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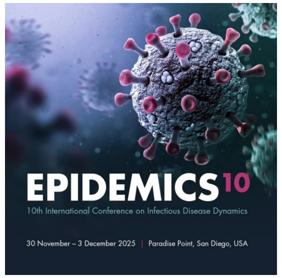

Unraveling the impact of non-pharmaceutical interventions on pathogen mutation for SARS-CoV-2

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Epidemics 10
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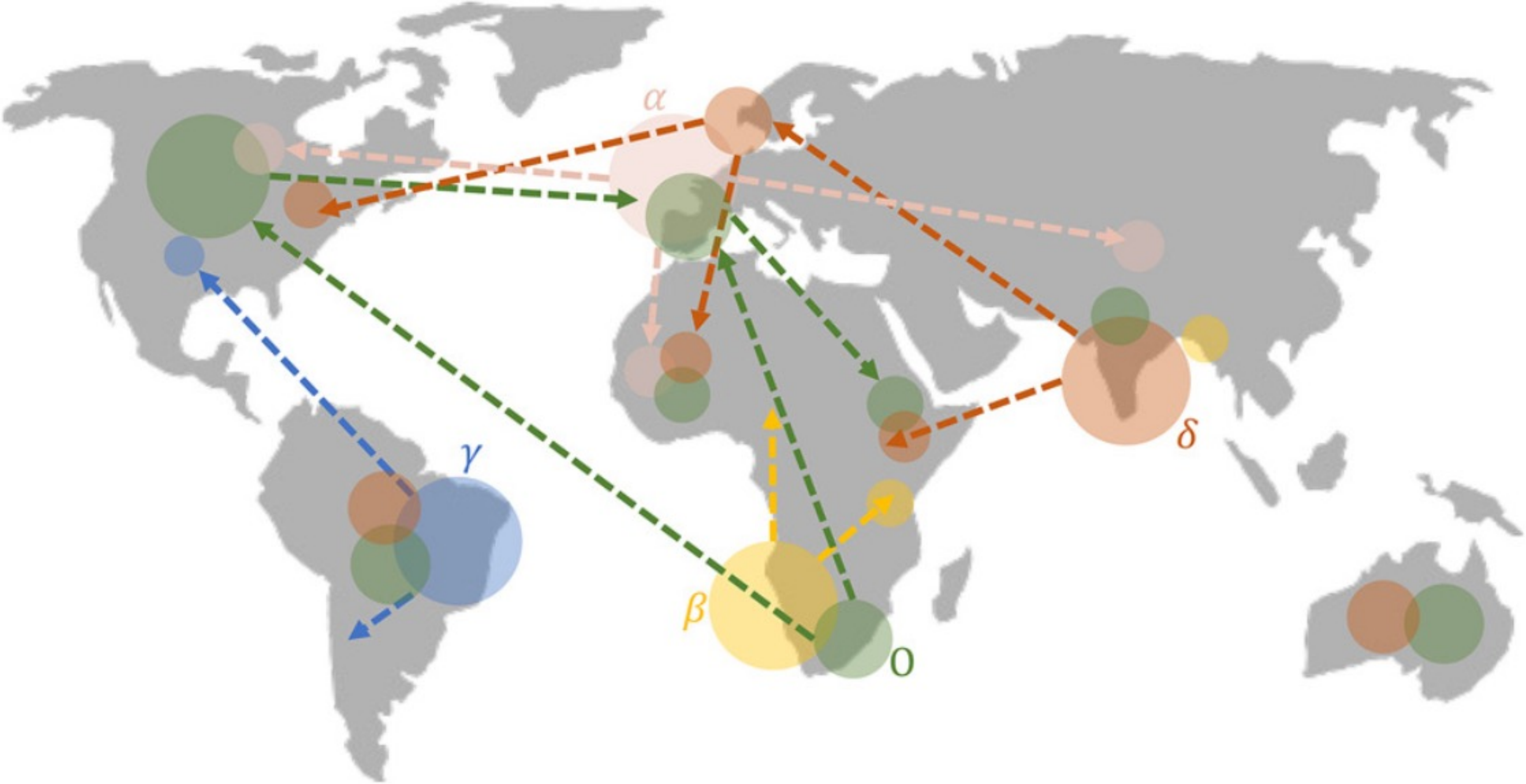
Background
&
Motivation

The origin of SARS-CoV-2 VOCs (Variants of concern)



