

# COVID-19の集団免疫レベルの低下と 再流行時期の予測

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東京財団政策研究所「健康危機に対するヘルス・レジリエンスの構築に関する研究」プログラムメンバー

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- 2022年11月10日現在，国内の新型コロナウイルス感染症の感染報告者数は2200万人を超え，ワクチンの累計接種回数は3億回を超えている  
(<https://vdata.nikkei.com/newsgraphics/coronavirus-japan-vaccine-status/>) .
- 相次ぐ流行の波とワクチン接種により国内の集団免疫レベルは高まっていると考えられる．数理モデルを用いてそのレベルを推計し，数値化することは，今後の流行動態を予測し，新たな波に備える上で重要である．

# 概要

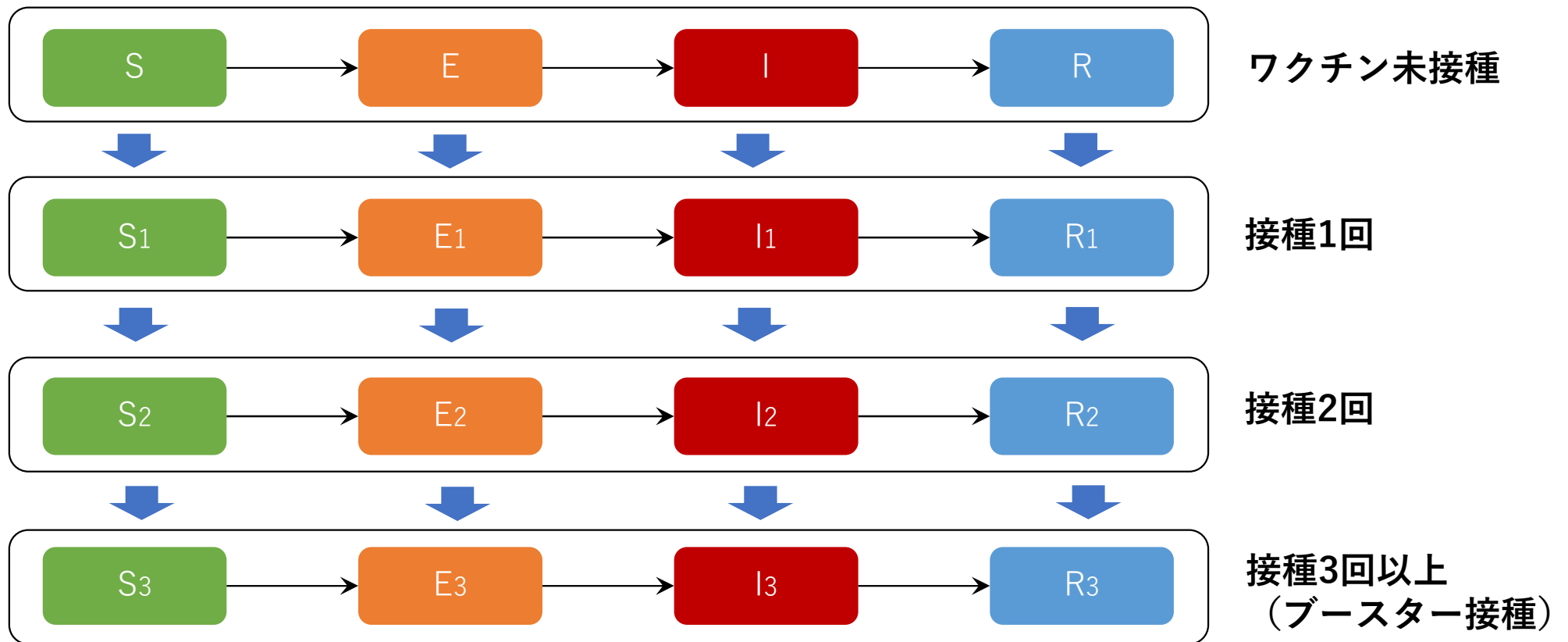
- 数理モデル（SEIRモデル）を用いて、主要都道府県の集団免疫レベルの推計を行った。
- 第6波、第7波を経て国内の集団免疫レベルは一時的に増加したが、現在は減少傾向にある。特に、ワクチンに由来する免疫の減少傾向が著しいため、感染を経験していない人を中心に追加接種を進めることが今後の流行に備える上で重要であると考えられる。

# モデル

- SEIRモデル（S：未感染，E：潜伏期，I：感染，R：回復）
- 考慮した要素
  - ワクチン接種（ブースター接種を含む）
  - 免疫の減衰
- 考慮していない要素
  - 再感染
  - 季節性，行動変容，ウイルス変異（推計では非明示的に考慮）
  - 都道府県間の相互作用

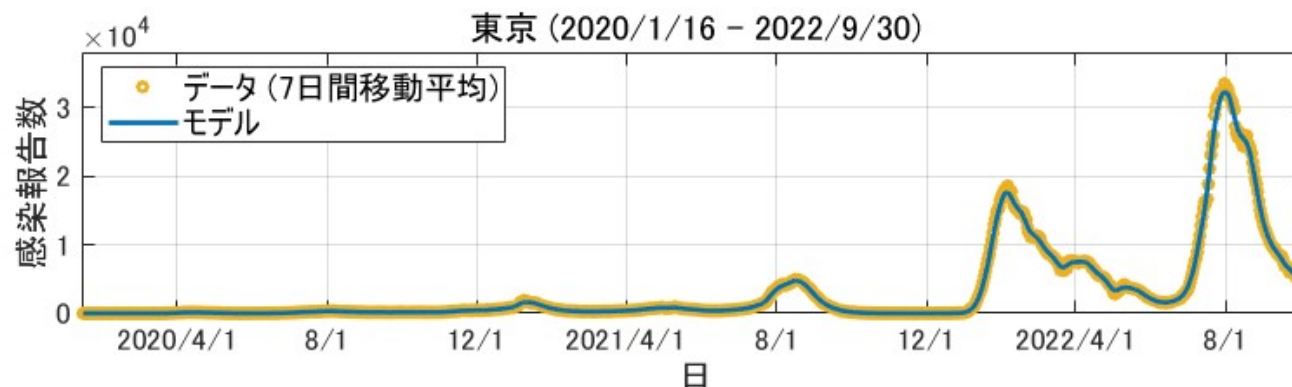
# モデル

- SEIRモデル (S: 未感染, E: 潜伏期, I: 感染, R: 回復)



# 利用したデータ

- **感染報告数** (NHK 特設サイト, <https://www3.nhk.or.jp/news/special/coronavirus/data/>)



感染率 (実効再生産数) を推計

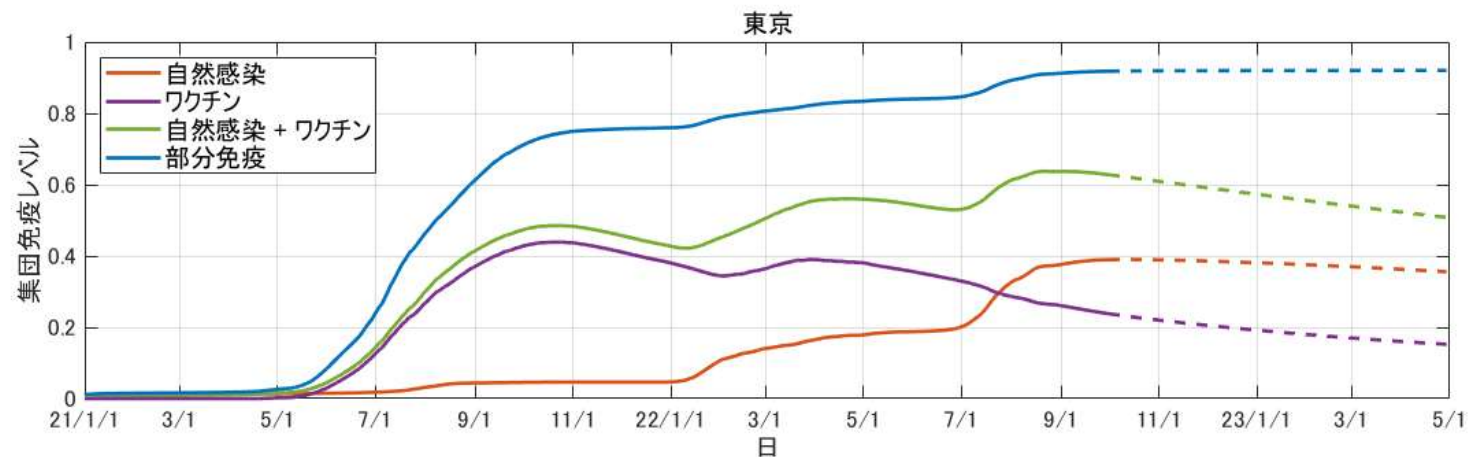
- **ワクチン接種回数** (デジタル庁 VRS, <https://info.vrs.digital.go.jp/>)



