Multi-stream data-driven forecasting of influenza activity and associated hospital admission burden: an implication for impact assessment of COVID-19 pandemic on 2019/20 winter influenza season in Hong Kong

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The authors report no potential conflicts of interest

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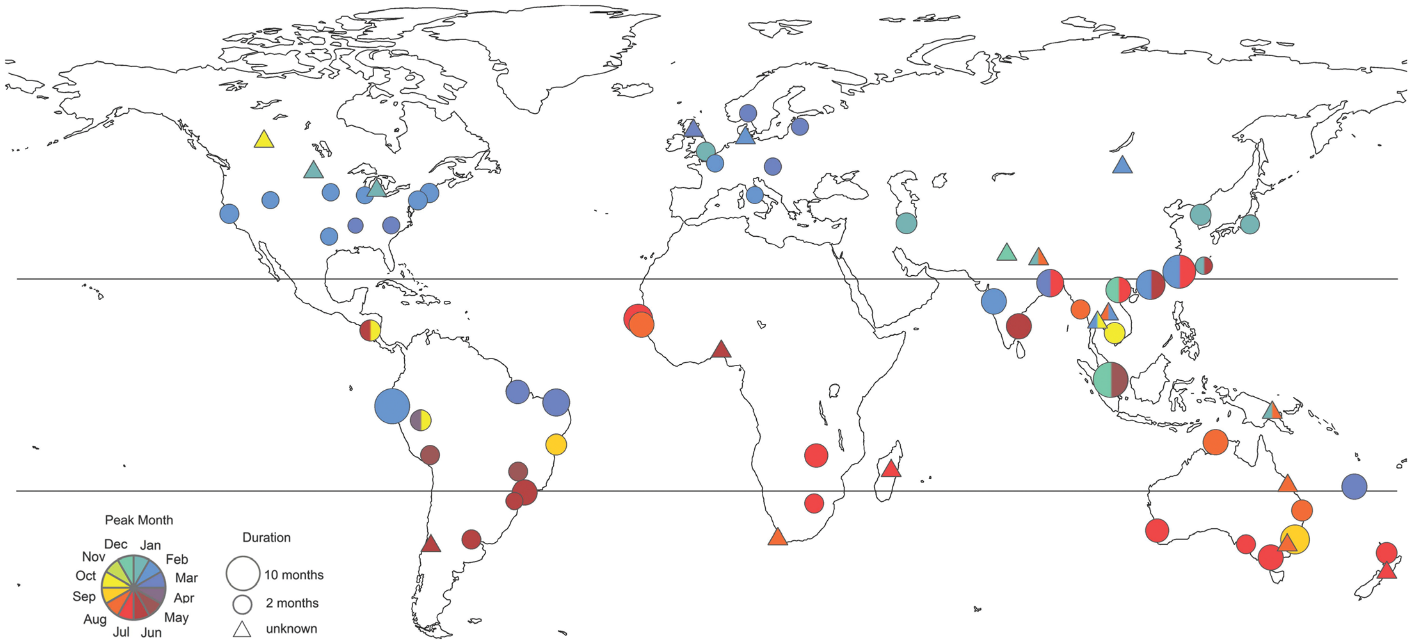
Background & Motivation

Influenza in Subtropics vs Temperate

- Influenza dynamics and seasonality in **temperate** Vs **tropical and subtropical** locations (Tamerius et al., 2011; Azziz et al.,2012; Tan et al.,2014)
  - Winter vs year-round
  - Single and multiple peaks

Fig. 1 Bloom-Feshbach et al. (2013): Global map of influenza peak timing and epidemic duration (n = 77 locations).



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- Various explanations have been put forward for such variations including.

Climatic or Meteorological effects: Temperature and humidity on the virus (Lowen et al.,2007; Shaman et al.,2009; Tamerius et al.,2013; te Beest et al.,2013)

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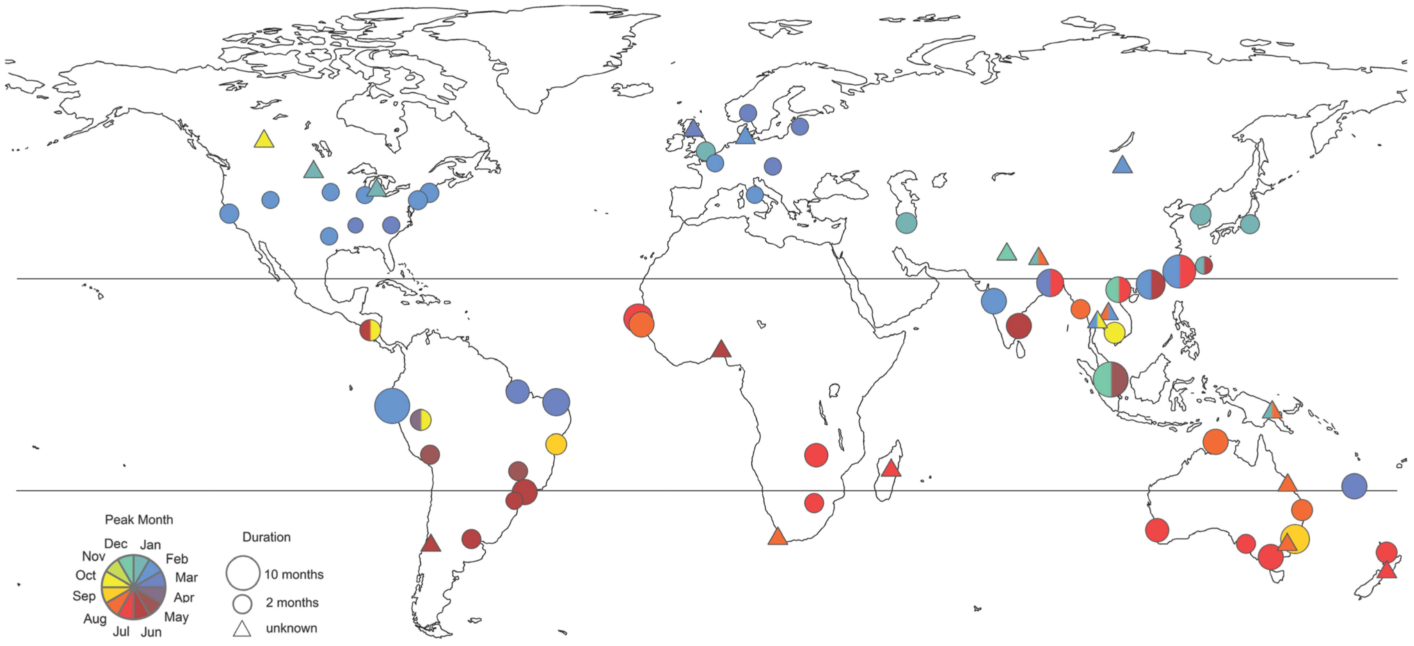