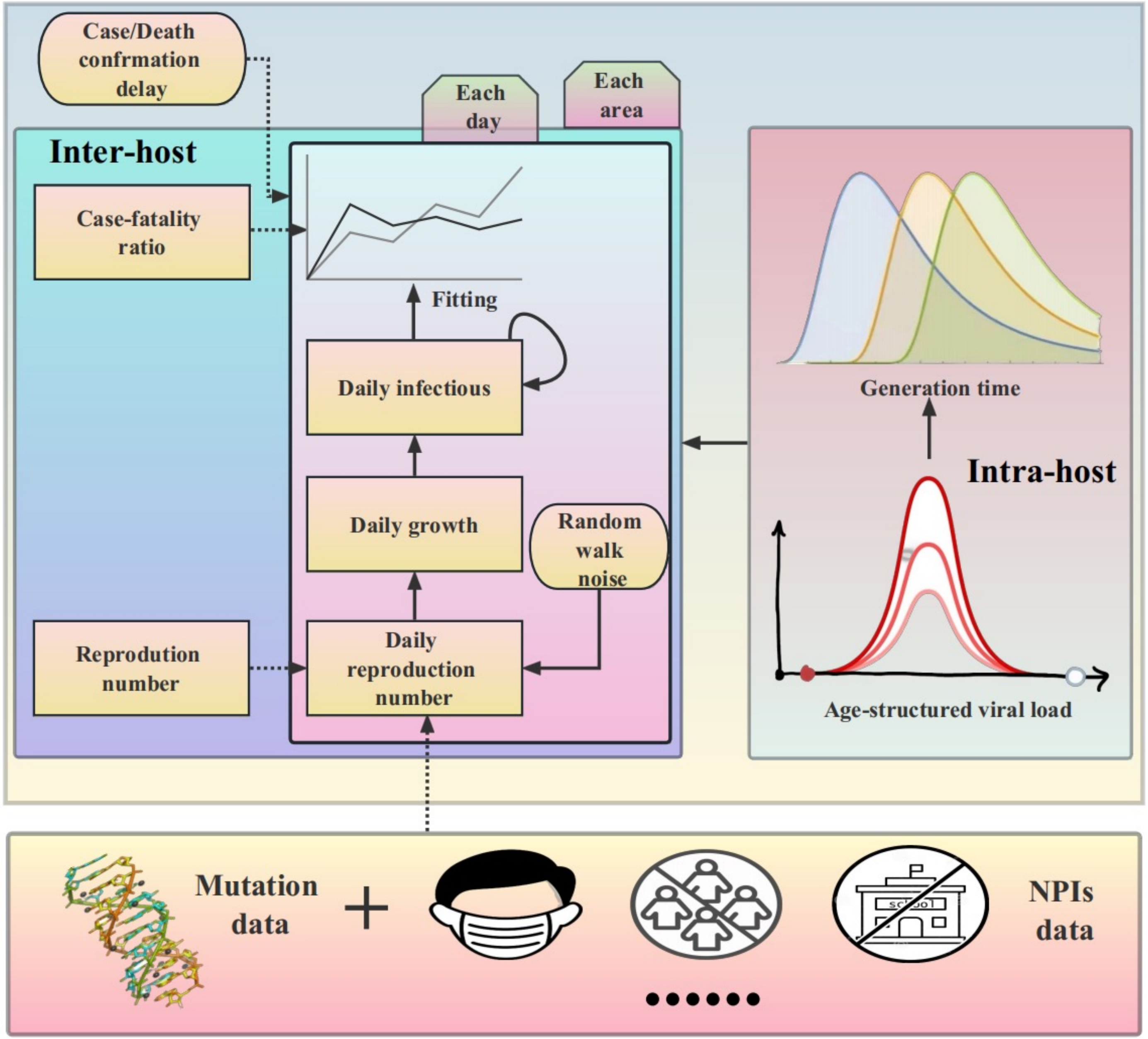
[1] Tegally H, Wilkinson E, Tsui J L H, et al. Dispersal patterns and influence of air travel during the global expansion of SARS-CoV-2 variants of concern[J]. Cell, 2023, 186(15): 3277-3290. e16.

- Why did the Alpha variant originate in the UK and spread rapidly during the second wave of the pandemic in Europe, while other European countries seemed to lag behind?

- Why do new variants of the COVID-19 always seem to emerge outside of China?

Materials & Methods

Intra- and inter-host model



Inter-host model:
Bayes machine learning

Intra-host model:
Mechanistic (ODE)

NPIs: Macro-level

Mutation: Micro-level

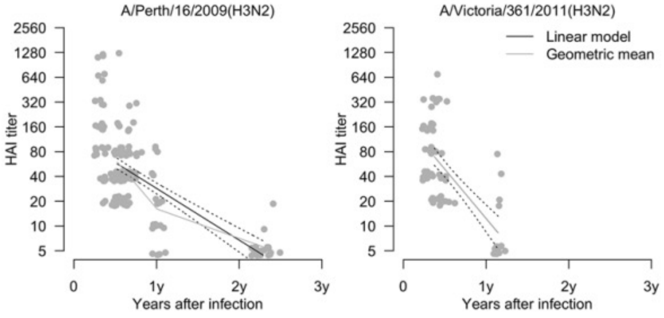
Studying cross-scale problems with multi-scale model

Transmission process

$$R_t^i = R_0^i \, exp\left(-\alpha_i N_{i,t,r} - \beta_j S_{j,t,r} - \gamma_k IM_{k,t,r}\right) \, exp\left(\Delta_t\right)$$

$$IM_{nat}^i\left(t\right) \quad IM_{cro}^i\left(t\right) \quad IM_{vac}^i\left(t\right) \quad D^i\left[t, s\right]$$