ワクチン接種率を推計

# グラフ

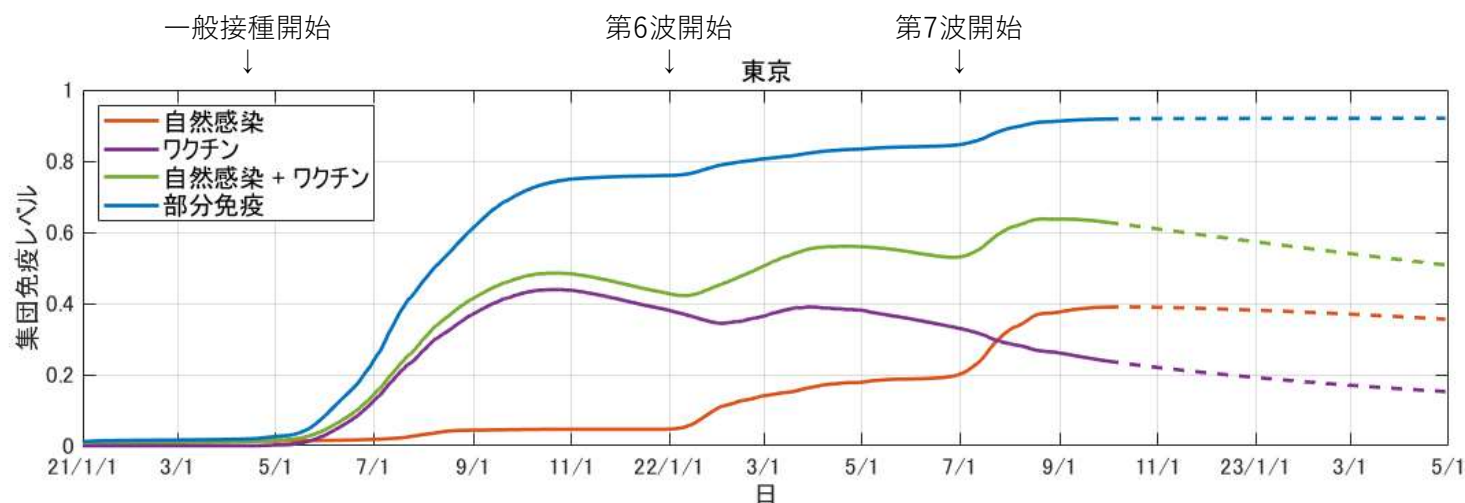
- 実線：2022年9月30日までの推計 点線：2023年5月1日までの予測



- 各曲線の意味

- **自然感染**：自然感染により免疫を獲得した人の割合（ブレイクスルー感染含む）
- **ワクチン**：ワクチン接種により免疫を獲得した人の割合（未感染に限る）
- **自然感染 + ワクチン**：上の2つの和
- **部分免疫**：自然感染かワクチン接種のいずれかあるいは両方の経験がある人の割合

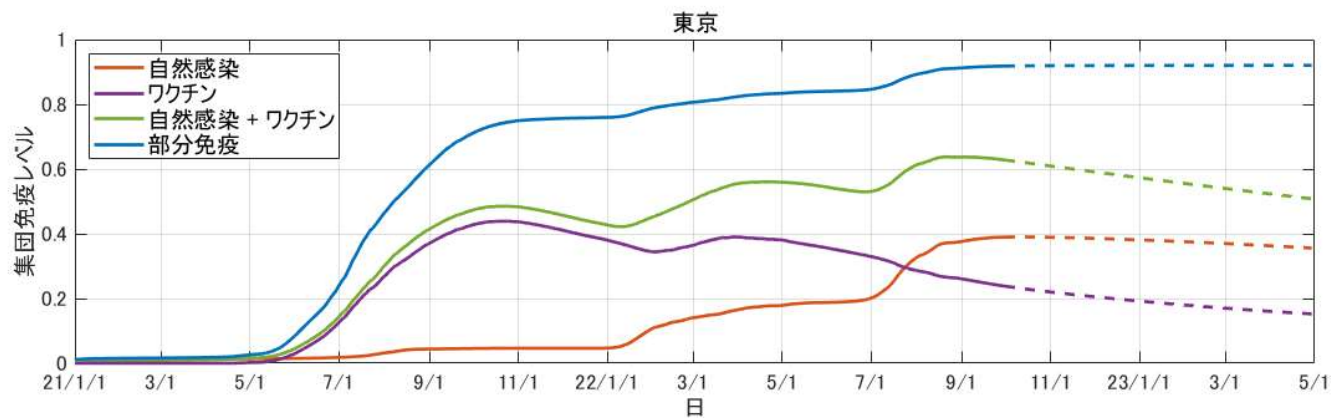
# 東京の推計結果



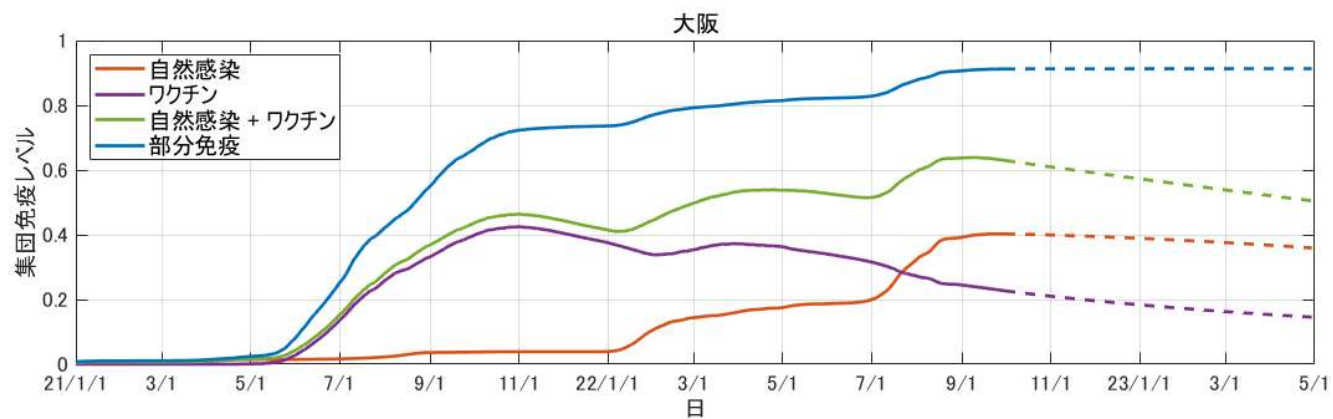
- **自然感染**：第6波，第7波のタイミングで大きく上昇
- **ワクチン**：一般接種を開始した2021年に上昇したが，現在は減少（ピーク時の半分程度）
- **自然感染 + ワクチン**：減少傾向．免疫の減衰を考慮しているため，**部分免疫**よりも実態に近いと考えられる．第6波，第7波はいずれもこの曲線が減少傾向のときに起こっており，この値が低下したタイミングで第8波が起ると予想できる．



