COLUMBIA UNIVERSITY | MAILMAN SCHOOL of PUBLIC HEALTH

Seasonality of Respiratory Infections: From Laboratory to Model, Forecast, and Public Health Action

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Outline

with a focus on influenza and COVID-19:

- **Epidemiology:** What is the seasonality of respiratory infections?
- **Laboratory studies:** How and why?
- **Modeling:** How to translate the mechanisms into models?
- **Forecasting:** Can seasonality models help forecast?
- **Public Health Action:** How all the above can help public health?

Acknowledgements

- **Collaborators**
  - Flu studies:
    - Virginia Tech: Linsey Marr (phd work);
    - Columbia University: Jeff Shaman, Max O'Donnell, Mat Cummings; Haokun Yuan, Sarah Kramer
    - University of Hong Kong: Ben Cowling, Eric Lau
    - Uganda Virus Research Institute: Barnabas Bakamutumaho, John Kayiwa, Nicholas Owor, Barbara Namagambo, Timothy Byaruhanga, Julius J. Lutwama
  - COVID studies:
    - Columbia: Jeff Shaman, Sasi Kandula, Haokun Yuan
    - NYC DOHMH: Sharon Greene, Anne Fine, Jaimie Shaff, and many others

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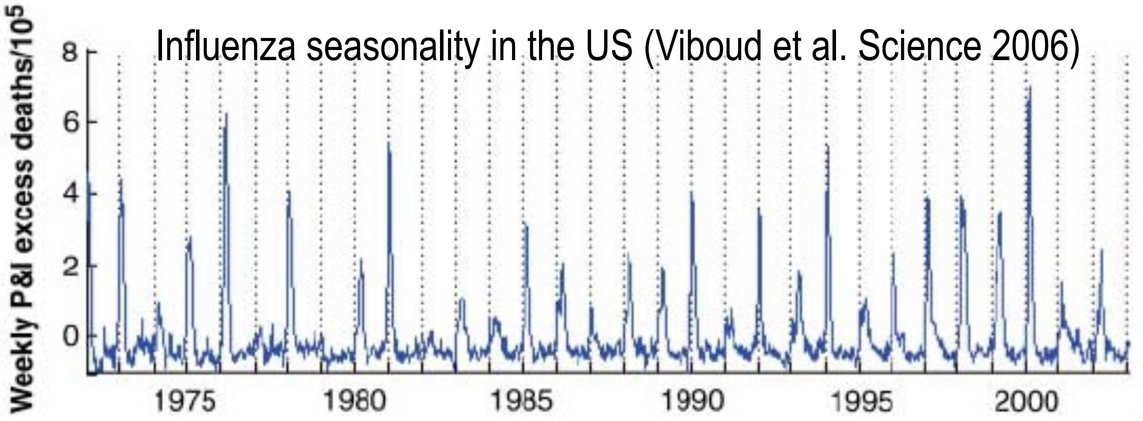
  - NYC DOHMH