Wei et al. PLoS One 2020

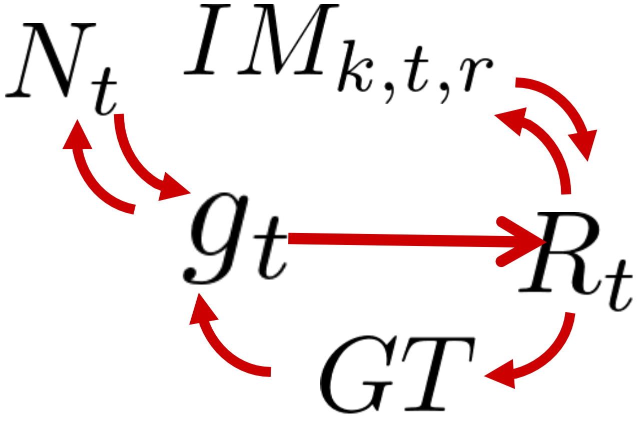


$$IM_{\text{nat}}^i\left(t\right) = \sum_{s=1}^{m.\text{lag}} im_{nat}\left(t-s\right) I^i\left(s\right) \exp\left(-\phi^i \times D^i\left[t,s\right]\right)$$

$$IM_{\text{cro}}^i\left(t\right) = \sum_{j \neq i = 1}^{n} \sum_{s=1}^{m.\text{lag}} \left\{r_{ij} \times im_{\text{cro}}\left(t-s\right) I^i\left(s\right) \exp\left(-\phi^i \times D^i\left[t,s\right]\right)\right\}.$$

$$g_{t,c} = \exp\left(\beta_{\text{GI}}\left(R_{c,t}^{\frac{1}{\alpha_{\text{GI}}}} - 1\right)\right) - 1$$

$$N_{t,c}^{(C)} = N_{0,c}^{(C)} \prod_{\tau=1}^{t} \left[\left(g_{t,c}+1\right) \cdot \exp \epsilon_{t,c}^{(C)}\right]$$



