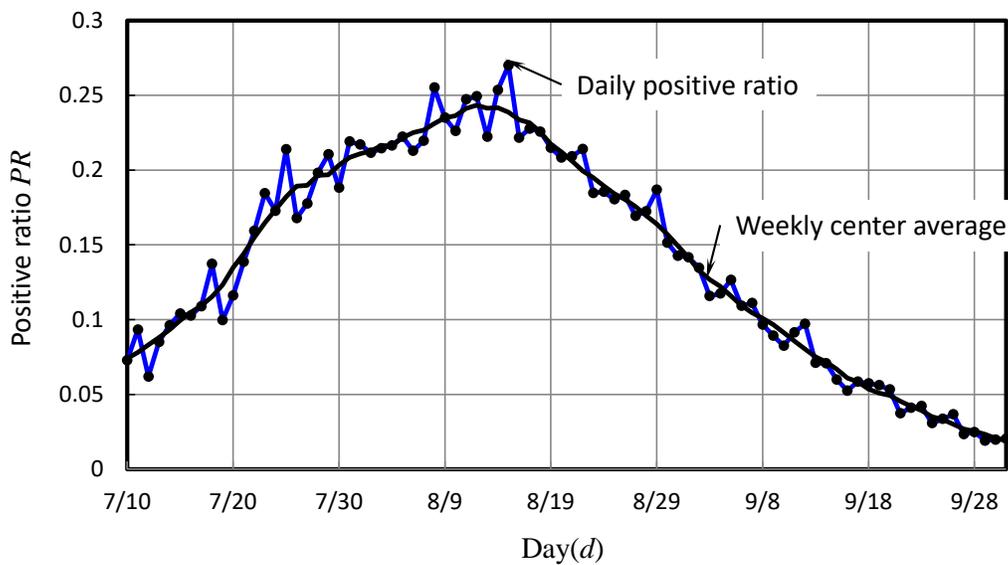
infection, they would have avoided establishing special four-day and three-day holidays for the Olympic Games. Alternatively, if a series of holidays were to be set up, a special inspection system as daily corona tests applied to all members of Olympic officials should have been applied also to citizen's inspection on four-day and three-day holidays to achieve the same number of people tested as on weekdays. In this case, the fifth wave would have been limited to at most 2,000 daily positives, and the number of daily positives would have decreased from mid-August, so that infected people treated at home due to the tight medical system could be reduced markedly, and the resulting serious illnesses and deaths would have been reduced significantly.



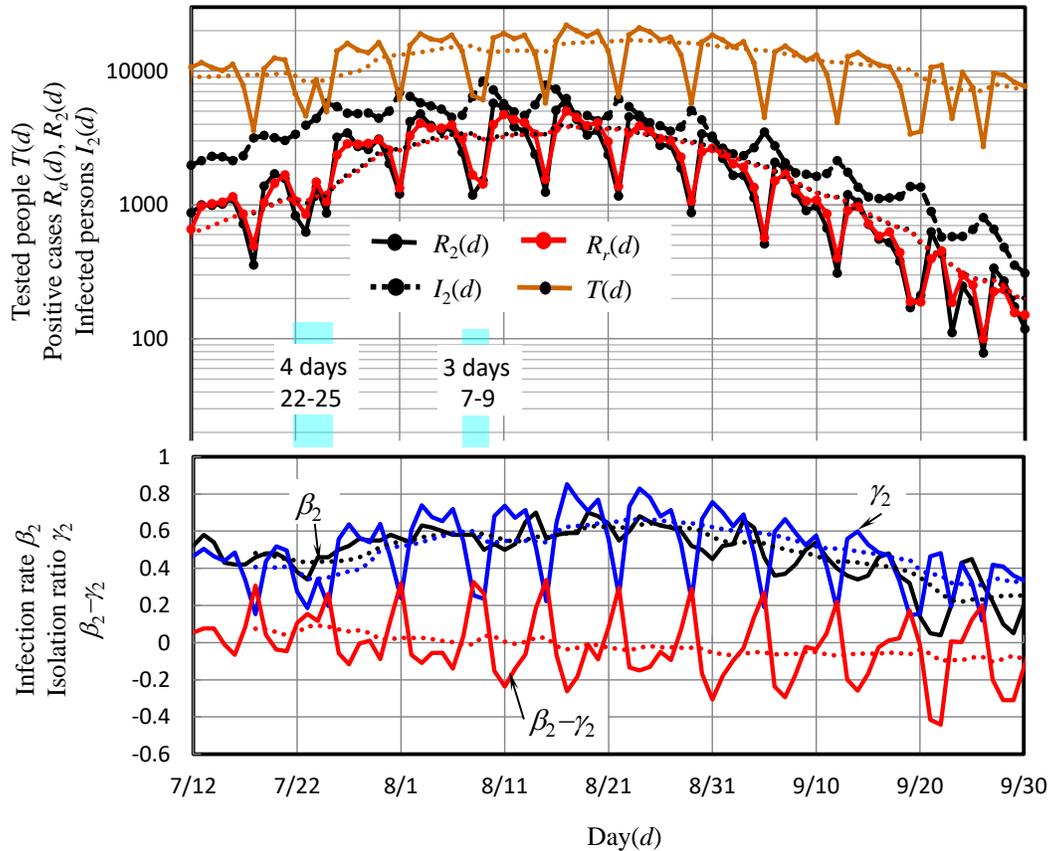
**Figure 3.** Daily number of people tested  $T(d)$  and daily number of actual positive cases  $R_a(d)$ . Theoretical daily number of positive cases  $R_1(d)$  and the number of infected persons in the city  $I_1(d)$ , daily infection rate  $\beta_1$  and testing/isolation rate  $\gamma_1$  (Analysis model 1)