# 主要都道府県の比較

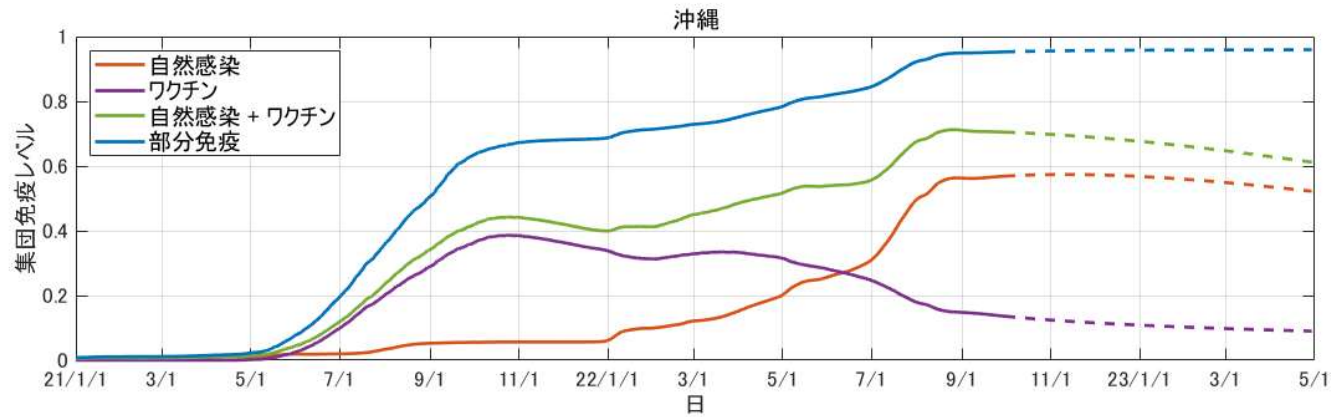


自然感染 > ワクチン

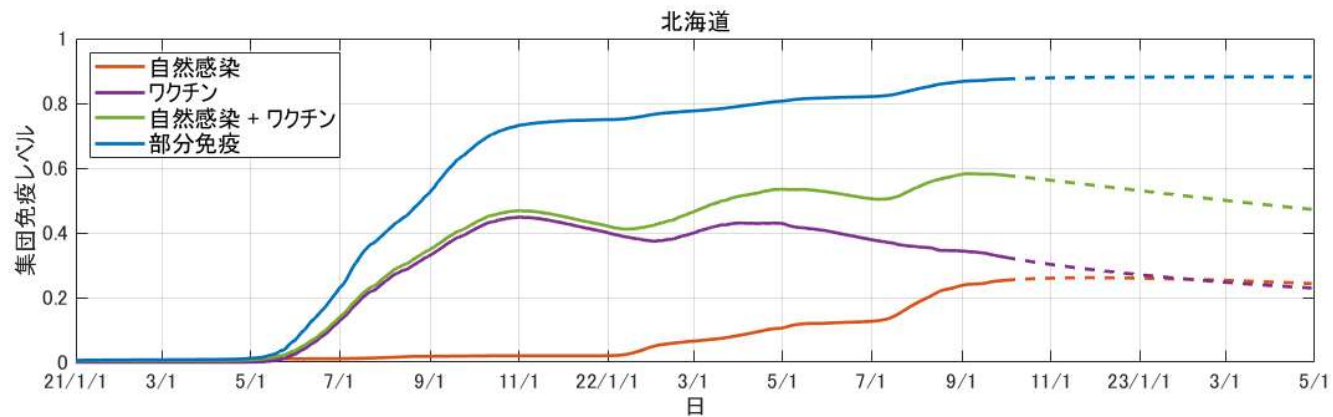


自然感染 > ワクチン

# 主要都道府県の比較



自然感染 ≫ ワクチン



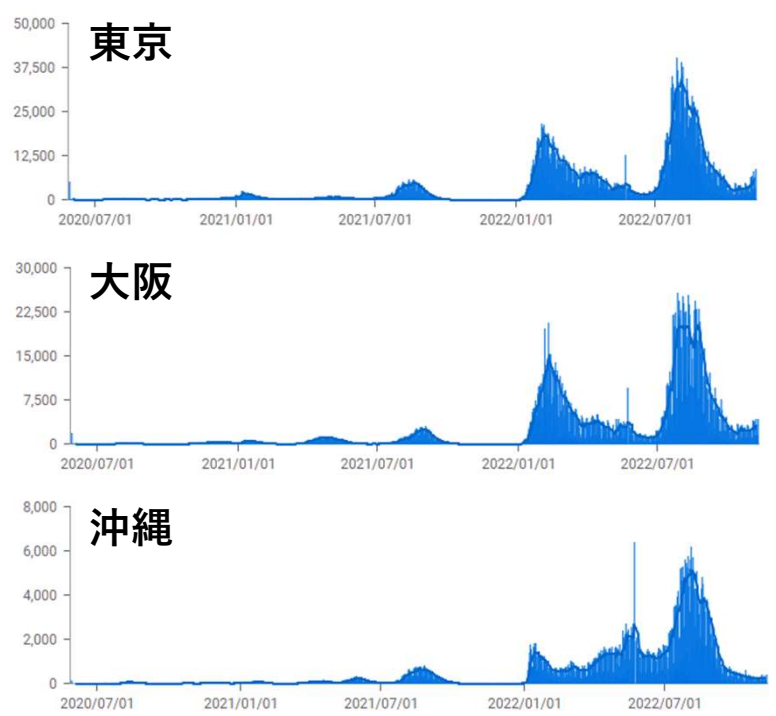
ワクチン > 自然感染

# 考察

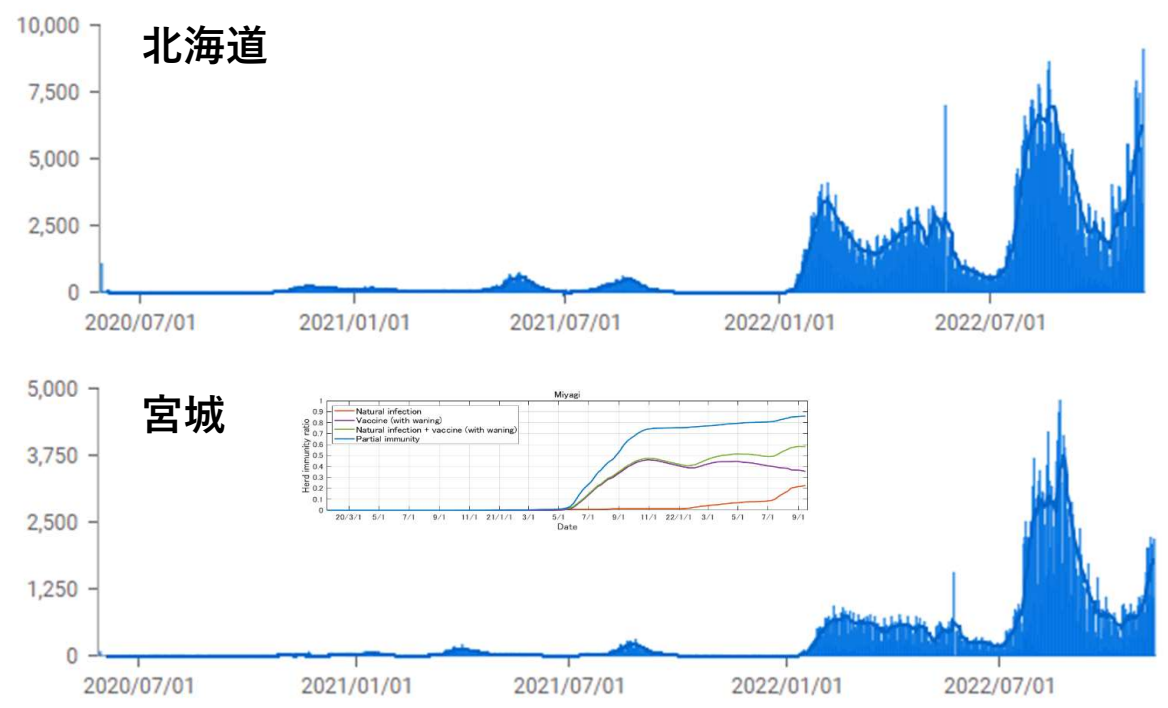
- ワクチン > 自然感染 の地域では第8波が早く起こる？

2022年11月8日までの感染報告数 (JHU CSSE COVID-19 Data, Google)

## 自然感染 > ワクチン



## ワクチン > 自然感染

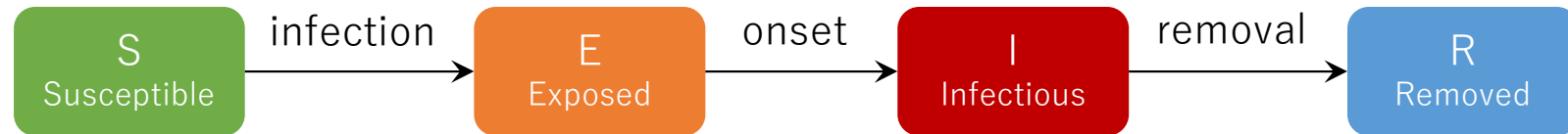


# まとめ

- 今回対象とした全ての都道府県で集団免疫レベルは減少傾向にある。特に、沖縄以外では、遅くとも2023年の春先までに第7波初期の水準まで集団免疫レベルが低下するため、第8波が起こる可能性がある（一部地域では既に起こっている）。
- 特にワクチンに由来する免疫の減少傾向が著しいため、自然感染を経験していない人を中心にワクチンの追加接種を進めることが効果的であると考えられる。
- 本稿のモデルは免疫の減衰を考慮できる点で現実的と言えるが、行動変容や季節性などによる個人の社会活動の時間変化（transient collective immunity）を考慮していない。そのため、集団免疫の過大評価や流行の過小評価の可能性があり、注意が必要である。

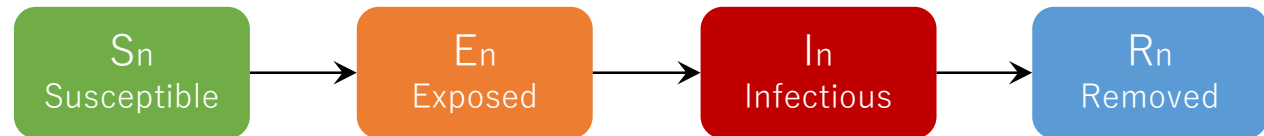
# Model (1/4)

- **SEIR model**



- We add more groups according to the vaccination times:

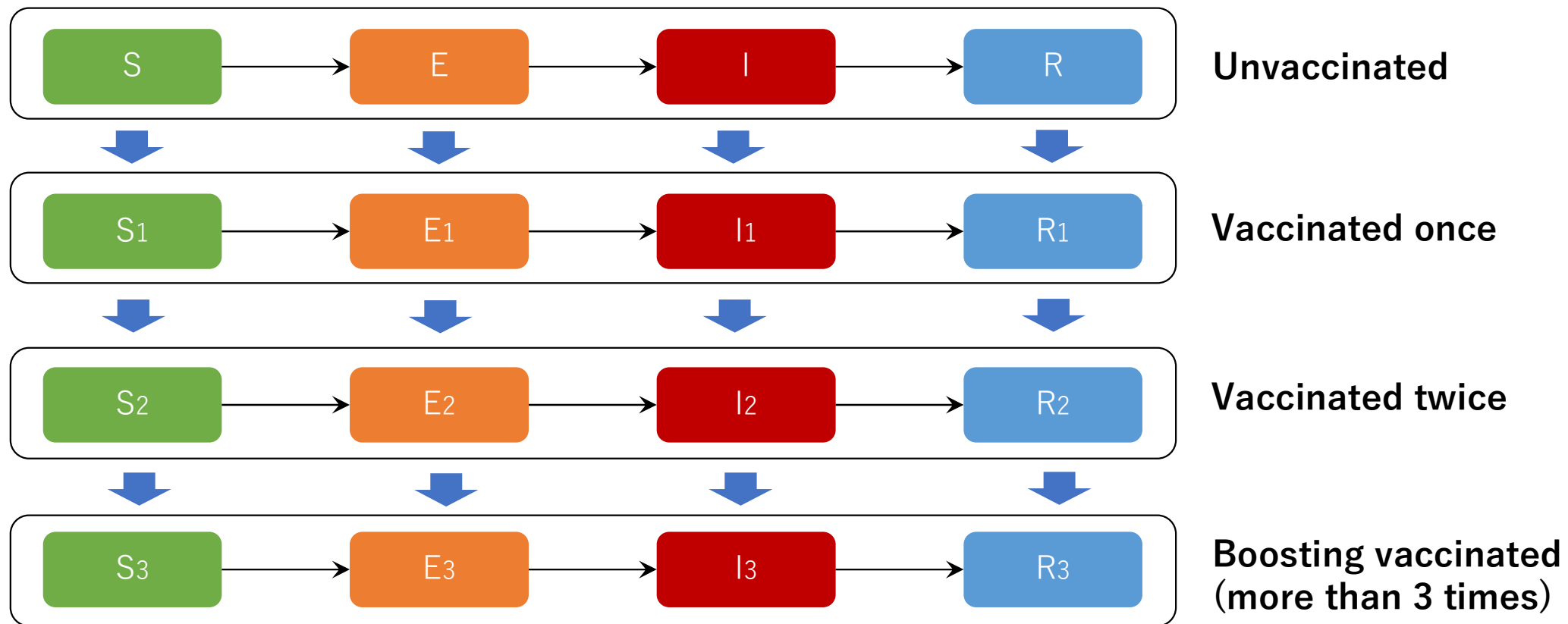
**Vaccinated n times**



$n=1,2,3$ . Here,  $n=3$  means the boosting shots and includes vaccinated four times.