micro

macro

Viral-load → Generation time → Growth rate

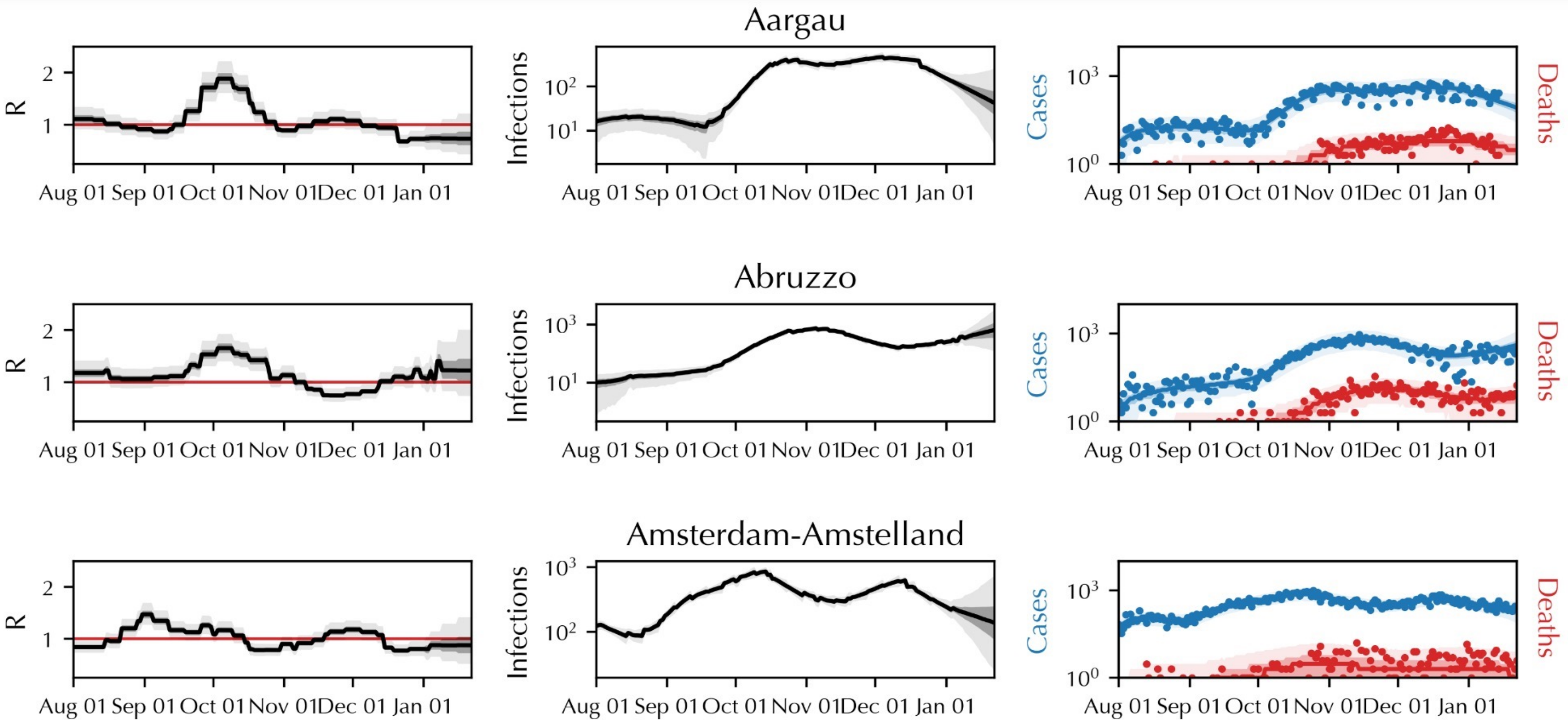
$R_{t,r}$

[2] Flaxman, S, et al. (2020). Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature.

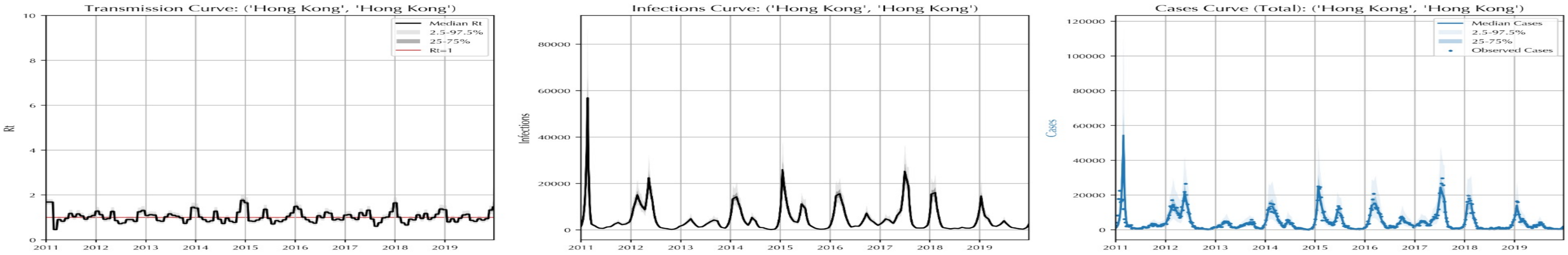
Results
&
Discussion

The fitting results of 114 regions in Europe.

Covid-19 :