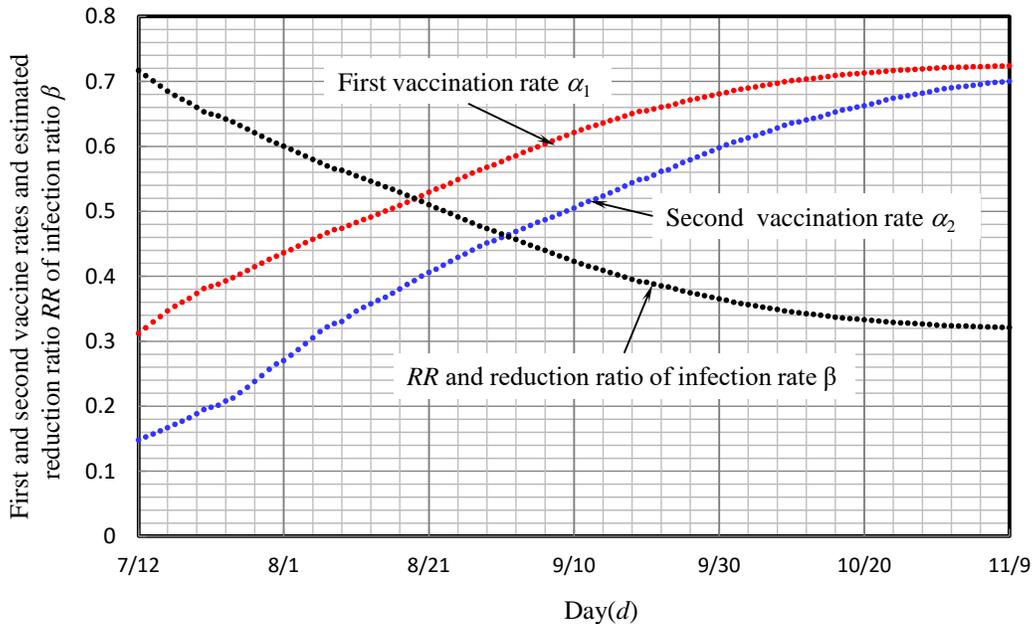
**Figure 4.** Number of consultations on fever and illnesses received at the Tokyo Metropolitan Fever Consultation Center. The dates 7/22-25 are four consecutive holidays and the dates 8/7-9 are three consecutive holidays related to the Olympic Games. The date 9/18-20 is a three-day weekend related to Senior Citizen's Day.