# Model (2/4)

- SEIR model



# Model (3/4)

- SEIR model

## Unvaccinated

$$S'(t) = -\lambda(t)S(t) - v_1S(t),$$

$$E'(t) = \lambda(t)S(t) - (\varepsilon + v_1)E(t),$$

$$I'(t) = \varepsilon E(t) - (\gamma + v_1)I(t),$$

$$R'(t) = \gamma I(t) - v_1R(t).$$

## Vaccinated once

$$S'_1(t) = v_1S(t) - \sigma\lambda(t)S_1(t) - v_2S_1(t),$$

$$E'_1(t) = v_1E(t) + \sigma\lambda(t)S_1(t) - (\varepsilon + v_2)E_1(t),$$

$$I'_1(t) = v_1I(t) + \varepsilon E_1(t) - (\gamma + v_2)I_1(t),$$

$$R'_1(t) = v_1R(t) + \gamma I_1(t) - v_2R_1(t).$$

$t$	Time (day)
$\lambda(t)$	Force of infection
$\varepsilon$	Transition rate from E to I
$\gamma$	Removal rate
$v_n$	Vaccination rate for n-th
$1 - \sigma$	Efficacy of the 1st vaccination
$\beta$	Transmission coefficient

$$\lambda(t) = \beta \left[ I(t) + I_1(t) + \sum_{n=2}^3 \int_0^{\infty} I_n(t, a) da \right].$$

# Model (4/4)

- SEIR model

Vaccinated more than twice (n=2,3)

$$S_n(t, 0) = \begin{cases} v_2 S_1(t), & n = 2, \\ v_3 \int_T^\infty S_2(t, a) da + v_4 \int_T^\infty S_3(t, a) da, & n = 3, \end{cases}$$

$$E_n(t, 0) = \begin{cases} v_2 E_1(t), & n = 2, \\ v_3 \int_T^\infty E_2(t, a) da + v_4 \int_T^\infty E_3(t, a) da, & n = 3, \end{cases}$$

$$I_n(t, 0) = \begin{cases} v_2 I_1(t), & n = 2, \\ v_3 \int_T^\infty I_2(t, a) da + v_4 \int_T^\infty I_3(t, a) da, & n = 3, \end{cases}$$

$$R_n(t, 0) = \begin{cases} v_2 R_1(t), & n = 2, \\ v_3 \int_T^\infty R_2(t, a) da + v_4 \int_T^\infty R_3(t, a) da, & n = 3, \end{cases}$$

$$\left( \frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) S_n(t, a) = -p(a)\lambda(t)S_n(t, a) - q_n(a)S_n(t, a),$$

$$\left( \frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) E_n(t, a) = p(a)\lambda(t)S_n(t, a) - [\varepsilon + q_n(a)]E_n(t, a),$$

$$\left( \frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) I_n(t, a) = \varepsilon E_n(t, a) - [\gamma + q_n(a)]I_n(t, a),$$

$$\left( \frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) R_n(t, a) = \gamma I_n(t, a) - q_n(a)R_n(t, a),$$

$$q_n(a) = \begin{cases} 0, & a < T, \\ v_{n+1}, & \text{otherwise.} \end{cases}$$

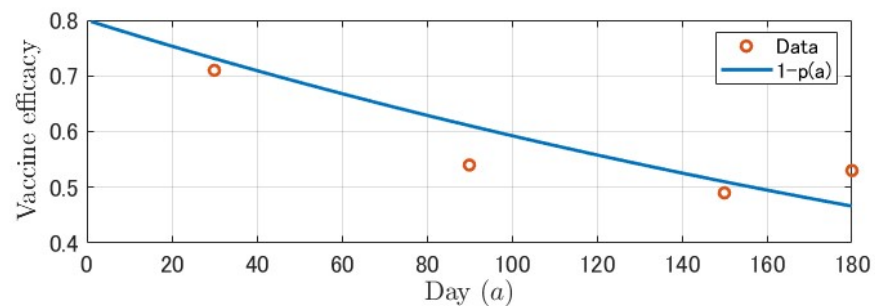
$a$	Vaccination age (day)
$T$	Vaccination interval by the boosting shot

$1 - p(a)$	Age-dependent vaccine efficacy
$q_n(a)$	Age-dependent vaccination rate for n-th



# Parameter setting (1/4)

- $\varepsilon = 0.2$  : the average incubation period  $1/\varepsilon = 5$  days (Lauer et al. 2020)
- $\gamma = 0.1$  : the average infectious period  $1/\gamma = 10$  days (Byrne et al. 2020)
- $\sigma = 0.54$  : the efficacy of the first vaccination is  $1 - \sigma = 0.46$  (NIID 2022)
- $T = 180$  days (before 2022/5/25) and **150** days (after 2022/5/25)
- $1 - p(a) = 0.8e^{-0.003a}$  : estimated using the data in (NIID 2022)



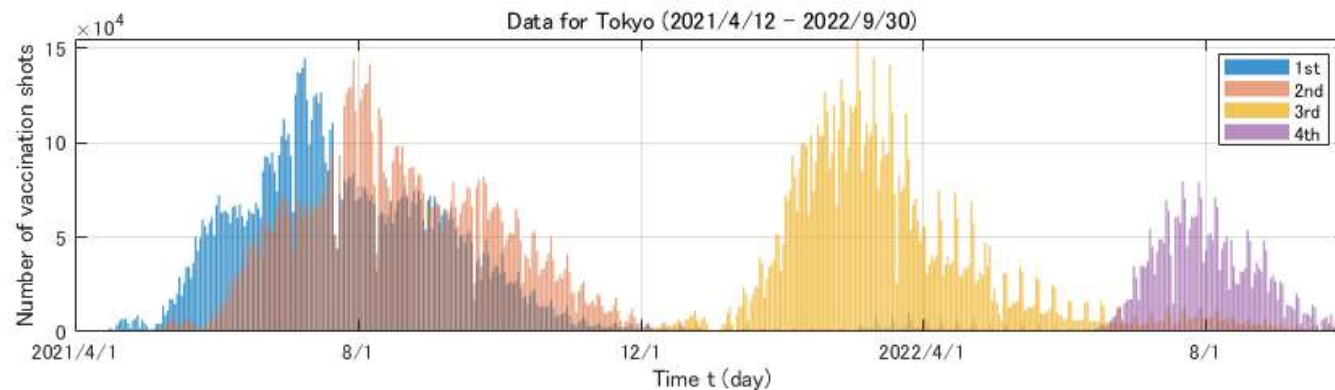
# Parameter setting (2/4)

- Vaccination rate

$$v_1(t) = \frac{(\text{number of the first vaccination at time } t)}{[S(t) + E(t) + I(t) + R(t)] \times N}.$$

$$v_n(t) = \begin{cases} \frac{(\text{number of the second vaccination at time } t)}{[S_1(t) + E_1(t) + I_1(t) + R_1(t)] \times N}, & n = 2, \\ \frac{(\text{number of the } n\text{-th vaccination at time } t)}{\int_T^\infty [S_{n-1}(t, a) + E_{n-1}(t, a) + I_{n-1}(t, a) + R_{n-1}(t, a)] da \times N}, & n \geq 3. \end{cases}$$

<https://info.vrs.digital.go.jp/opendata/>



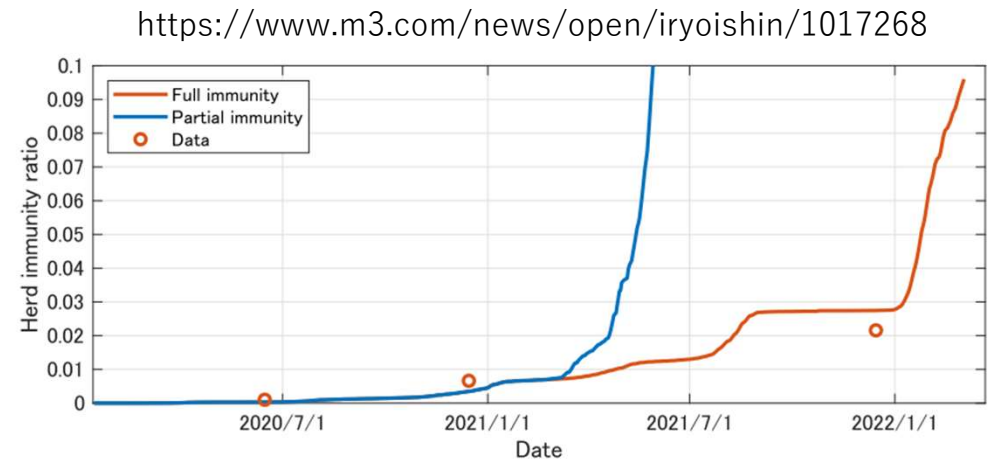
# Parameter setting (3/4)