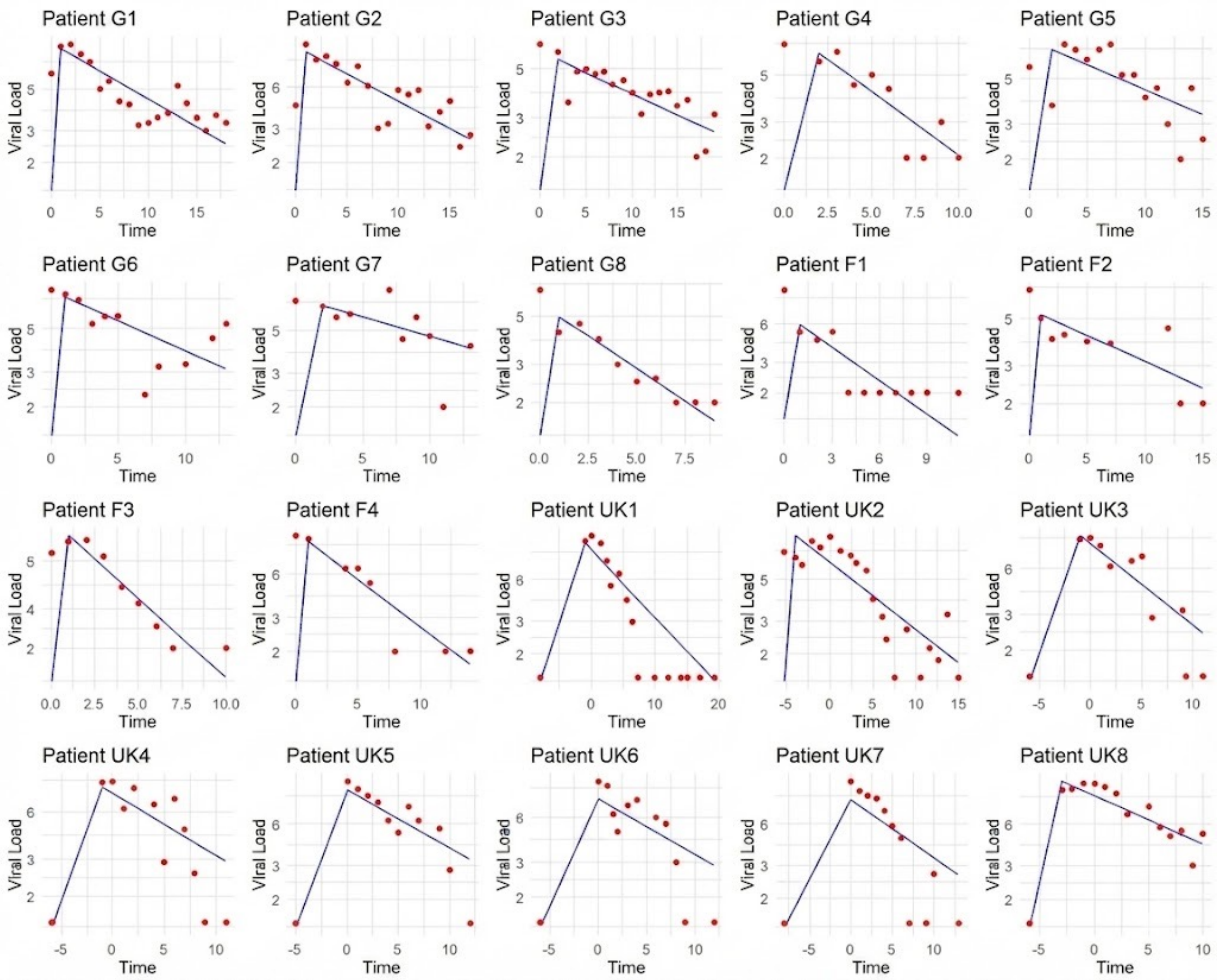


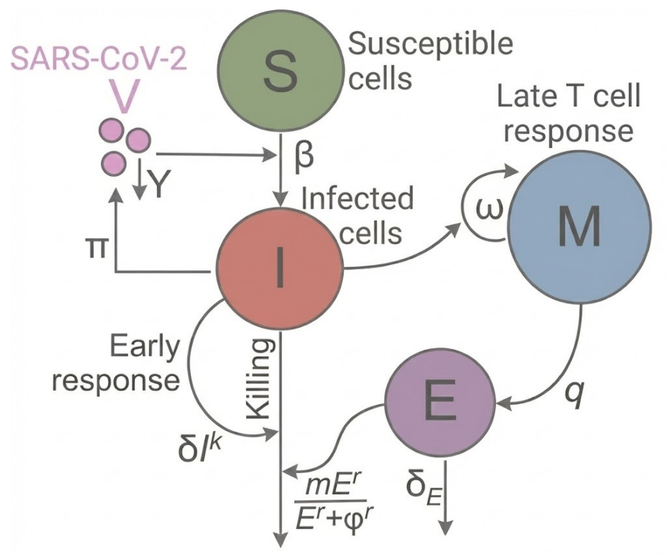
Influenza :