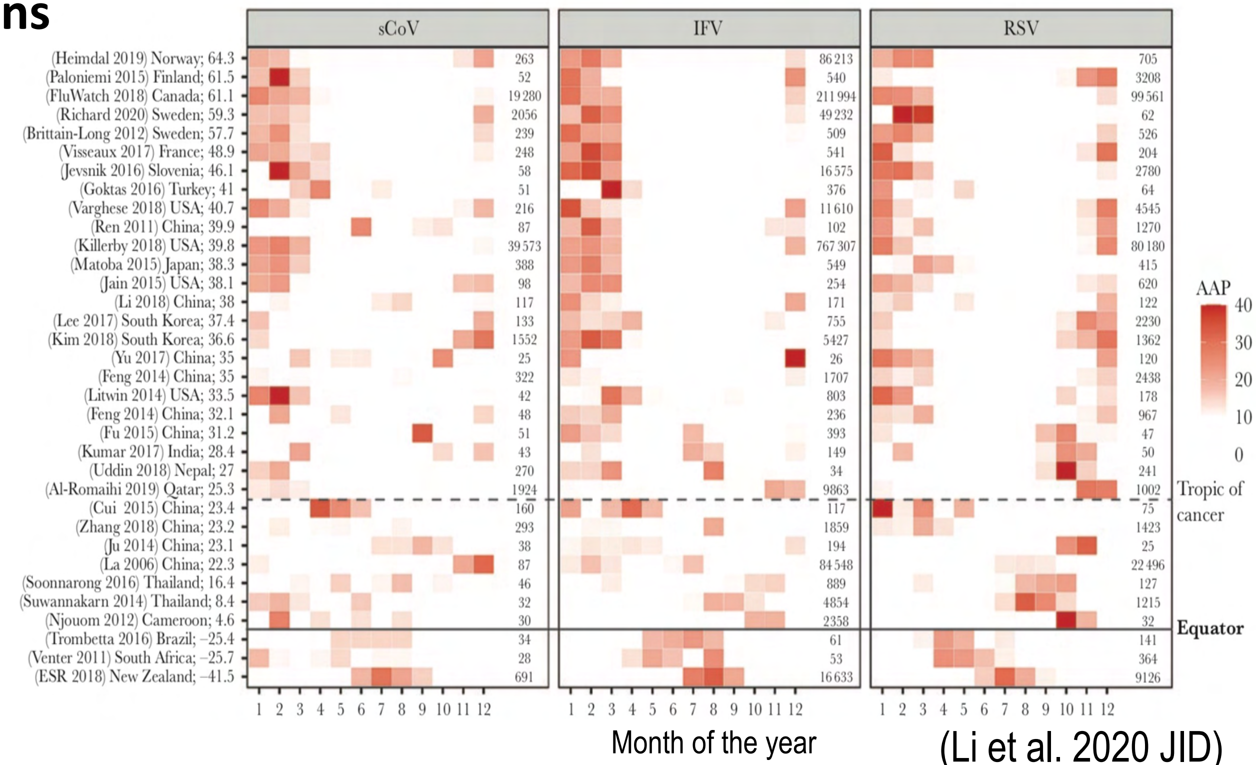
RESPIRATORY INFECTION SEASONALITY: EPIDEMIOLOGY

Seasonality of common respiratory infections

- **Influenza tends to surge in the winter in temperate regions**


Influenza seasonality in the US (Viboud et al. Science 2006)

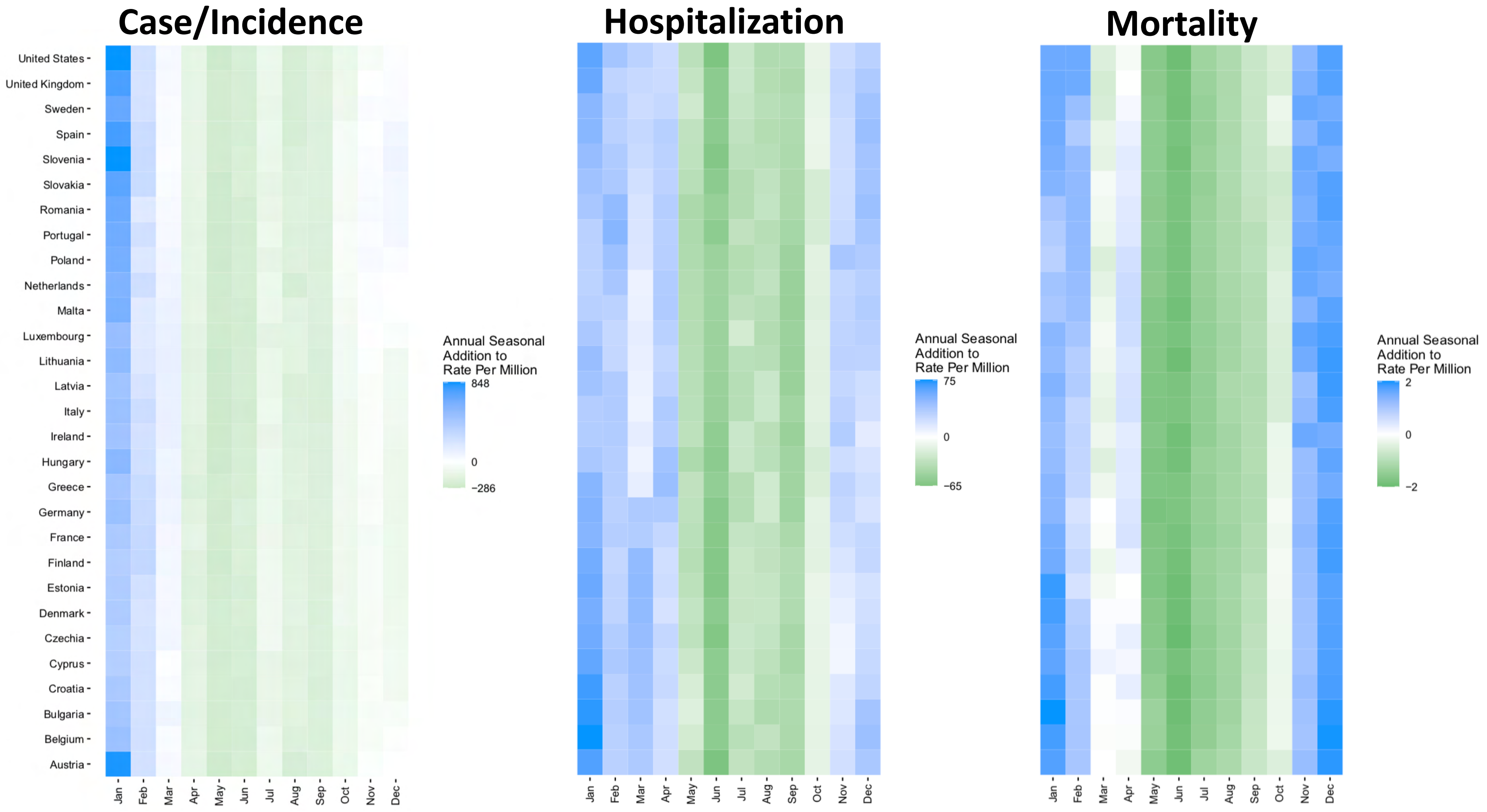
- **Many respiratory infections seem to follow similar seasonal pattern:**
  - Temperate regions: cold winter-months
  - Tropical/subtropical: two peaks, or year round (less studied)



