

## Title: Reconstructing susceptibility against chickenpox: A mathematical modelling study

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In Japan, routine two-dose immunization against varicella has been conducted among children at ages of 12 and 36 months since 2014, and the vaccination coverage has reached around 90%. To understand the impact of routine varicella vaccination, we reconstructed the epidemiological dynamics of varicella in Japan. Moreover, public health and social measures (PHSMs) targeting the coronavirus disease 2019 (COVID-19) pandemic have potentially affected the epidemiological dynamics of endemic infectious diseases. In this study, we investigated the impact of PHSMs for COVID-19, with a particular focus on varicella dynamics in Japan. Epidemiological and demographic datasets over the past three decades were analyzed to reconstruct the number of susceptible individuals by age and year. To estimate the annual risk of varicella infection, we fitted a balance equation model to the annual number of cases from 1990 to 2019. Using parameter estimates, we reconstructed varicella dynamics starting from 1990 and modeled future dynamics until 2033. Moreover, we adopted the susceptible-infectious-recovered type of mathematical model to reconstruct the epidemiological dynamics of varicella from Jan. 2010 to Sep. 2021. We analyzed epidemiological and demographic data and estimated the within-year and multi-year component of the force of infection and the biases associated with reporting and ascertainment in three periods: pre-vaccination (Jan. 2010-Dec. 2014), pre-pandemic vaccination (Jan. 2015-Mar. 2020) and during the COVID-19 pandemic (Apr. 2020-Sep. 2021).

Overall varicella incidence declined over time and the annual risk of infection among children younger than 10 years old decreased monotonically starting in 2014. Conversely, varicella incidence among teenagers (age 10 to 14 years) has increased each year since 2014. A substantial number of unvaccinated individuals born before the routine immunization era remained susceptible and aged without contracting varicella, while the annual risk of infection among teenagers aged 10 to 14 years increased starting in 2011 despite gradual expansion of varicella vaccine coverage. The number of susceptible individuals decreased over time in all age groups. Modeling indicated that susceptibility rates among pre-school children aged 1 to 4 years will remain low.

In the COVID-19 related analysis, by using the estimated parameter values, we reconstructed and predicted the varicella dynamics from 2010 to 2027. Although the varicella incidence dropped drastically during the COVID-19 pandemic, the change in susceptible dynamics was minimal; the number of susceptible individuals was almost stable.

Routine varicella vaccination has successfully reduced infections in pre-school and early primary school age children, but has also resulted in increased infection rates among adolescents. This temporary increase was caused both by the increased age of susceptible individuals and increased transmission risk among adolescents resulting from the dynamic nature of varicella transmission. Monitoring susceptibility among adolescents will be important to prevent outbreaks over the next decade. In addition, our prediction showed that the risk of a major outbreak in the post-pandemic era may be relatively small. However, uncertainties, including age-related susceptibility and travel-related cases, exist and careful monitoring would be required to prepare for future varicella outbreaks.

### Biography

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