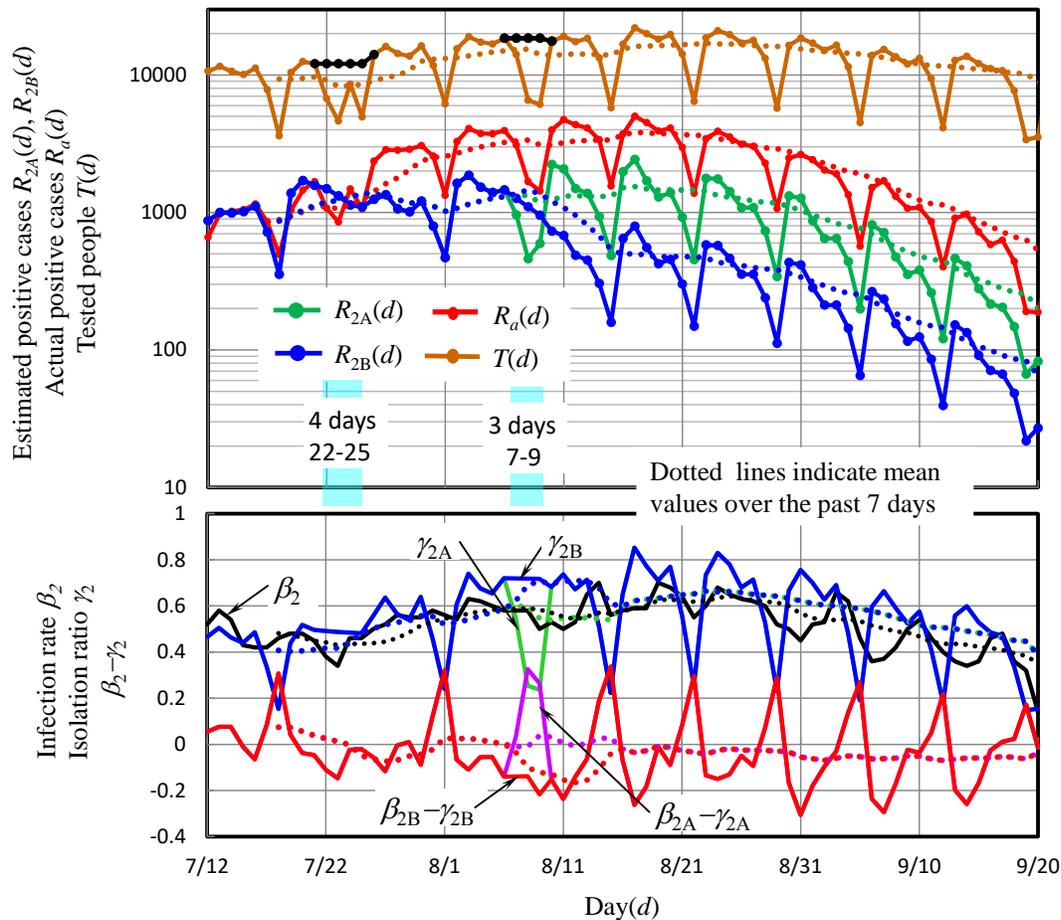
**Figure 5.** Variation of daily and seven-day median average positive ratios *PR*



**Figure 6.** Daily number of people tested  $T(d)$  and daily number of actual positive cases  $R_a(d)$ . Theoretical daily number of positive cases  $R_2(d)$  and number of infected persons in the city  $I_2(d)$ , daily infection rate  $\beta_2$  and testing/isolation rate  $\gamma_2$  (Analysis model 2)



**Figure 7.** The first and second vaccination rate and estimated  $RR$  and reduction ratio of infection ratio  $\beta$  in Tokyo city as a function of day



**Figure 8.** Daily number of positive cases when  $T(d)$  of the previous day is maintained on the consecutive days of Olympic Games opening and closing ceremonies in Analysis Model 2. The green line  $R_{2A}$  shows the daily number of positive cases when  $T = T(7/21) = 12090$  is maintained for the period from 7/22 ~25 (Model A). The blue line  $R_{2B}(d)$  shows the daily number of positive cases when  $T = T(8/6) = 18528$  is also maintained during 8/7~9 (Model B). The infection rate is assumed to maintain  $\beta_2$  in figure 6. The testing and isolation rate  $\gamma_{2A}$  in Model A is shown by the green line in the lower panel, and the testing and isolation rate  $\gamma_{2B}$  in Model B is shown by the blue line.  $\beta_{2A} - \gamma_{2A}$  is shown by the purple line, while  $\beta_{2B} - \gamma_{2B}$  are shown in red line.

## Discussion

### 1. Considerations on the prevailing infectious disease theory and the justification of IR theory

First, the validity and justification for using IR theory to investigate the primary mechanism of the COVID-19 epidemic wave are presented. Prof. Nishiura and his team have been the sole researchers in Japan who have studied infectious disease outbreaks mathematically. Their main goal is to use the most recent stochastic process theory to forecast the effective reproduction number and to suggest the essential action criteria for infection suppression (2,3,8). Based on his findings, he claims that 80 percent of socioeconomic activities must be avoided to prevent the first wave of infection from spreading. He computed the effective reproduction number in the first and second waves in Osaka City, Japan and stressed the importance to quickly design and introduce complex intervention measures to reduce the effective reproduction number below 1 (3).