(Li et al. 2020 JID)

Seasonality of common respiratory infections

- **COVID-19/SARS-CoV-2: higher incidence, hospitalization, and mortality in the winter in temperate regions**



Case/Incidence

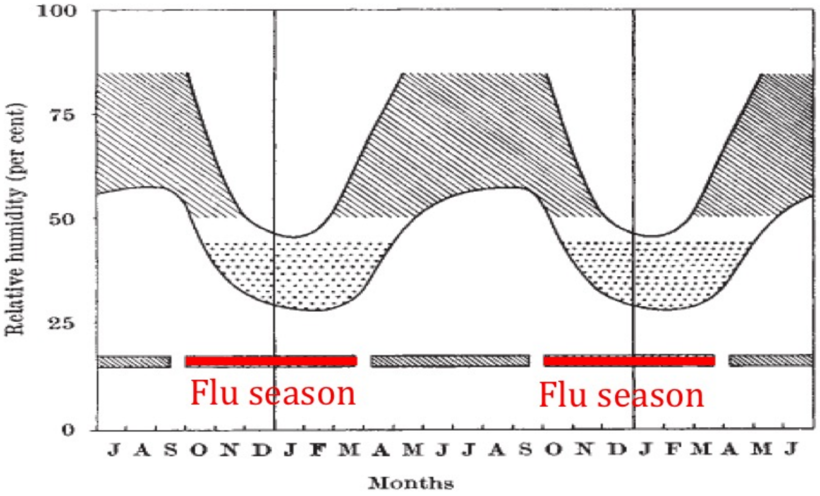
Hospitalization

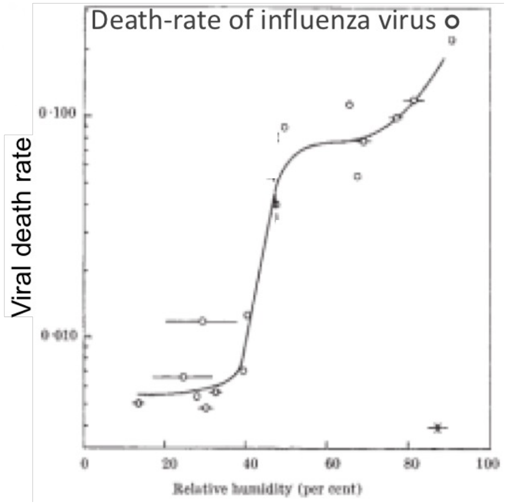
Mortality

Wiemken et al. 2023 Scientific Reports.