Biological effects: Host immunity during winter (Dowell,2001; Lipsitch, et al.,2009)
Social effects: Indoor crowding in winter (Lofgren et al.,2007), Holidays and School closures (Ferguson et al.,2006; Cowling et al.,2008; Wu et al.,2010)

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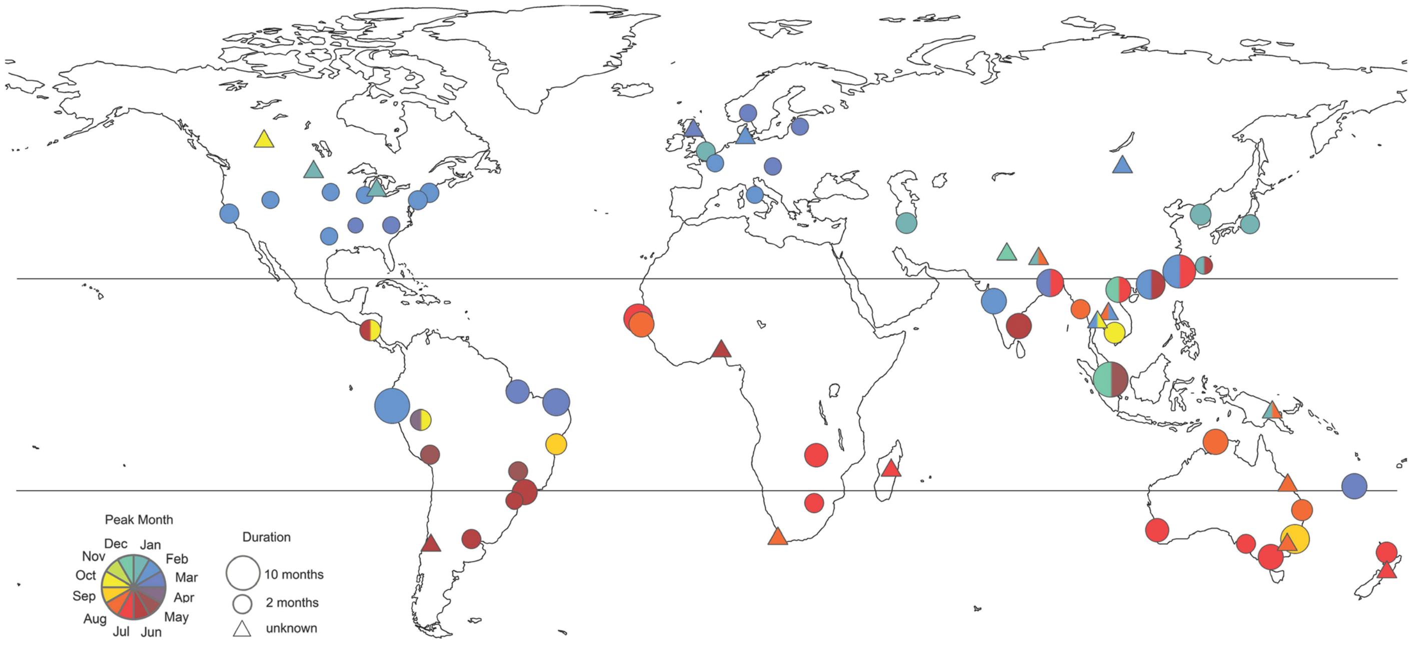

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- Where a tiny seasonal change in transmissibility by these drivers may cause a large sustained oscillation in incidence of influenza outbreaks (Dushoff et al,2004).