However, from the author's point of view, the theory of Nishiura and colleagues raises the following questions:

1. Although the method of calculating the effective reproduction number based on stochastic process theory is well suited to sexually transmitted diseases, Covid-19 infections, which necessitate rapid testing and isolation of all positive cases, including close contacts, are almost all one-generation infections and can be analyzed with a simple (S) IR model.
2. Nishiura's theory does not include a parameter for the testing and isolation rate, and as a result, he has never highlighted the significance of testing and isolation.
3. Although he was primarily interested in determining the effective reproduction number, it is more important to understand the changes in infection and testing/isolation rates separately in order to determine the prevailing mechanism of infection expansion and contraction.

Following the first wave, many people criticized the fact that the number of PCR tests in Japan was lower than in the least developed countries, as indicated in the introduction. Prof. Nishimura, the foremost theoretical expert, however, never highlighted the significance of testing and isolation. This is because of his theory, which served to support administrators and infectious disease doctors who clung to old notions.

Although the author is not an epidemiologist, he believes that the IR model, which expresses the number of infected people in a city by using the infection rate  $\beta$  and testing/isolation rate  $\gamma$ , should be able to forecast the number of infected people in a city easily. Since around March 2020, the author has been

researching a method for estimating the number of infected persons,  $\beta$ , and  $\gamma$ , based on actual data from daily positive cases and people tested. Around the same time, the author learned that Dr. Kikuchi, a colleague at our university laboratory, was working on a simulation study using SIR theory to estimate the number of infected people, infection rates, and testing/isolation rates. Since the first wave of infection, there was a common collaboration on this research, analyzing, and reporting on the mechanics of infection expansion and contraction (5,6).

In the case of COVID-19 infection, the median serial interval is 4 days, which is shorter than the mean incubation period of 5 days (9,10). This means that the mean latency period  $D$  is expected to be about 2 days. Therefore, the (S)EIR model, which takes into account the relationship that exposed persons  $E$  becomes infectious persons  $I$  with a time constant  $\epsilon (= D^{-1})$ , is more rigorous than (S)IR model. However, Kikuchi has shown that when the infection rate  $\beta$  and the testing/isolation rate  $\gamma$  change slowly, the number of infected persons  $I$  calculated from the (S)IR model using the measured values of daily positive cases corresponds to  $E+I$  in the (S)EIR model. Although the values of  $\beta$  and  $\gamma$  of the (S)IR model are smaller than those of the (S)EIR model, they can be transformed by a coefficient that depends on  $\epsilon$ , and the infection rate and the testing and isolation rate of the (S)EIR model can be obtained. As described before, when the number of people tested increases rapidly from Sunday to Monday,  $R = \gamma(I+E)$  is detected, while  $E$  is not immediately detected in  $R_a$ , so  $R > R_a$  on Monday, and then  $R < R_a$  on Wednesday and Thursday since it is detected later. This transient phenomenon can be observed evidently by IR theory.

In comparison to the other advanced mathematical models mentioned above, the author and Kikuchi believed that the simplest IR model is the best approach to elucidate the dominant mechanism of infection expansion and contraction of the Covid-19 disease, and they used the IR model to analyze the first, second, and third waves (5, 6). The fifth wave is analyzed using the same IR model, but the infection rate and inspection/isolation rate calculation methods are more advanced than in earlier articles (5,6).

### 2. Effective reproduction number

As a measure of the intensity of infection and the state of spread or contraction of an infectious disease, the effective reproduction number, expressed as  $R_t$ , is generally used.

In IR theory,  $R_t$  is expressed by  $R_t = \beta/\gamma$  for the following reason. From equation 1, the increments of infected persons can be expressed as  $dI(t) = (\beta - \gamma)I(t)dt$ .

Substituting  $dt = 1/\gamma$ ,  $dI/I = \beta/\gamma - 1 = Rt - 1$  can be obtained. Thus,  $dt = 1/\gamma$  implies a period during which all infected persons  $I$  in the city can be tested and isolated, under the condition  $\beta = 0$  since  $dI/I = -1$ . Therefore,  $Rt = (dI + I)/I$  means the ratio of the infected people during the period of  $1/\gamma$ . In the analysis of the fifth wave, the changes in  $\beta$ ,  $\gamma$ , and  $\beta - \gamma$  has been shown separately throughout the entire course of the expansion and contraction of infection and made clear the effect of the number of people tested on the rate of testing and isolation, the change in delta strains on the infection rate, and the effect of vaccination rate on the infection rate.