Fitting method: Bayesian DL MCMC

The fitting results of viral load

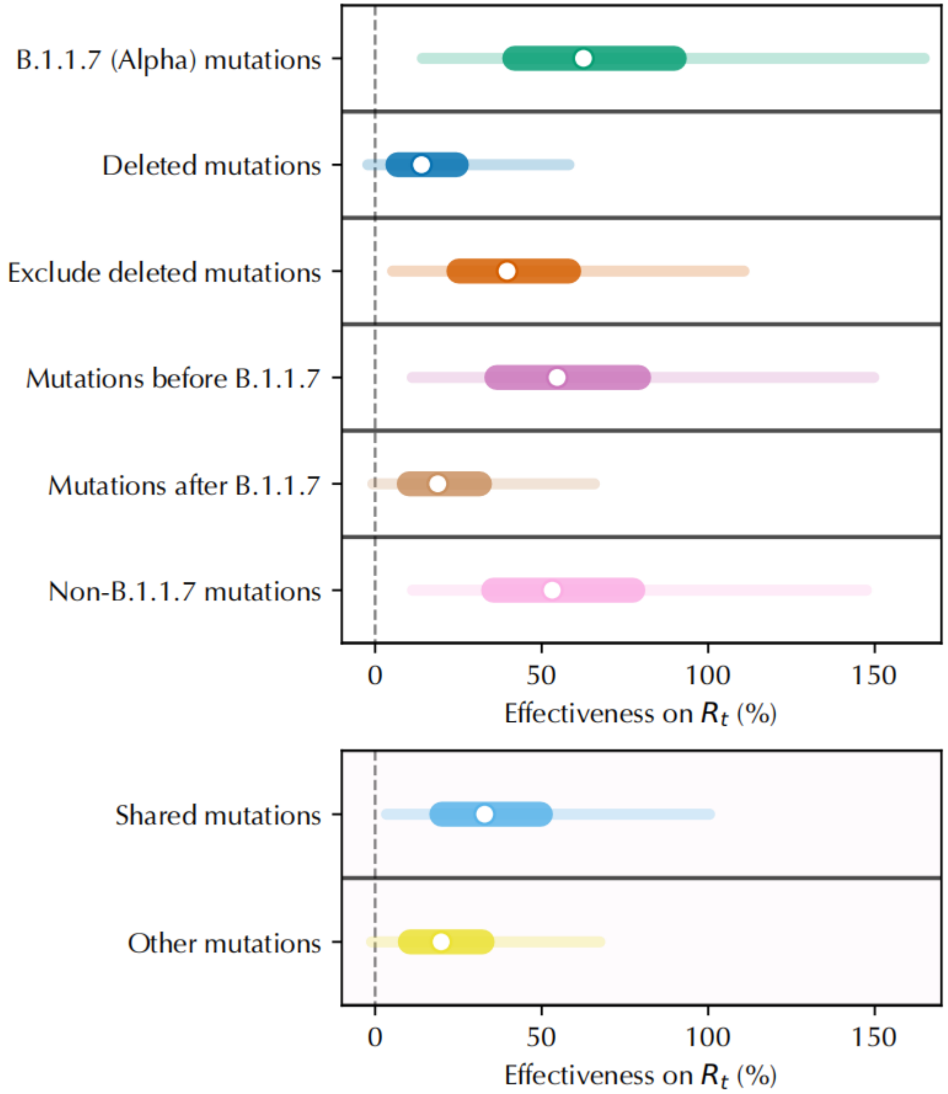


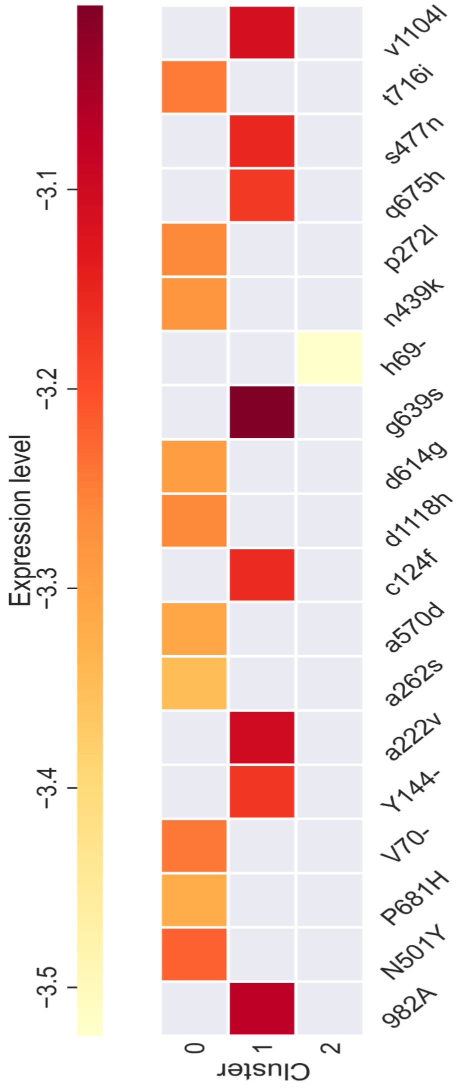


Viral-load ⟶ Generation time

Growth rate ⟶ $R_{t,r}$

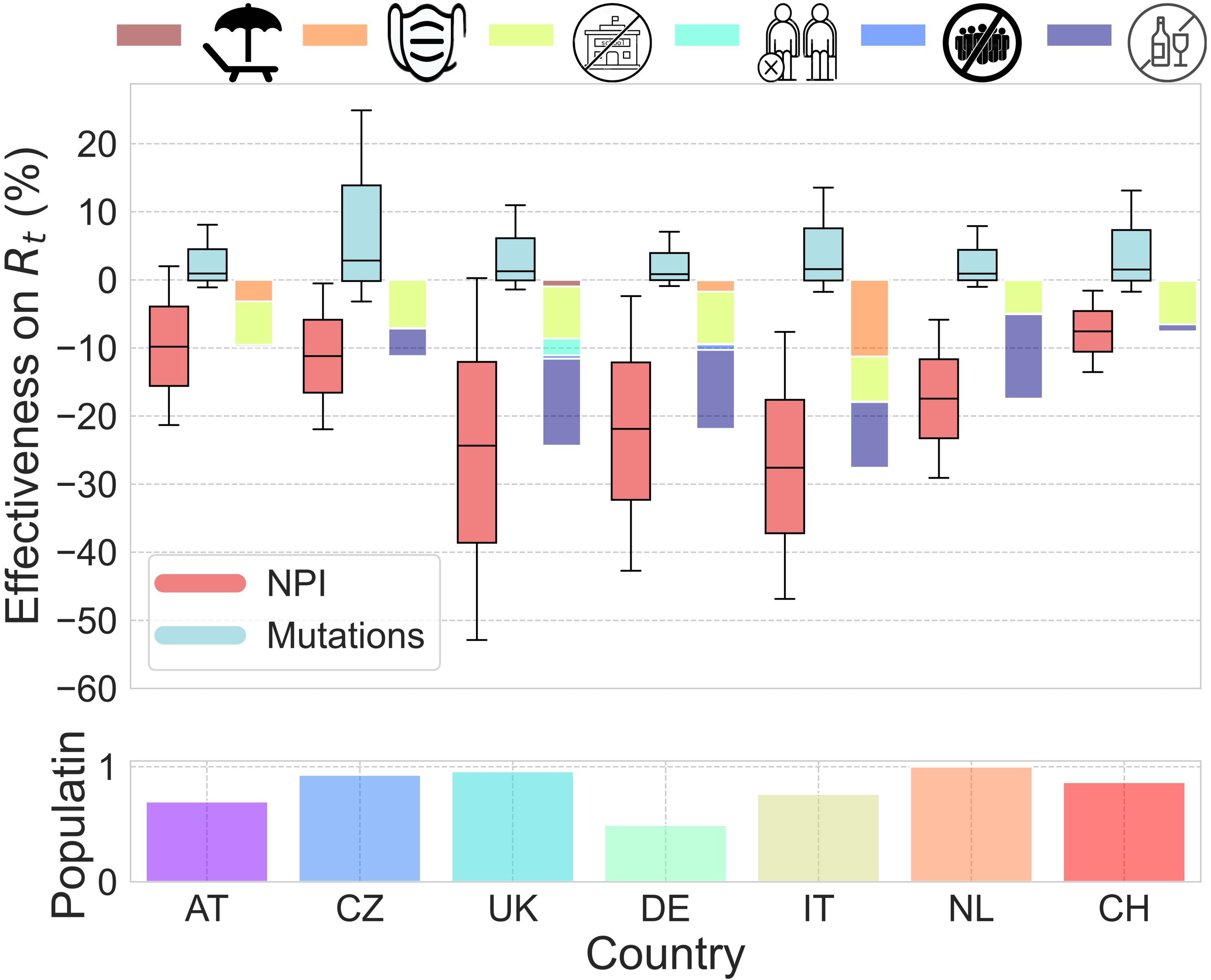
Genetic mutations effectiveness under default model settings.