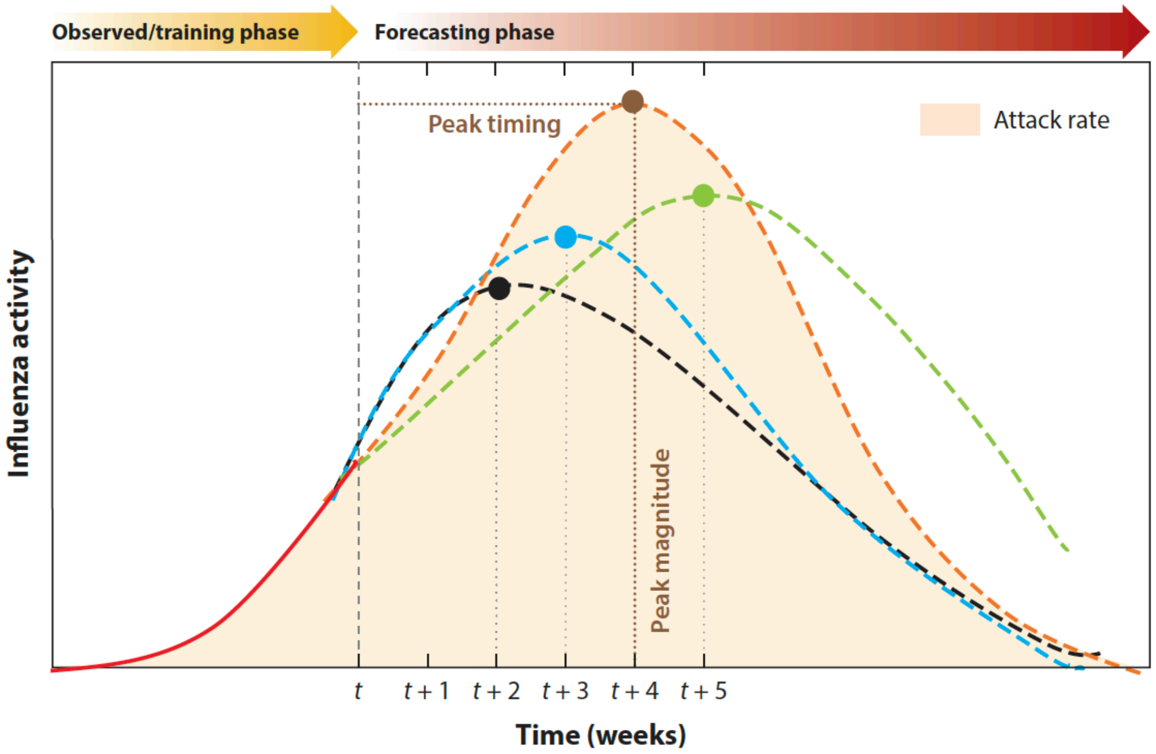
Objectives

Hong Kong is a subtropical location, having **year-round** influenza circulation with **multiple peaks**.

- To assess the impact of these drivers on influenza **transmissibility** and **seasonality** in Hong Kong
- To construct a statistical and mechanistic model based **predictive** frameworks using multi-stream data.
- To use these models to provide forecasts (short-term, medium-term and long-term) of influenza **outcomes**: activity/attack rate, peak timing and peak magnitude in subtropical city Hong Kong.

Fig. 2

Ali ST Ann. Rev. PH 2022



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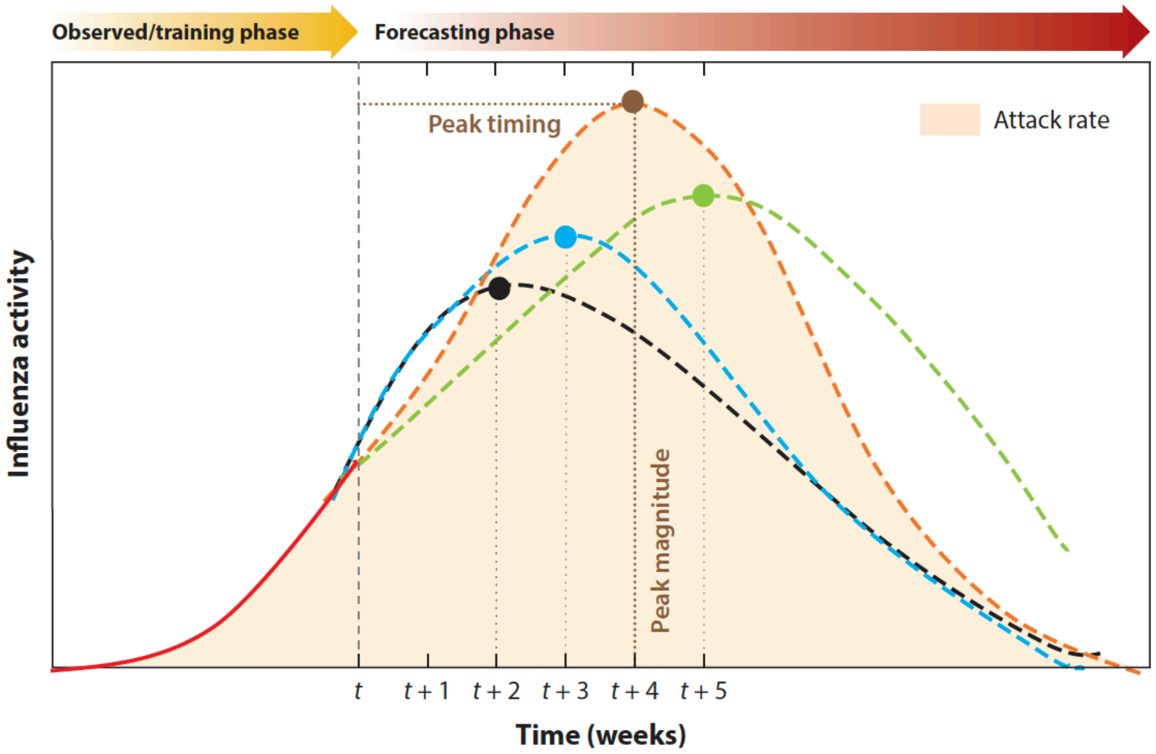


