Respiratory syncytial virus outbreaks are predicted after the COVID-19 pandemic in Tokyo, Japan

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Running Head: RSV outbreaks after COVID-19 pandemic in Tokyo

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Abstract:

The nonpharmaceutical interventions (NPIs) on COVID-19 can impact current and future dynamics of respiratory syncytial virus infections (RSV). In Tokyo, RSV activity declined by 97.9% (95%CI: 94.8% - 99.2%) during NPIs. A longer period of NPIs could expand susceptible populations, enhancing the potential for larger RSV outbreaks after NPIs ends.

In response to COVID-19 pandemic, the Japanese government has adopted non-compulsory nonpharmaceutical interventions (NPIs), including public school closure from 02 March 2020 to 02 April 2020, emergency state from early April 2020 to 31 May 2020, international border controls, and the maintenance of “new lifestyle” until now. These measures may also reduce the transmission of other directly transmitted, respiratory infections and increase the susceptibilities during NPIs, e.g., respiratory syncytial virus (RSV)- one of the most important directly transmitted, viral respiratory diseases circulating in the population (1,2). A growing concern posed by the relaxation of NPIs after the pandemic, raises the possibility of an outbreak of these other infections, since the susceptible population has been accumulating as a result of NPI implementation (3). Here, we used the surveillance data on RSV infections in Tokyo to investigate the impact of NPIs on the current and future dynamics of RSV infections.

We collected weekly RSV cases in Tokyo from 1st week of 2016 to 53rd week of 2020 from Infectious Disease Surveillance Center, National Institute of Infectious Diseases. Annual population and birth were collected from Statistics of Tokyo (4,5). We consider NPIs in Tokyo started from 02 March 2020 and continued until the end of 2020, our study period.
We used interrupted time series analysis to examine the effect of NPIs on current RSV infections (6). We applied a quasi-Poisson regression model with a linear term for time to model long-term trends and a cyclic cubic B-Spline with three equally spaced knots for the week of the year to model seasonality (Model 1). We assumed the strengths of intervention remained the same during our study period and used a dummy variable for the intervention.

\[ Y_t \sim \text{quasi-Poisson} \]

\[ \log(E(Y_t)) = \beta_0 + \beta_1 \times \text{time}_t + \beta_2 \times \text{NPI}_t + \text{seasonality} \]

Model 1

Where, \( E(Y_t) \) is the expected RSV infection cases at week \( t \); \( \text{time}_t \) is a continuous variable indicating time in weeks of year, which is used to control for the long-term trend; \( \text{NPI}_t \) is a dummy variable indicating the before-NPIs period (coded 0) and the after-NPIs period (coded 1). \( \beta_1 \) is the change in RSV infection risk associated with a one-week increase to represent the trend before NPIs; \( \beta_2 \) is the level change following the NPIs, which can be described as the differences between the weekly RSV risk in the before-NPIs period and after-NPIs period and therefore represents the effects of the NPIs on RSV infection.

Next, we calculated transmission rate and generated forward simulation by using the time-series Susceptible-Infected-Recovered (TSIR) model based on RSV infection data from 2016 to 2019 (3,7):

\[ \ln \left( E[I_{t+1}] \right) = \ln(\beta_t) + \alpha \ln(I_t) + \ln(\bar{S} + Z_t) - \ln(N_t) \]

Model 2

where \( E[I_{t+1}] \) is the expected number of weekly infected individuals at \( \text{time}_{t+1} \); \( \beta_t \) are biweekly factors representing the transmission rate; \( \alpha \) represents the epidemic saturation and also a correction factor for switching from continuous to discrete time, and was fixed at 0.97 (3,8); \( \bar{S} \) is the estimated mean number of susceptible individuals in the population across the time-series; \( Z_t \)
describes the shape of the susceptible dynamics, which was specified by spline regression with 2.5 degrees freedom; $N_t$ is the total population size at $t$. This model was fitted using a quasi-Poisson regression with log link.

In order to estimate the reductions in transmission rate during NPIs in 2020, we generated forward simulation by assuming different reductions in transmission rate ranging from 0-90% with 10% intervals by using TSIR model and compared the predictions with the observed RSV infections in 2020 (3). The reduction in transmission rate which showed the lowest mean absolute error between the observations and predictions were used for the next simulation.

We then simulated forward until 2030 by assuming a one-year length of NPIs (02 March 2020 - 02 March 2021) with the reduced transmission rate. The RSV transmissibility after NPIs ends (02 March 2021) was assumed to remain the same as before NPIs (2016-2019). We used the average population and average birth rates between 2016 and 2020 and assumed a constant population and birth rate over the simulation period. We run the simulation for 40 years to remove transient dynamics (3). We also run the simulation by varying our assumptions on the lengths of NPIs and the reduction in transmission rate.

During the NPIs, RSV activity declined by 97.9% (95%CI: 94.8% - 99.2%) (i.e., $\beta_2$ obtained from Model 1, Figure 1), and its transmission rate reduced by 40%. By assuming a one-year period for NPIs (i.e., 02 Mar 2020 – 02 Mar 2021) with 40% reduction in RSV transmission rate, we found that a severe outbreak is likely to occur in 2022-2023 after NPIs has ended, which can be more than five times larger than previous outbreaks (Figure 2). Moreover, a longer NPI period and a larger reduction in transmission rate may increase the susceptibility and subsequently lead to a larger outbreak (Figure 3).
Our analysis showed that the NPIs for COVID-19 had limited the spread of RSV infections in Tokyo. A longer period of NPIs could expand susceptible populations, enhancing the potential for larger outbreaks once control measures were lifted. Similar findings were also reported in a recent study conducted in the US (3).

Our results need to be interpreted with cautions. First, an overestimation of the impact of NPIs on RSV transmission is likely, as the total number of RSV tests might have been impacted by the pandemic. However, such information is unavailable for current study. Second, our simulation did not account for possible imported cases, virus interferences, and possible changes in transmission rate over time, suggesting further uncertainty in our predictions.

Our results suggest that the healthcare systems may need to prepare for the possible large outbreaks of other infections in the future after relaxing NPIs, especially when the current healthcare systems have stretched beyond their capacity by the COVID-19 pandemic.

**Conflict of interest:** None to declare.

**References:**


**Figure legends:**

**Figure 1.** The time series of weekly RSV cases in Tokyo from 2016 to 2020.

*Black points are observed weekly RSV cases; red lines are predictions from ITS model; grey areas are the period for NPIs (02 Mar – the end of 2020)*

**Figure 2.** RSV simulation under the assumptions of a 40% reduction in transmission rate for one-year period for the NPIs in Tokyo

*Black points represent the RSV weekly cases from the surveillance data; grey areas represent the NPIs period assuming for a one-year of length; red line is the proportion infected (Infection
cases/ total population (I/N)); black line is proportion susceptible (susceptible population/total population (S/N)).

**Figure 3.** Respiratory syncytial virus simulation under different assumptions on the reduction of transmission rate and the lengths of NPI period ranging from 43 to 53 weeks starting from 10th week of 2020

*Surface plots show the change in peak incidence per capita (left) and peak susceptibility per capita (middle) relative to pre-2020 maxima. The right panel show the timing of peak incidence.*
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