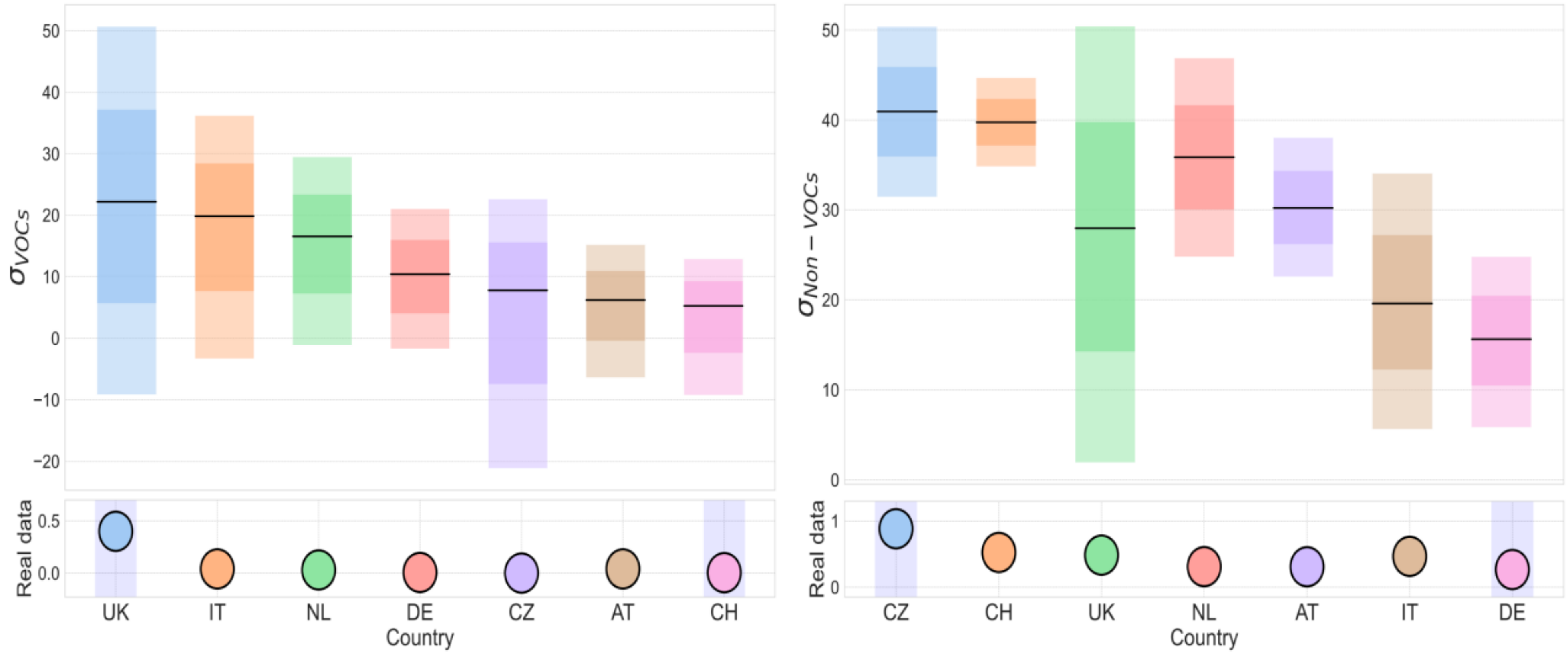
Shared mutations play a more significant role in the transmission dynamics of SARS-CoV-2

Effectiveness of NPIs and mutations in different countries



Measures such as wearing masks are very effective in reducing R_t.