- To estimate the transmission coefficient  $\beta$ , we fit

$$Y(t) := (\text{detection rate } \delta) \\ \times (\text{newly removed } \gamma \left[ I(t) + I_1(t) + \int_0^\infty I_2(t, a) da \right]) \\ \times (\text{total population } N),$$

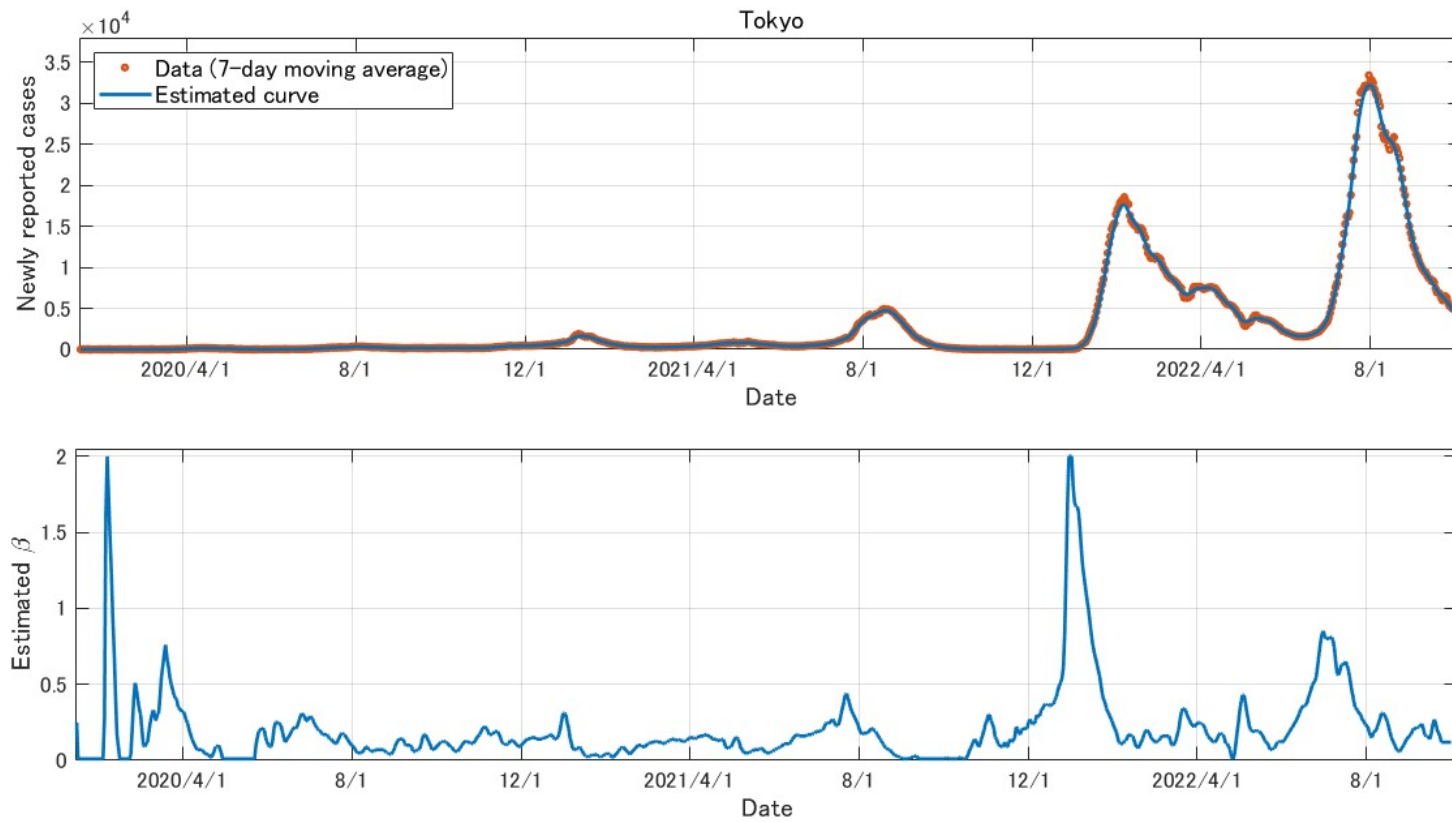
to the actual data of reported cases.

- $\delta = 0.5$  : estimated from the data.



# Parameter setting (4/4)

- Estimation of  $\beta$  (estimated epidemic curve)



# Estimation of the herd immunity level

- We will plot four kinds of curves:

- **Natural infection**  $\sum_{n=0}^3 M_n(t)$ : proportion of individuals who have been immunized by natural infection, where

$$M_0(t) = E(t) + I(t) + R(t), \quad M_1(t) = E_1(t) + I_1(t) + R_1(t),$$

$$M_n(t) = \int_0^\infty [E_n(t, a) + I_n(t, a) + R_n(t, a)] da, \quad n = 2, 3.$$

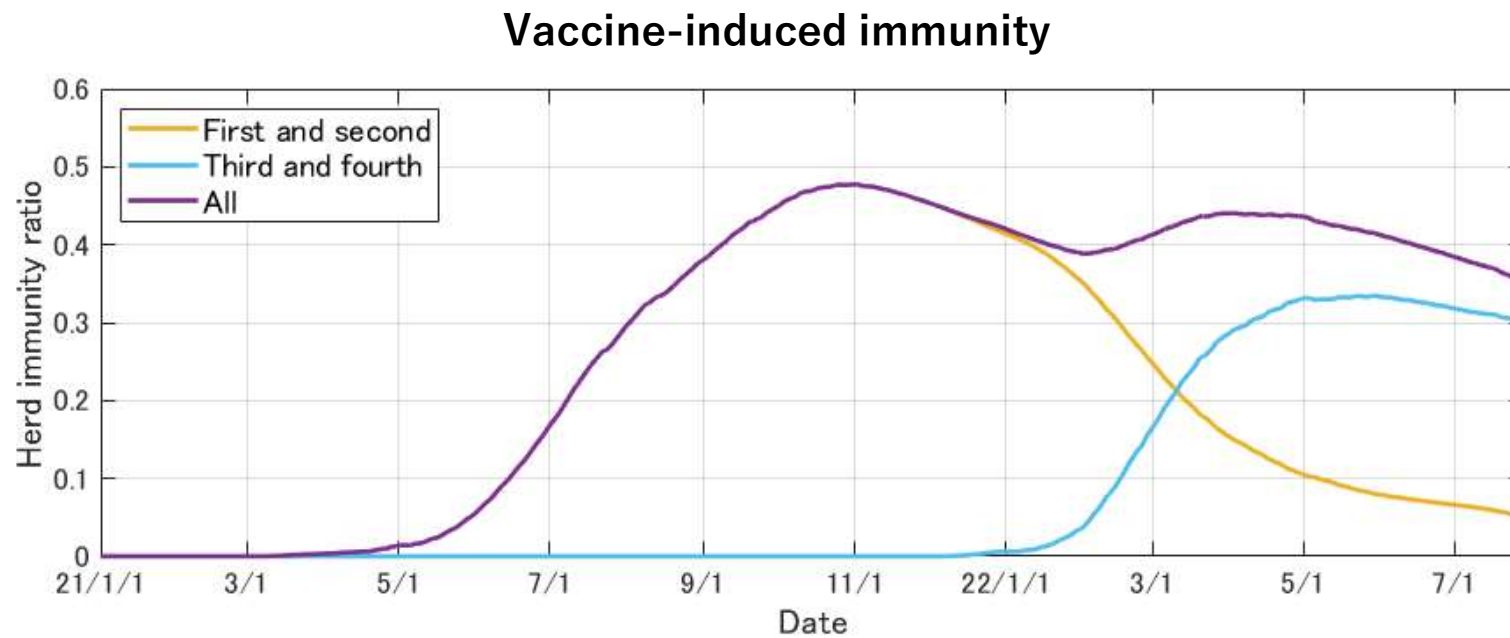
- **Vaccine**  $(1 - \sigma)S_1(t) + \sum_{n=2}^3 \int_0^\infty [1 - p(a)]S_n(t, a) da$ : proportion of individuals who have been immunized by vaccination.

- **Natural infection + Vaccine**: sum of the above two functions.

- **Partial immunity**  $1 - S(t)$ : proportion of individuals who have been immunized.