Emergence of COVID-19 Pandemic

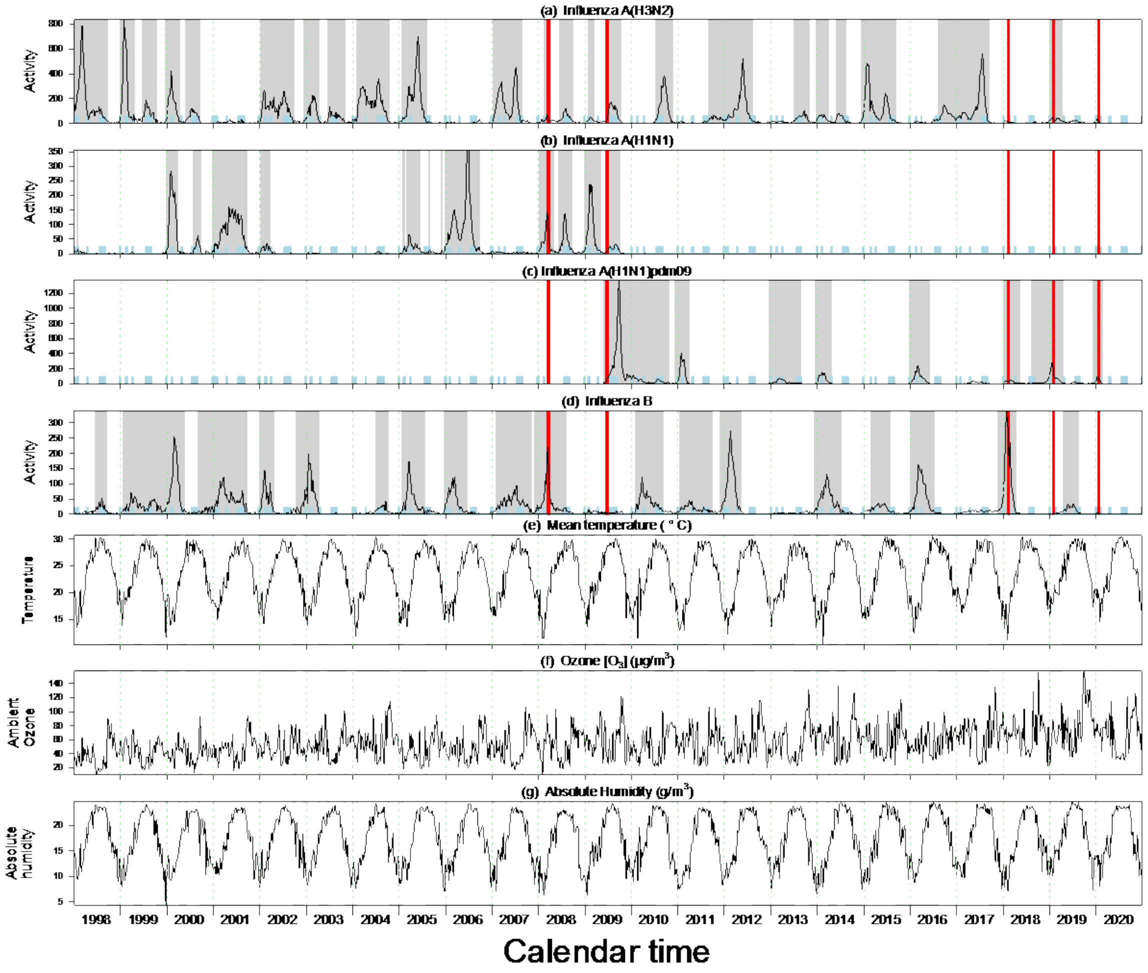
- To assess the impact of COVID-19 PHSMs on 2019/20 winter season in Hong Kong
  - Retrospective forecasting for influenza outcomes.
  - Associated hospital admission burden

Materials & Methods

Influenza Activity : During 1998-2020

Fig. 3

Ali ST et al Sc Tot Envs 2022 and Lau YC et al PLoS Comp Bio 2024



– **ILI+ proxy** (in lines)**:** (proportion of specimen tested **positive**) x (proportion of GP visits with **ILI**) [Wong JY et al., AJE 2013]. Grey shaded regions are identified epi-onset for influenza type and subtypes.

– Reactive school closure (Red) and holiday related school closure (small Blue bars).

– Extrinsic drivers (meteorological and environmental)

– ILI+ proxy ➔ R_t [Cori et al., AJE 2013]

– R_t ➔ β_t ($\beta_t = \frac{R_t}{S_t} \times \vartheta$ where, ϑ is recovery rate)

– Regression framework to identify the potential drivers and their form of association. [Ali ST et al., EID 2018]

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Statistical modelling framework

– ***Standard*** *Generalized Linear Model (GLM)* with log link,
$ln(\lambda(t+k)) = \alpha_k \boldsymbol{B}(t-1) + \sum_{l=1}^{L} \beta_{k,l} y(t-l) + \sum_{j=1}^{n} \psi_{k,j}(t-1)$
where, ILI+ proxy $y(t)$ ~ negative binomial distribution with $\lambda(t+k)$ is the expected ILI+ proxy for the coming k week with $k \in \{0,1,2,3\}$ at week t.

Absolute Humidity: U-shaped form ($\psi_{k,j}(t) = \{\gamma_{k,1,j} C_j(t) + \gamma_{k,2,j} C_j^2(t)\}$)

Ozone: Non-liner power form ($\psi_{k,j}(t) = \{C_j(t)\}^{\gamma_{k,1,j}}$)

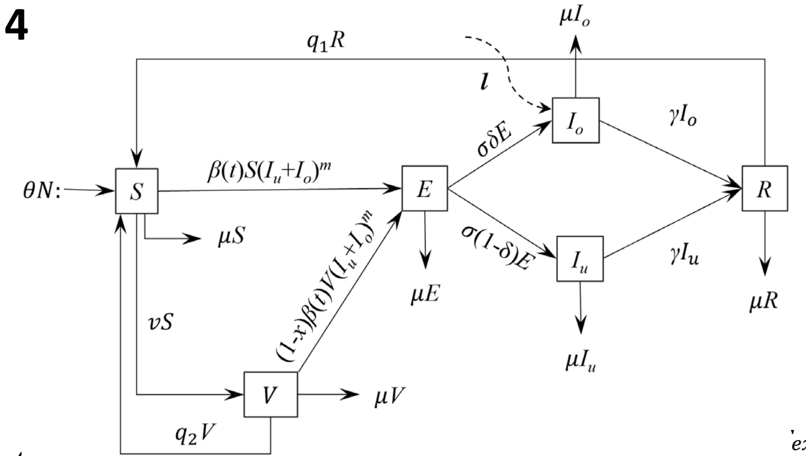
School closures: $\psi_{k,j}(t) = \begin{cases} 1, & (t) \; in \; regular \; week \\ 1-\varepsilon, & (t) \; in \; during \; the \; contorl \end{cases}$

– *Evaluation (short-term, medium-term and long-term)*
- Outcomes
- Cross-validation
- RMSE, RMSLE , MAE, WIS

Mechanistic modelling framework

– *Compartmental Model Construction*

Fig. 4



$\beta(t) = \beta_0 \left(1 + \beta_1 \sin\left(\frac{\ldots}{13} t + \phi\right)\right) \cdot \exp([a_1 q^2(t) + a_2 q(t)]) \cdot \left\lfloor \frac{\ldots c}{T(t)} \right\rfloor^{exp} \cdot \exp(-cO_3(t))\, \mathrm{d}\Gamma$