However, when the change in  $Rt$  during the process of infection spread is shown, it can immediately be known how much it is needed to change  $\gamma$  or  $\beta$  to make  $Rt < 1$ . Since  $\gamma \times Rt = \beta$ , to make  $Rt < 1$ , the number of people tested should be increased so that  $\gamma$  is more than  $\gamma Rt$  of the current value. On the other hand, since  $\beta/Rt = \gamma$ , administrative measures should be taken such as refraining from activities, restricting the flow of people, increasing the rate of vaccine intake, booster vaccination, etc. so that  $\beta$  is less than  $\beta/Rt$  of the current value.

## Conclusion

These are the main key findings of study:

1. An IR model based on the competition idea between the infection rate and the testing/isolation rate was used to investigate why the fifth wave of COVID-19 infections in Tokyo spread rapidly in time for the Olympic Games. The key explanation for the rapid spread of highly contagious delta strains from late July to early August was that the number of tests fell by half during the four-day Olympics opening ceremony and three-day Olympics closing ceremony holidays. If a special inspection system had been set up to keep the same number of people tested on weekdays during the four consecutive holidays and the three consecutive holidays, Tokyo's maximum daily number of positive cases would have been around 2,000 at most, and the infection would have entered a contraction period from August 3.

2. Even though the vaccination rate had progressed to more than 40% under the state of emergency, the overall infection rate  $\beta$  increased during the 10-day period following August 17, when the number of daily positive cases reached its peak. This was likely due to the spread of the highly infectious delta strain. Despite this, the number of daily positive cases reduced since the testing/isolation rate  $\gamma$  remained higher than the infection rate  $\beta$  due to the higher number of people screened.

3. According to analysis model 1, the mean value of

infection rate  $\beta$  decreased monotonically from 0.7 on August 27 to about 0.25 at the end of September. In analysis model 2, the mean value of  $\beta$  decreased from 0.65 to about 0.25. This decrease in  $\beta$  is thought to be mainly due to the subsequent rapid increase in vaccination rates, especially among the younger generation. The mRNA-based vaccine infection-prevention effects and the trend of vaccination rates in Tokyo indicate that vaccination reduced the infection rate to around 1/2 on September 10 and to 1/3 at the end of October. During this period, the daily number of positive cases decreased at a rate of about 1/2 per week, but this reduction rate could be achieved by the additional effect of the gradual decrease in the number of people tested maintaining the relationship  $\gamma \approx \beta + 0.1$ .

4. From the results of these analyses, it can be expected to achieve a society with coronas by controlling the number of people tested so that  $\gamma > \beta$  is maintained through vaccination and expansion of the possible number of people tested. When the vaccination rate reaches 80% or more, including among young people, if the breakthrough infection rate is less than about 0.3 under conditions of free social and economic activities with only infection-prevention measures such as wearing masks, disinfection, and hand washing when in proximity, it seems possible to restore pre-corona social and economic activities by establishing an immediate inspection system. In other words, immediate testing using free testing kits at schools, medical and welfare institutions, etc., and group testing once a week, if necessary, should be possible, and clusters of 10 or more people should never be generated. In addition, as is already the case in many developed countries, a system should be established so that the general public can receive free testing at pharmacies and other facilities as needed. It is also important to increase the vaccination rate up to more than 90%.

Japan's conventional strategy of reducing social and economic activities and suppressing infection by controlling the flow of people appears to be that of human beings who have been defeated by Covid-19 virus and are just staying at home and enduring. On the contrary, human beings have used science and technology to overcome the threats of nature and build a safe and secure society, and the way to proactively fight against COVID-19 virus using science and technology is to reduce the infection rate through vaccination and to establish a rapid inspection and isolation system to quickly find and isolate infected people. To stop the sixth wave of epidemics, it is more important to strengthen the front-line units of the coronal warfare rather than to expand the number of medical beds for the severely ill. The front-line forces

in the corona wars are the inspection and isolation personnel at public health centers. Based on this analytical study, the author believes that the following strategies can be used to win the sixth wave of coronas. First, during the period of spread of infection, it should not have consecutive weekends and holidays. In addition, during the critical period when infection spreads more than 2 times per week, it should be established a warfighting inspection system that can maintain the same number of inspections on weekends as on weekdays, with the cooperation of private inspection and medical institutions.

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