# In the early stage of the 7th wave (2/4)

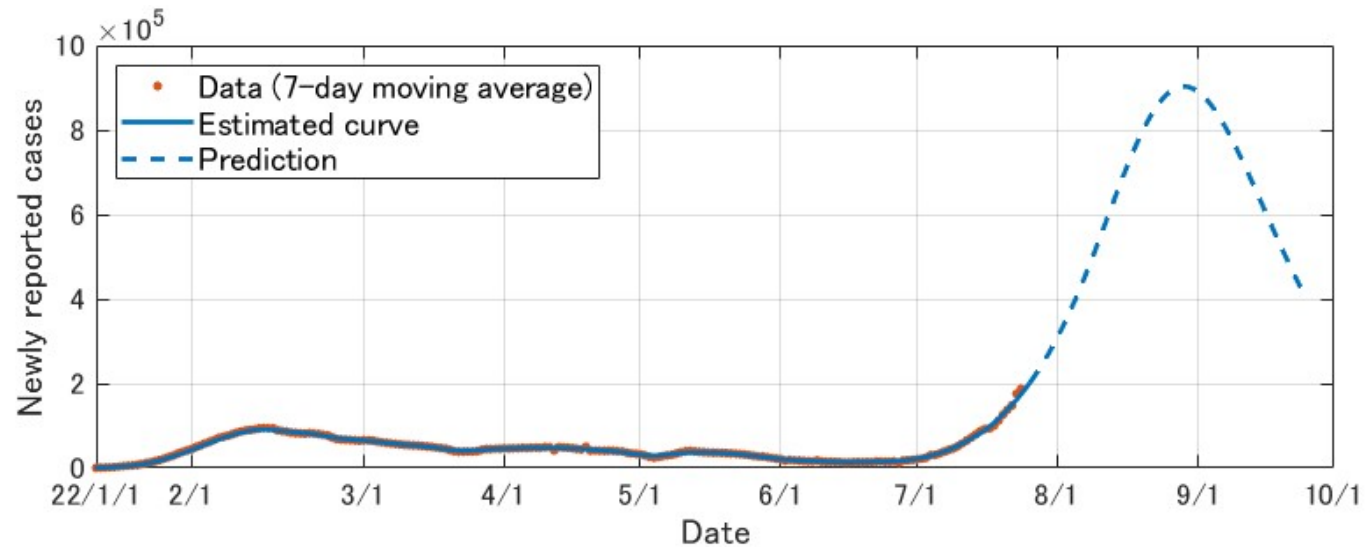
- For Japan (2020/1/14 – 2022/7/25)



- The herd immunity induced by vaccine has decreased.

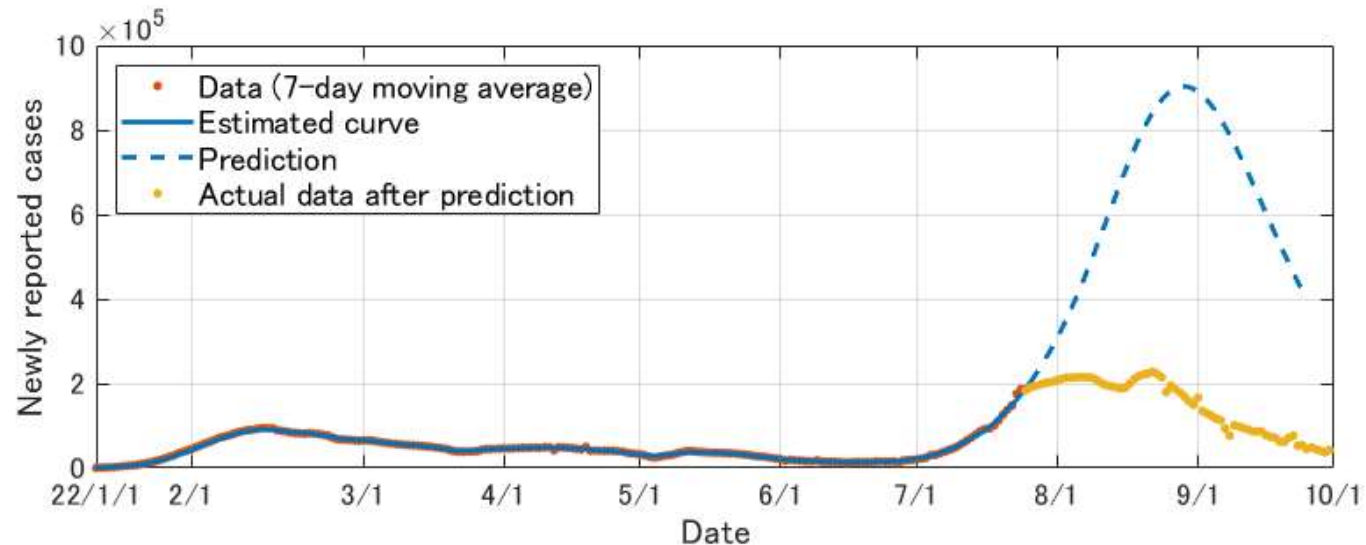
# In the early stage of the 7th wave (3/4)

- Prediction as of July 2022 (using the last 1 week data)



# In the early stage of the 7th wave (4/4)

- Prediction as of July 2022 (using the last 1 week data)



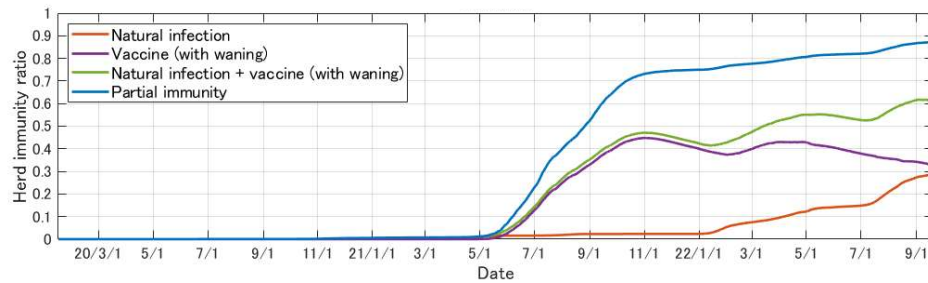
- Possible causes of overestimation:
  - well-mixed modeling in the whole Japanese population
  - transient collective immunity (behavior change, seasonality)



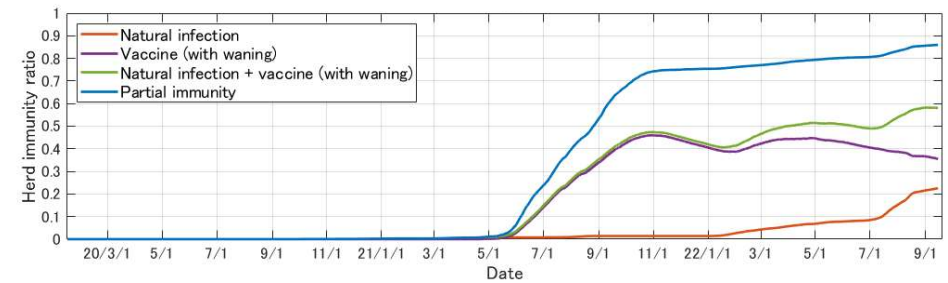
# After the 7th wave (1/5)

- For main 12 prefectures (2020/1/14 – 2022/9/14)

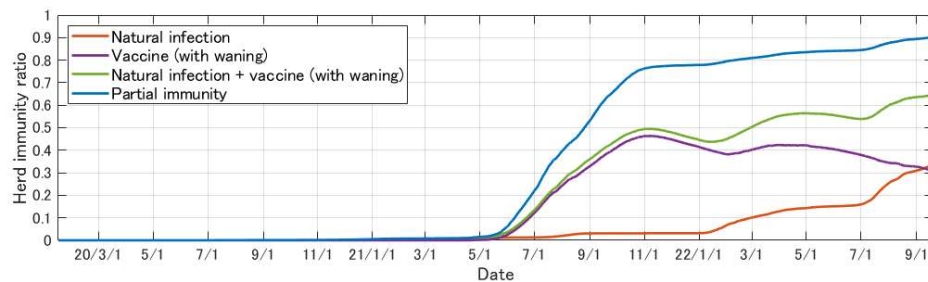
## Hokkaido



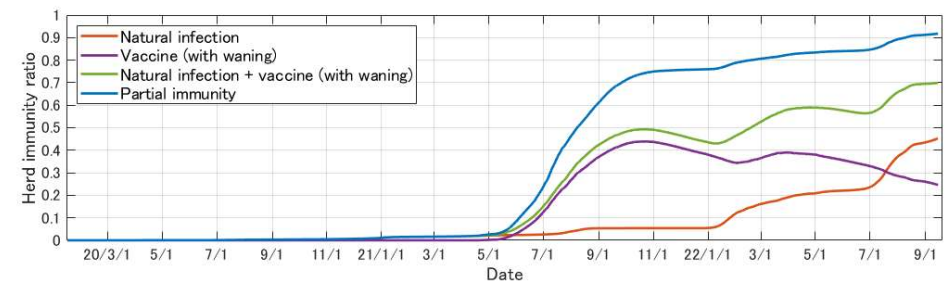
## Miyagi



## Saitama



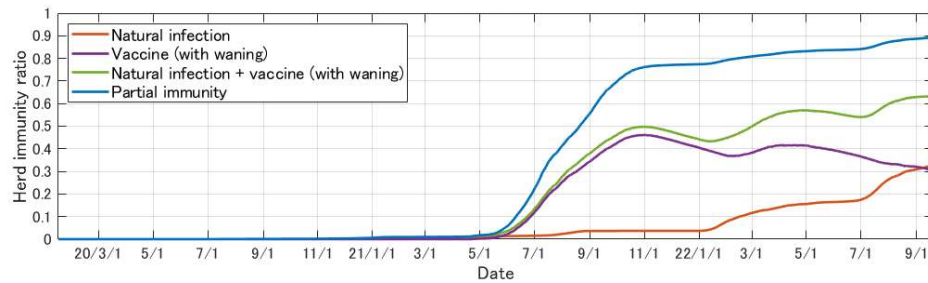
## Tokyo



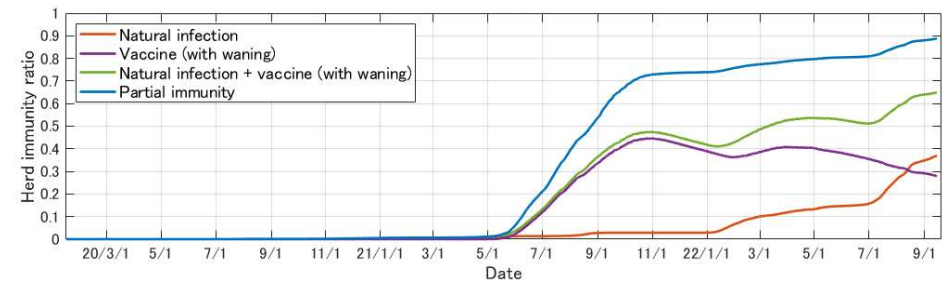
# After the 7th wave (2/5)