– *Parameters estimation:* POMP, particle filtering

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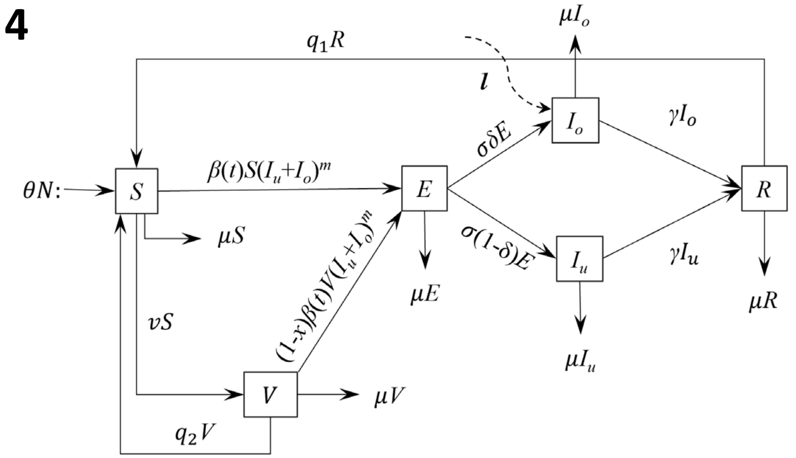

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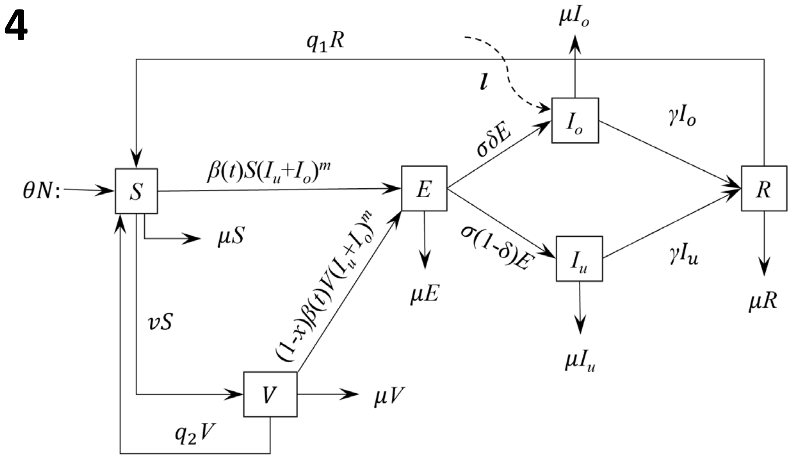

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Impact assessment of COVID-19 PHSMs on influenza transmission

- Retrospective forecast
- Training data (2010 to 2019) for forecast (2020)
- Reduction in transmissibility, attack rate, peak magnitude and delay peak timing

Results & Discussion

Impact of drivers on influenza transmissibility

Fig. 5 Non-linear form of association between ambient ozone concentration and transmissibility in Hong Kong (with p=0.7, P=0.3)

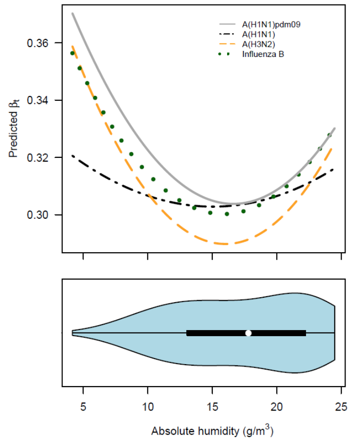


Fig. 6 Non-linear form of association between ambient ozone concentration and transmissibility in Hong Kong (with p=0.7, P=0.3)

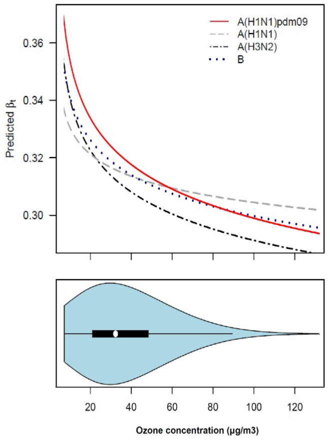
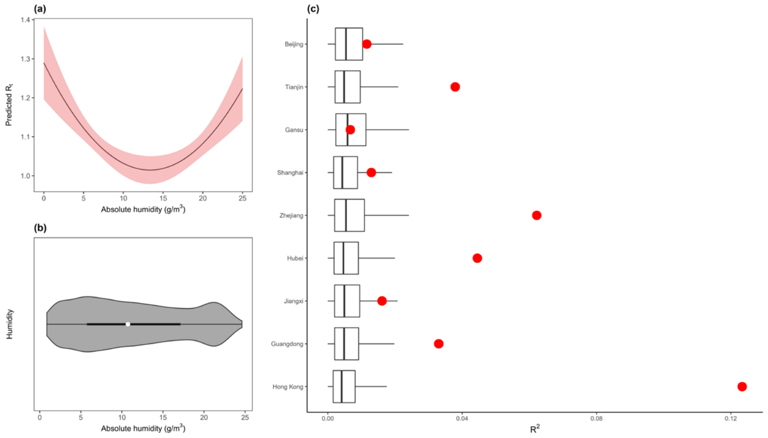


Fig. 7



- Absolute humidity (U shape)
- Ozone(power shape)
- School closure (negative)
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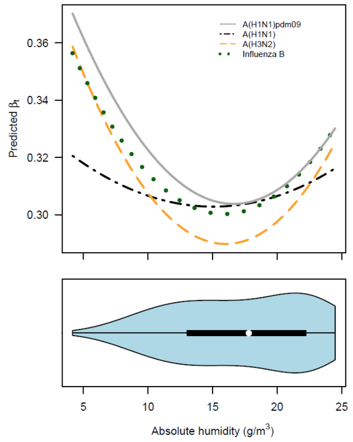

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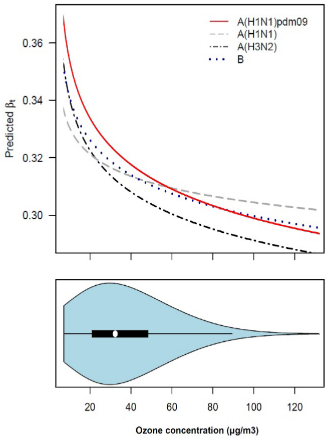