Comparison of simulated ranking results for VOCs and Non-VOCs from our model with real data.

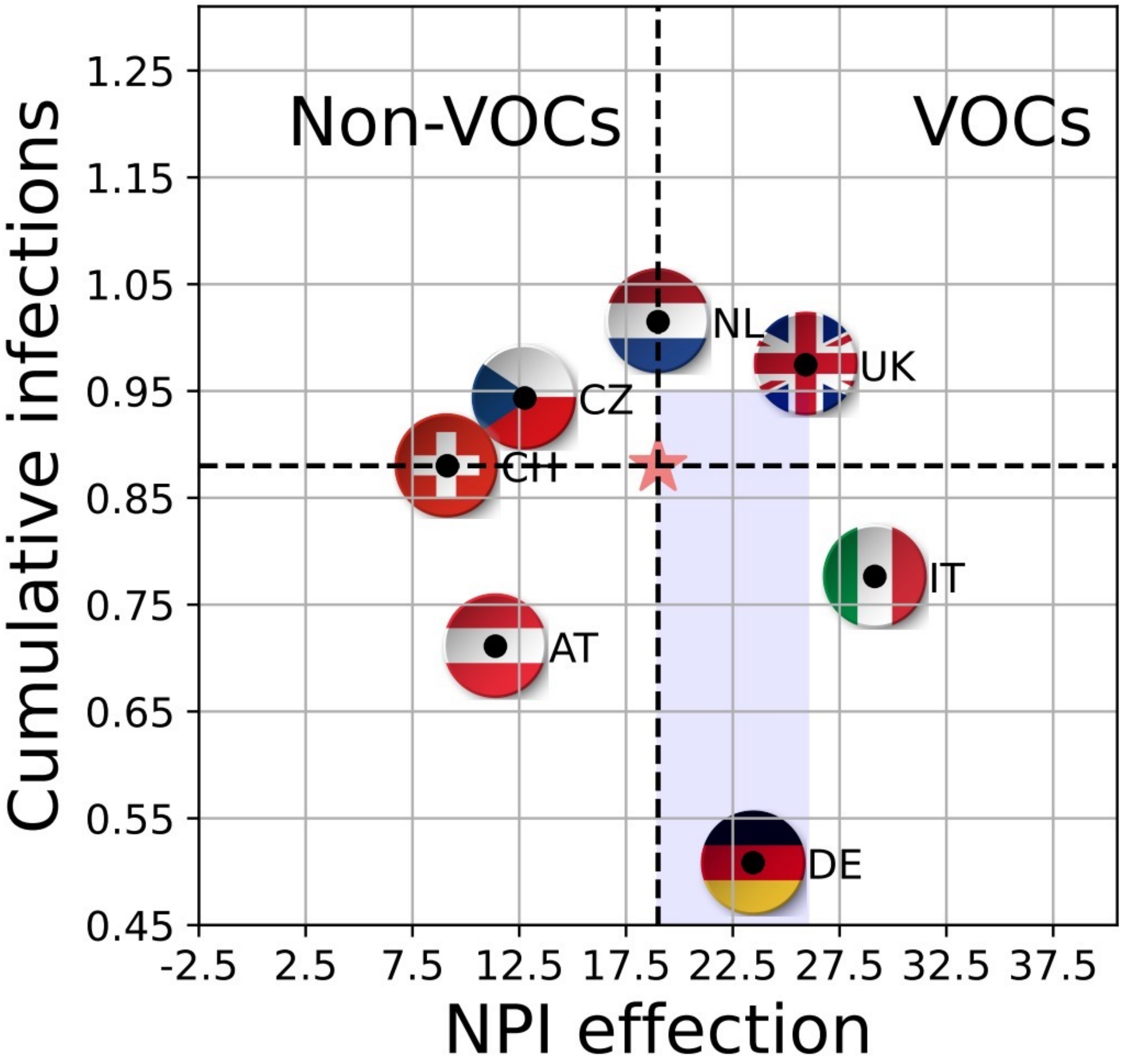


(a)

(b)

The results of our model align well with the rankings observed in the real-world scenario

Assessing the impact of NPIs and relative infections on mutations and predicting mutation priority.



High NPIs drive strain-specific mutations

Low NPIs incite random ones

The influence of NPIs on COVID-19 variant mutation is non-linear

Conclusions

- We quantified a crucial issue, the impact of NPIs on COVID-19 variants using a cross-scale model.
- Mutations associated with VOCs, such as shared mutations, have significantly influenced Rt.
- The influence of NPIs on the evolution of COVID-19 variants is non-linear.
- We forecasted the future mutation priorities for seven European countries.

Limitation & Future opportunities

- Mutation mechanisms (Select Presure)---Darwinian
- More data: Mobility, subtype...
- The risk of emergence of a new variant

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Thank You!

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