- For main 12 prefectures (2020/1/14 – 2022/9/14)

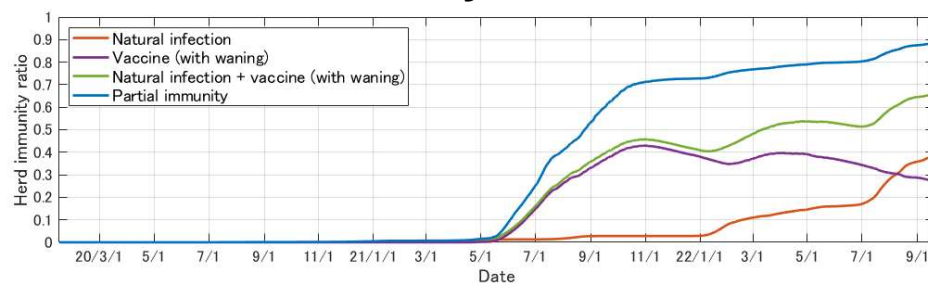
## Kanagawa



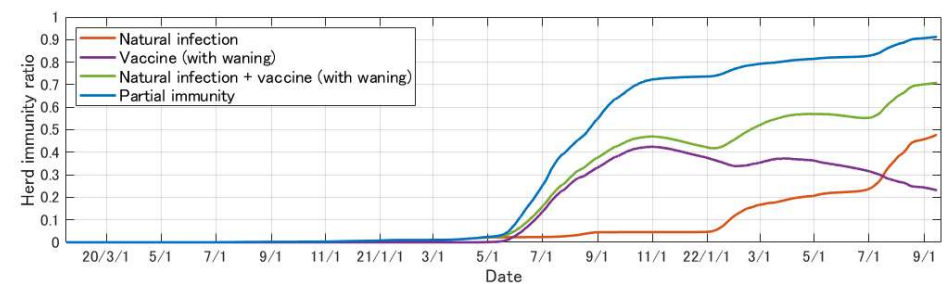
## Aichi



## Kyoto

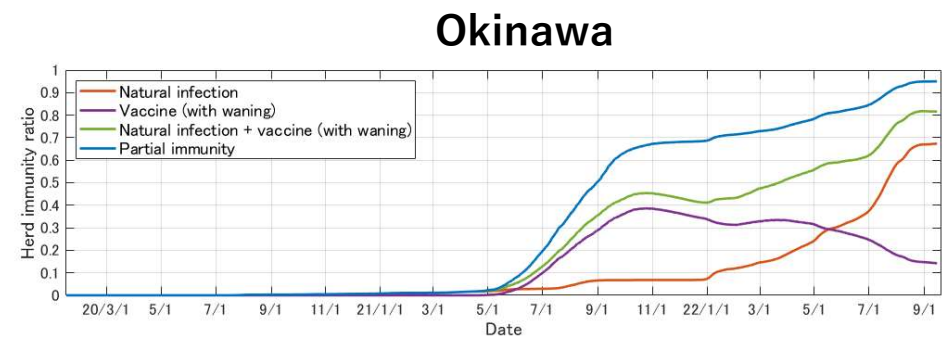
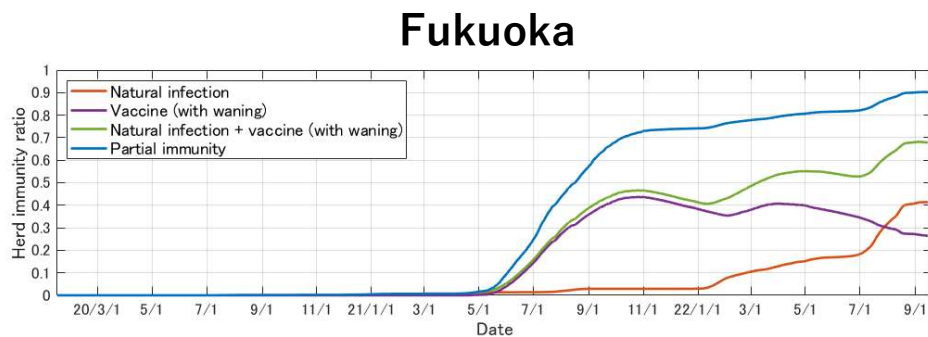
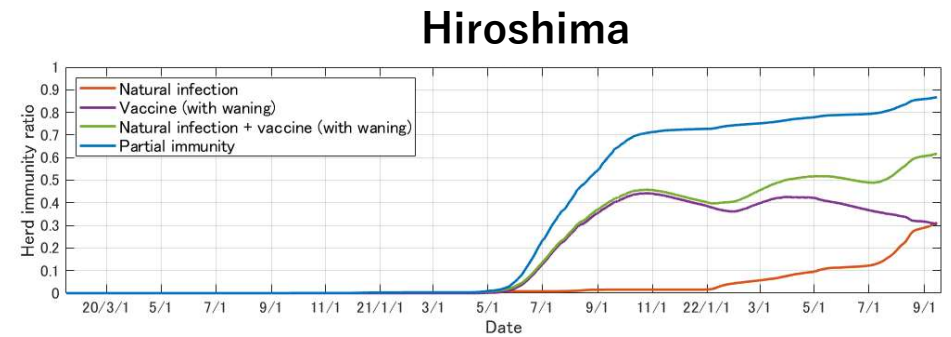
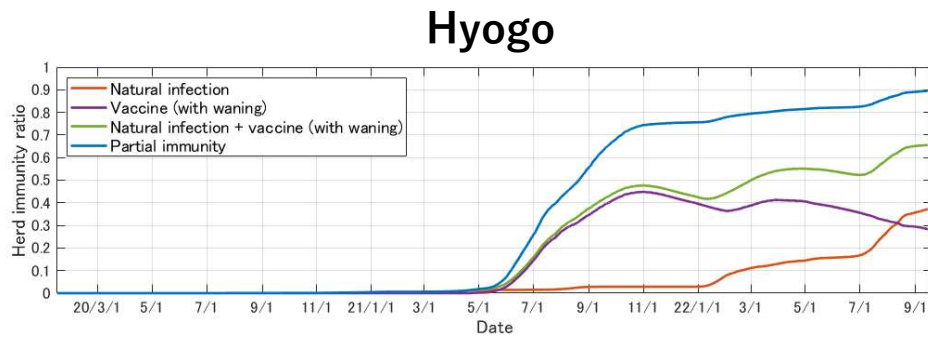


## Osaka



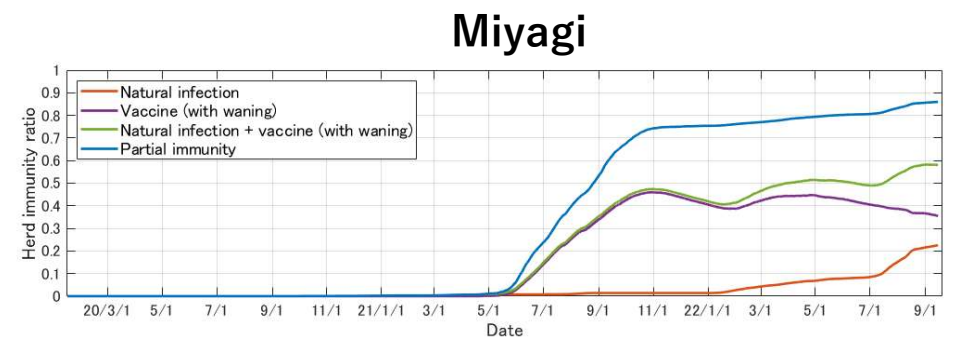
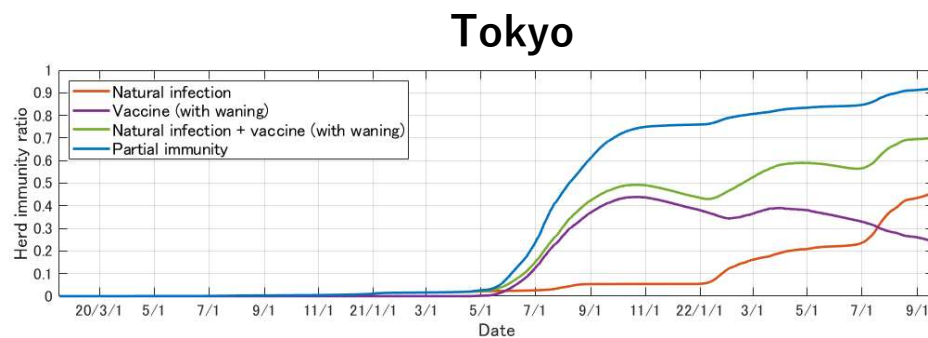
# After the 7th wave (3/5)

- For main 12 prefectures (2020/1/14 – 2022/9/14)



# After the 7th wave (4/5)

- The herd immunity level has steadily increased in all prefectures.
- In Tokyo, Osaka and Okinawa, the **immunity by natural infection** greatly exceeds the **immunity by vaccine**. On the other hand, in Hokkaido and Miyagi, the **immunity by vaccine** exceeds the **immunity by natural infection**. Will the next wave arrive earlier in Hokkaido and Miyagi?