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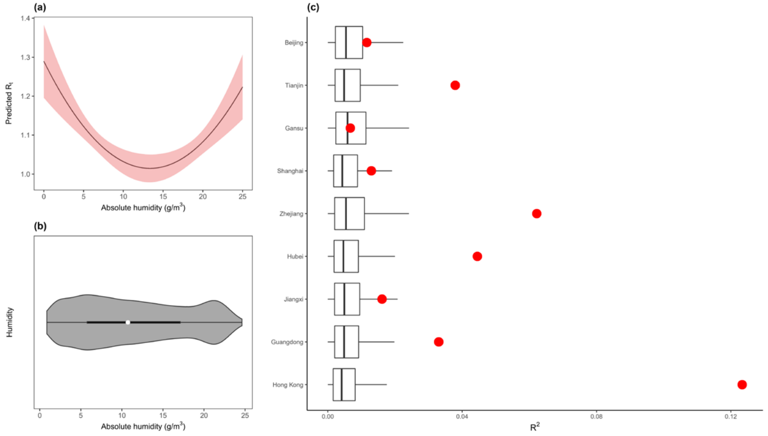

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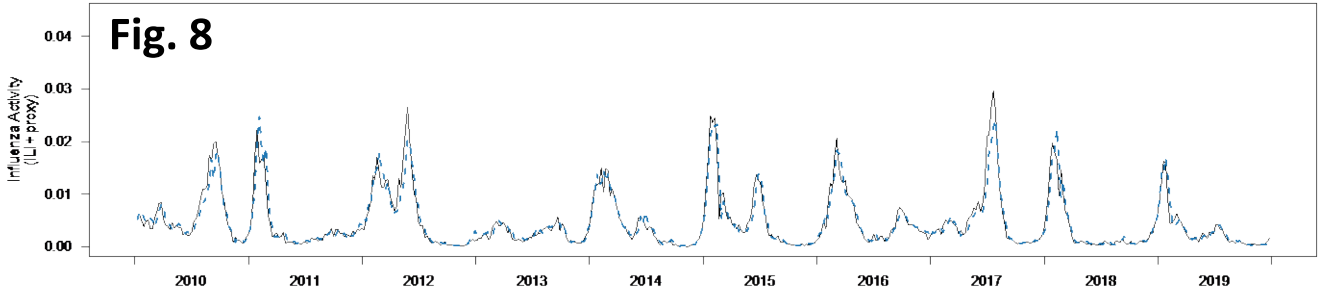
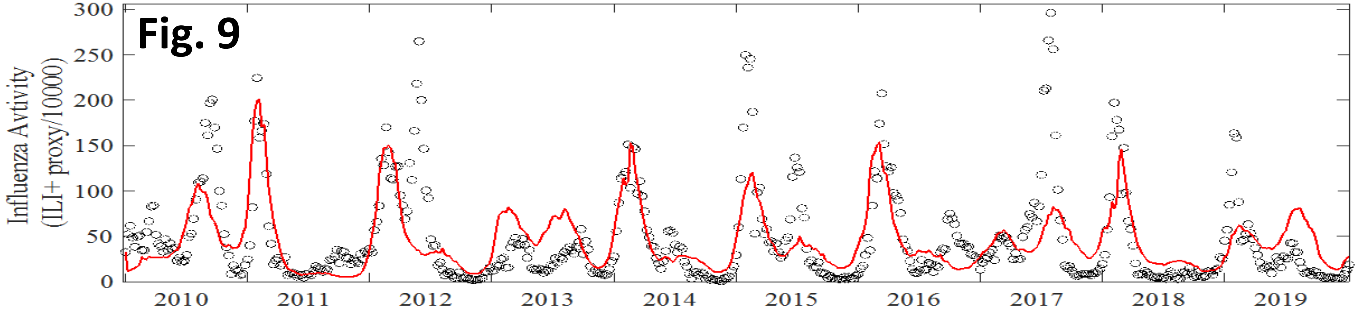
Statistical and mechanistic model based prediction of influenza activity





– Both frameworks show comparable predictive performance

– Suggests some other potential drivers need to be included

Forecasting influenza activity in 2020 and assessing the impact of COVID−19 PHSMs

Fig. 10

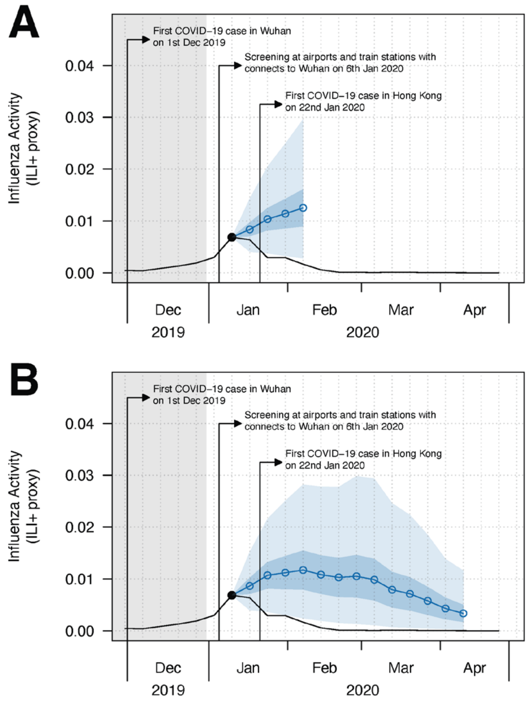
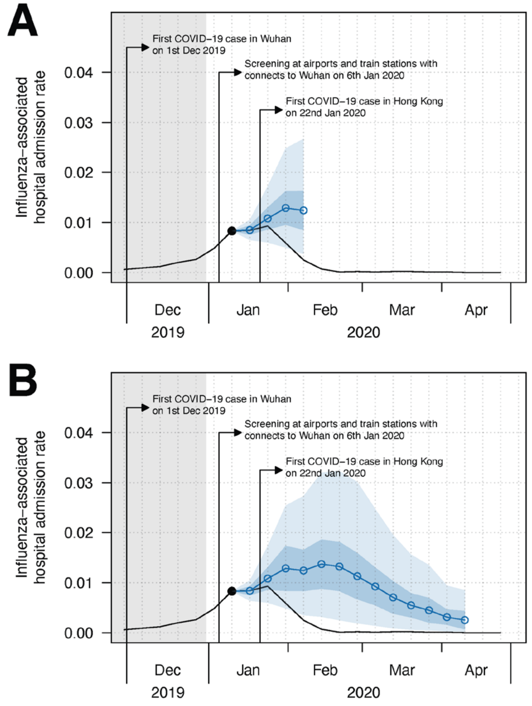


Fig. 11



– Short term (1-4 weeks), medium-term (13 weeks) and long-term (beyond a season)

– Influenza infection and hospital burden

– Peak for 2020 influenza winter-spring season could have peak in early February.

– COVID-19 PHSMs could reduce

➔ 44.6% (95% CrI: 38.6% - 51.9%) in transmissibility

➔ 75.5% (95% CI: 73.0% - 77.6%) in attack rate

➔ 41.5% (95% CI: 13.9%– 55.7%) peak magnitude.

➔ 63.1% (95% CI: 59.3% - 66.3%) in the admission rate during the winter-spring season in 2019/20

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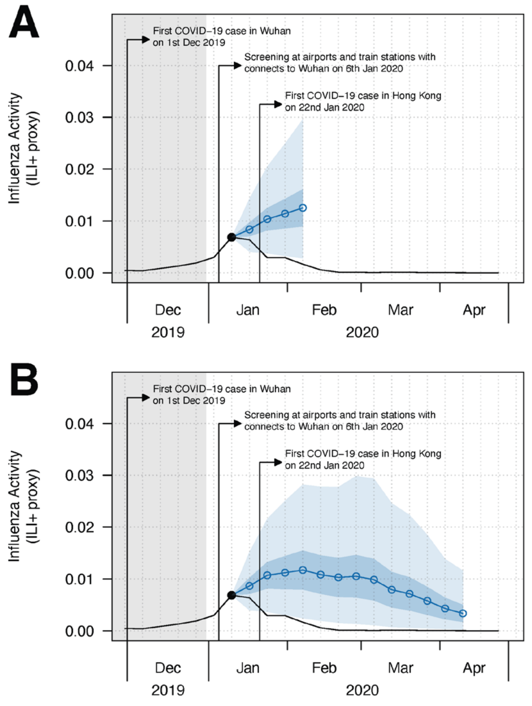

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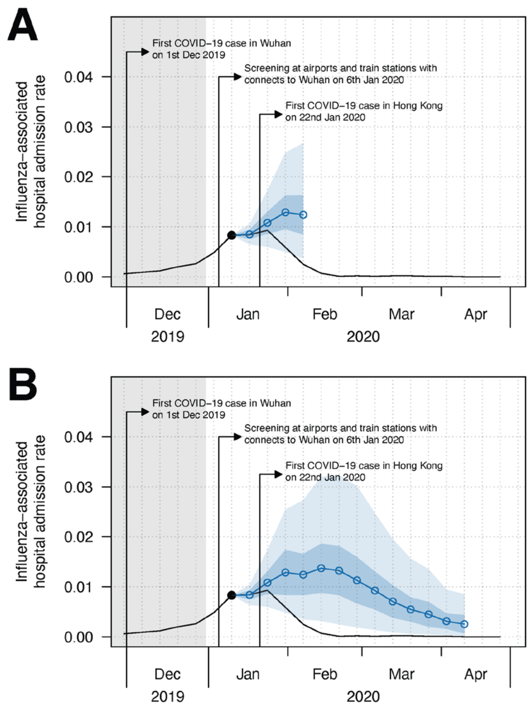

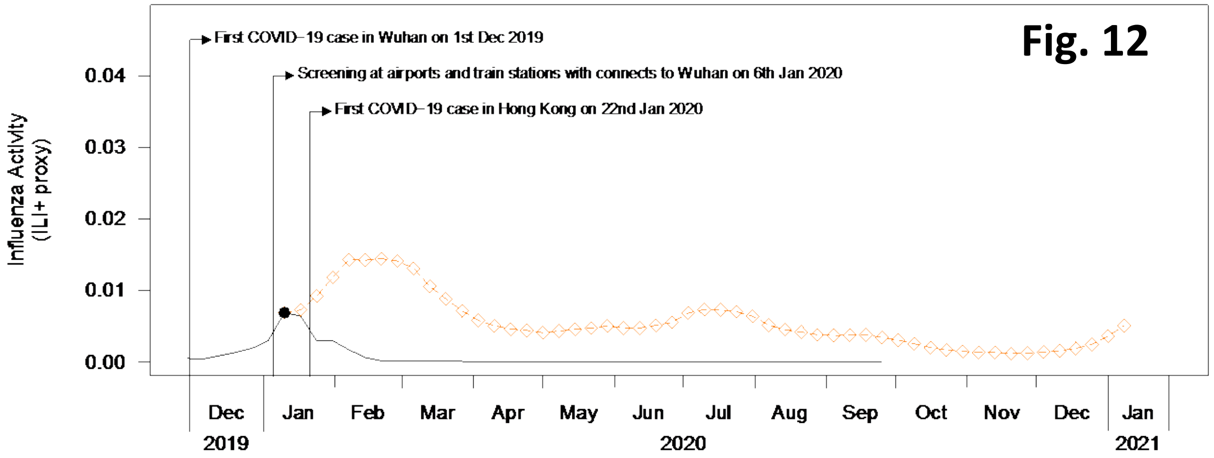

Fig. 12

– Short term (1-4 weeks), medium-term (13 weeks) and long-term (beyond a season)

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– Long term forecast suggested a peak in February, followed by a summer epidemic with lower magnitude

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Forecasting influenza activity in 2020 and assessing the impact of COVID−19 PHSMs