# After the 7th wave (5/5)

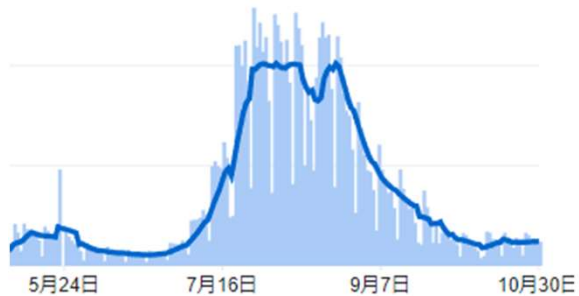
- The latest reported cases (JHU CSSE COVID-19 Data, Google)

**Natural infection > Vaccine**

**Tokyo**



**Osaka**

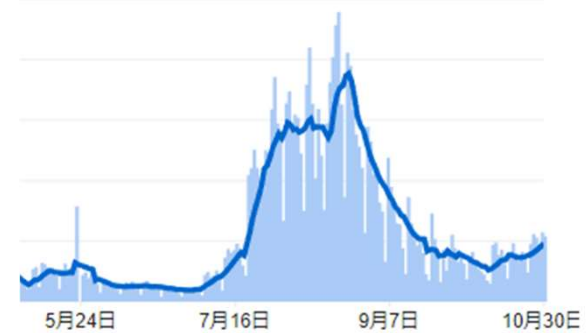


**Natural infection < Vaccine**

**Hokkaido**



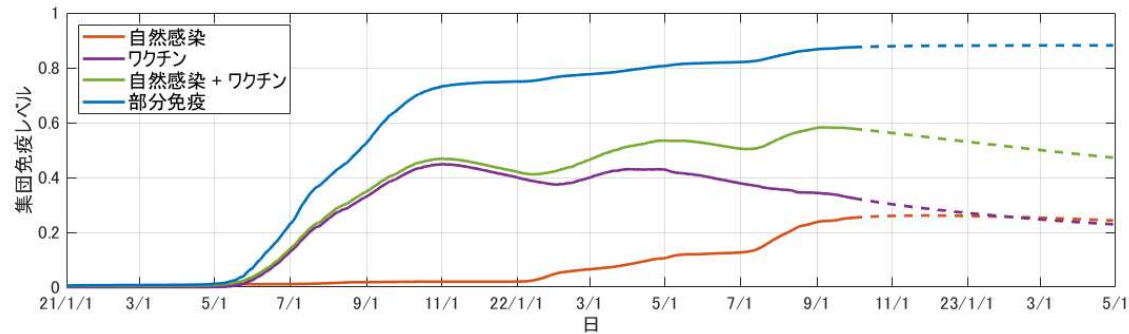
**Miyagi**



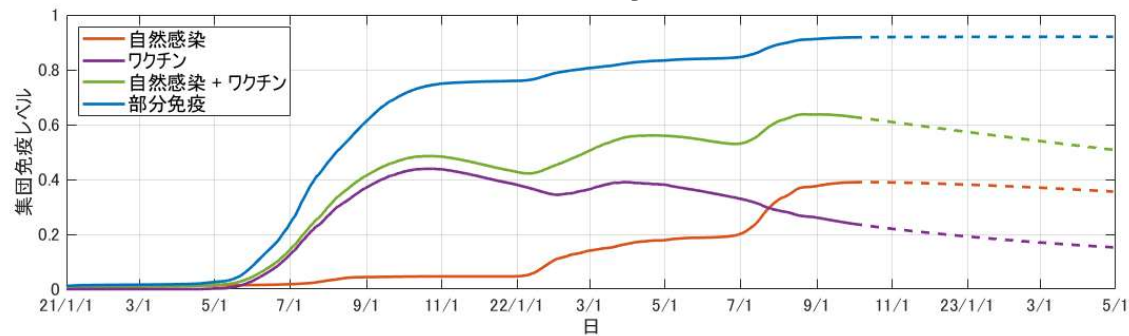
# Prediction of the next wave

- For main 5 prefectures (2021/1/1 – 2023/5/1)

## Hokkaido



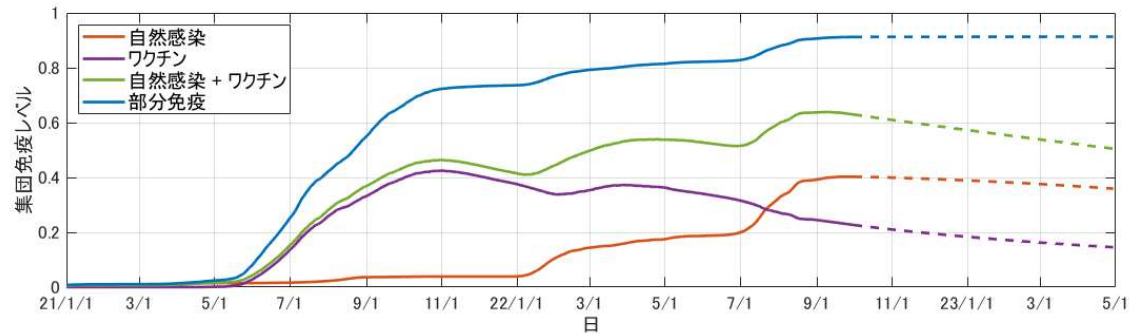
## Tokyo



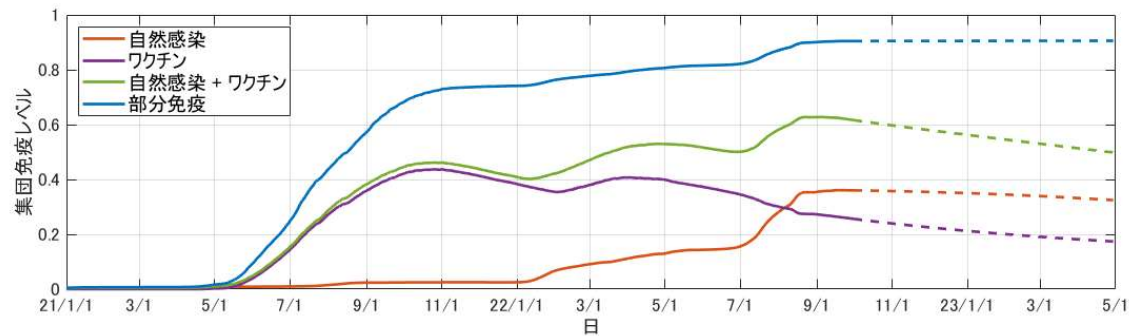
# Prediction of the next wave

- For main 5 prefectures (2021/1/1 – 2023/5/1)

## Osaka



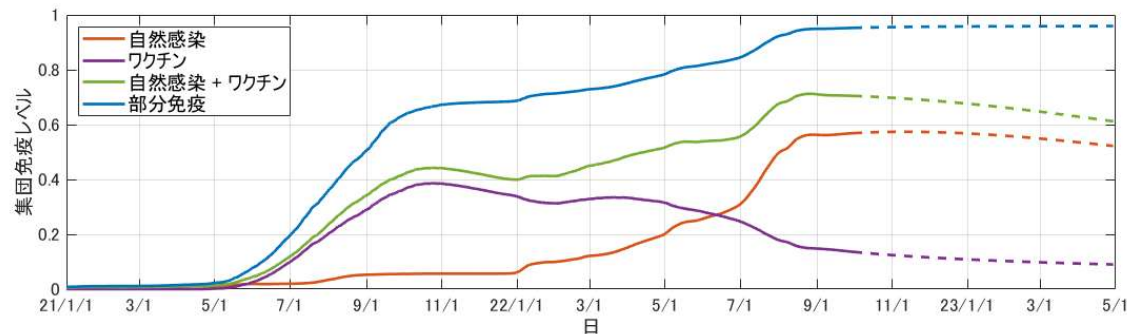
## Fukuoka



# Prediction of the next wave

- For main 5 prefectures (2021/1/1 – 2023/5/1)

## Okinawa



- In four prefectures except Okinawa, the herd immunity ratio could decrease to the level at the pre-7th wave before the next spring.



# Summary

- Using an age-structured model, we have kept working on the estimation of the herd-immunity level for COVID-19 in Japan.
- The herd-immunity level has steadily increased in most of prefectures after the 7th wave. However, the immunity will wane and the next wave could occur when it decreases to a low level.
- In some prefectures such as Hokkaido and Miyagi, the vaccine-induced immunity is larger than the infection-induced immunity. The next wave may come earlier in such prefectures.

# Limitations

- The following factors are not considered in the model:
  - Interaction between different prefectures
  - Virus mutation and immune escape
  - Behavior change and seasonality
- Prediction was done using the last 1 week data. Such prediction may have much uncertainty due to the change of climate, situation and environment.