Fig. 13

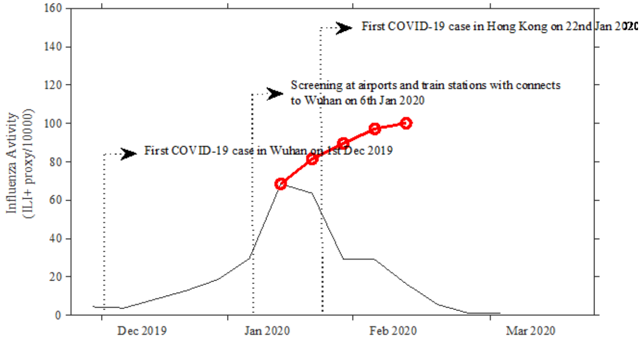
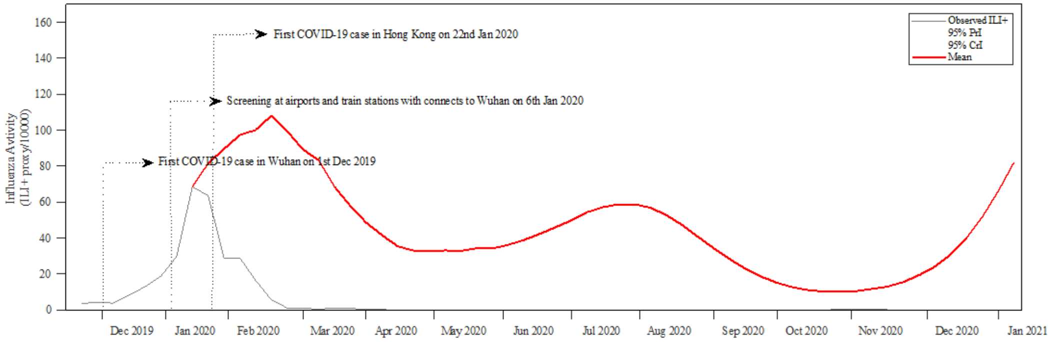


Fig. 14



– **Mechanistic framework**

– Comparable results for short-term and long-term

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Forecasting influenza activity in 2020 and assessing the impact of COVID–19 PHSMs

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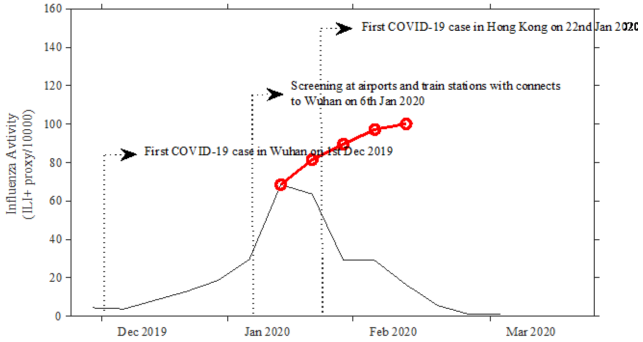
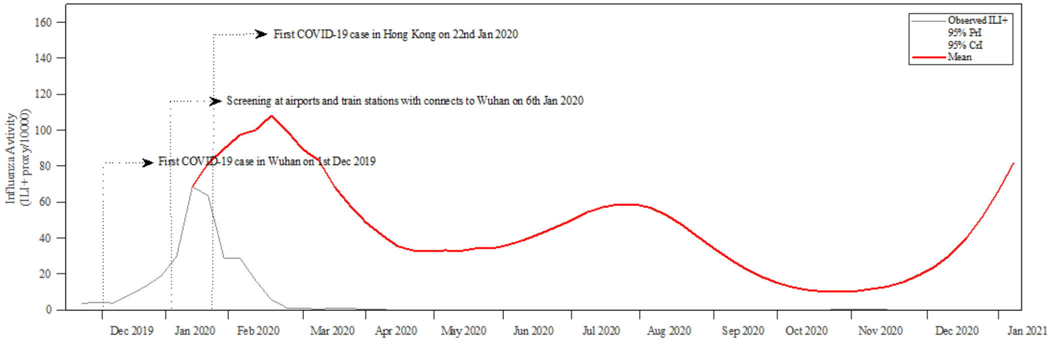


Fig. 14



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Conclusion

– Data-driven statistical frameworks to predict and forecast less regular dynamics of seasonal influenza and associated hospital admissions burden in Hong Kong

– To early detection of the influenza outbreak and enabled timely decision-making for the public health policymakers with better healthcare preparedness including stockpiling, implementation of better interventions (PHSMs) and vaccination scheme to mitigate the upcoming epidemics.

– Such forecasting frameworks also has the potential to quantify the direct/indirect impact of interventions for similar directly transmitted diseases (e.g. COVID-19 and influenza) on their associated burden of infections and hospitalization

Limitation and Future opportunities

– We have not considered **other drivers** into the model (population immunity, antigenic changes, importation risks etc.)

– Post-COVID-19 pandemic, interaction, co-existence, co-circulation of respiratory viruses

Acknowledgements

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Publications and Dissemination

1. Ali ST, Cowling BJ, Wong JY, Chen D, Shan S, Lau EHY, He D, Tian L, Li Z, Wu P; Influenza seasonality and its environmental driving factors in mainland China and Hong Kong, ***Science of the Total Environment***, 2022, 818, 151724. [**IF 8.00** (2021), rank **25/274** Environmental Sciences].
2. Ali ST, Cowling BJ; Influenza Virus: Tracking, Predicting and Forecasting. ***Annual Review of Public Health***, 2021, 42:43-57. [**IF 21.98** (2021), rank **4/203** Public Health, Environmental and Occupational Health (Science)]
3. Lau, YC, Shan S, Wang D, Chen D, Du Z, Lau EYC, He D, Tian L, Wu P, Cowling BJ, Ali ST†; Forecasting of Influenza Activity and Associated Hospital Admission Burden and Estimating the Impact of COVID-19 Pandemic on 2019/20 Winter Season in Hong Kong. ***PLOS Computational Biology.***, 2024. 20(7): e1012311. [**IF 4.78** (2021), rank **3/20** Bioinformatics and computational Biology]

Results of the study were presented in international conferences including **Epidemics7** 2019, USA, **Epidemics8** 2021, Italy; and **Option XI** 2022, Belfast, UK.

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Thank YOU!