General mechanisms behind this seasonality

- **Three main mechanisms** (Moriyama et al. 2020 Annual Review of virology)
  - Host vulnerability
  - Host behavior
  - Viral stability (Environmental factors: temperature, humidity)
- **Flu seasonality v. humidity**
  - H: Low wintertime humidity drives flu epidemic (Hemmes et al. 1960)
    - Temperate regions: Flu epidemic coincides with low indoor humidity
    - Influenza virus survives better at lower humidity
  - *Supports the seasonality in temperate regions, but not the (sub)tropics*



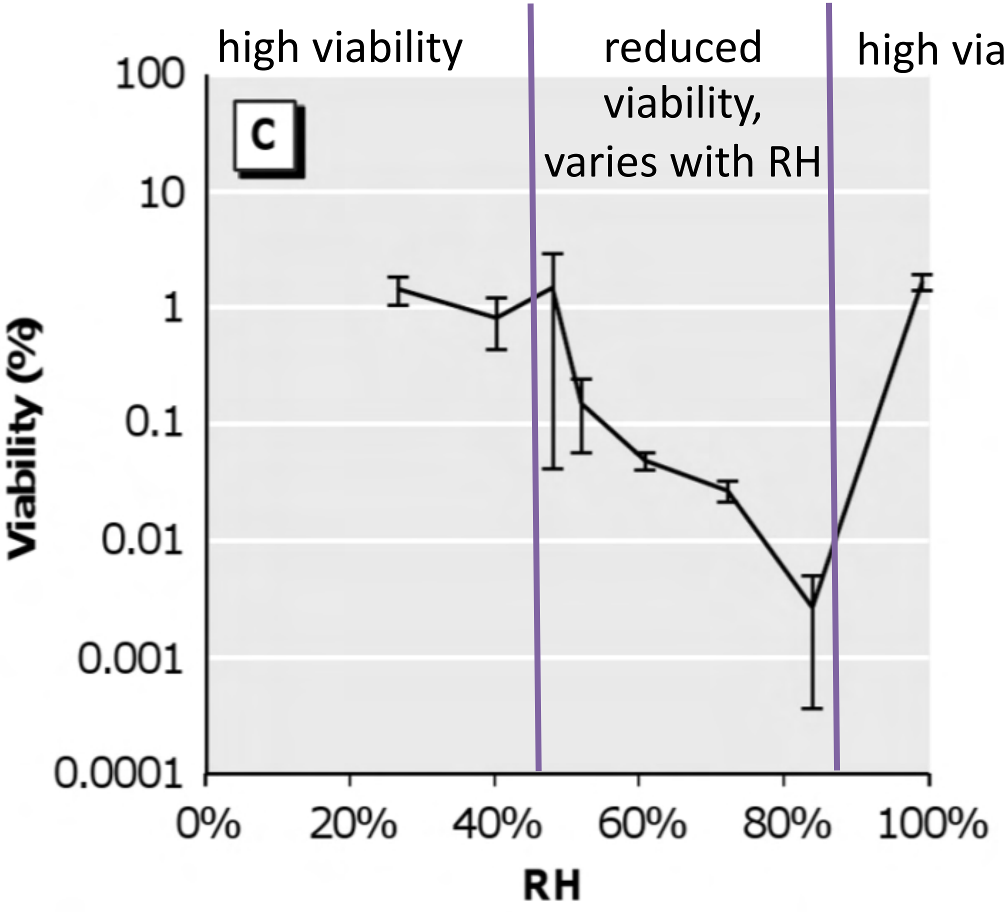


Hemmes et al. Nature 1960

(SELECT) LABORATORY STUDIES: ENVIRONMENTAL FACTORS, AND UNDERLYING MECHANISMS

Laboratory studies: Influenza

- **Study:** Testing flu viability in mucus, under a wide range of humidity
  - Including humidity near 100%
- **Result: Bimodal response**



high viability

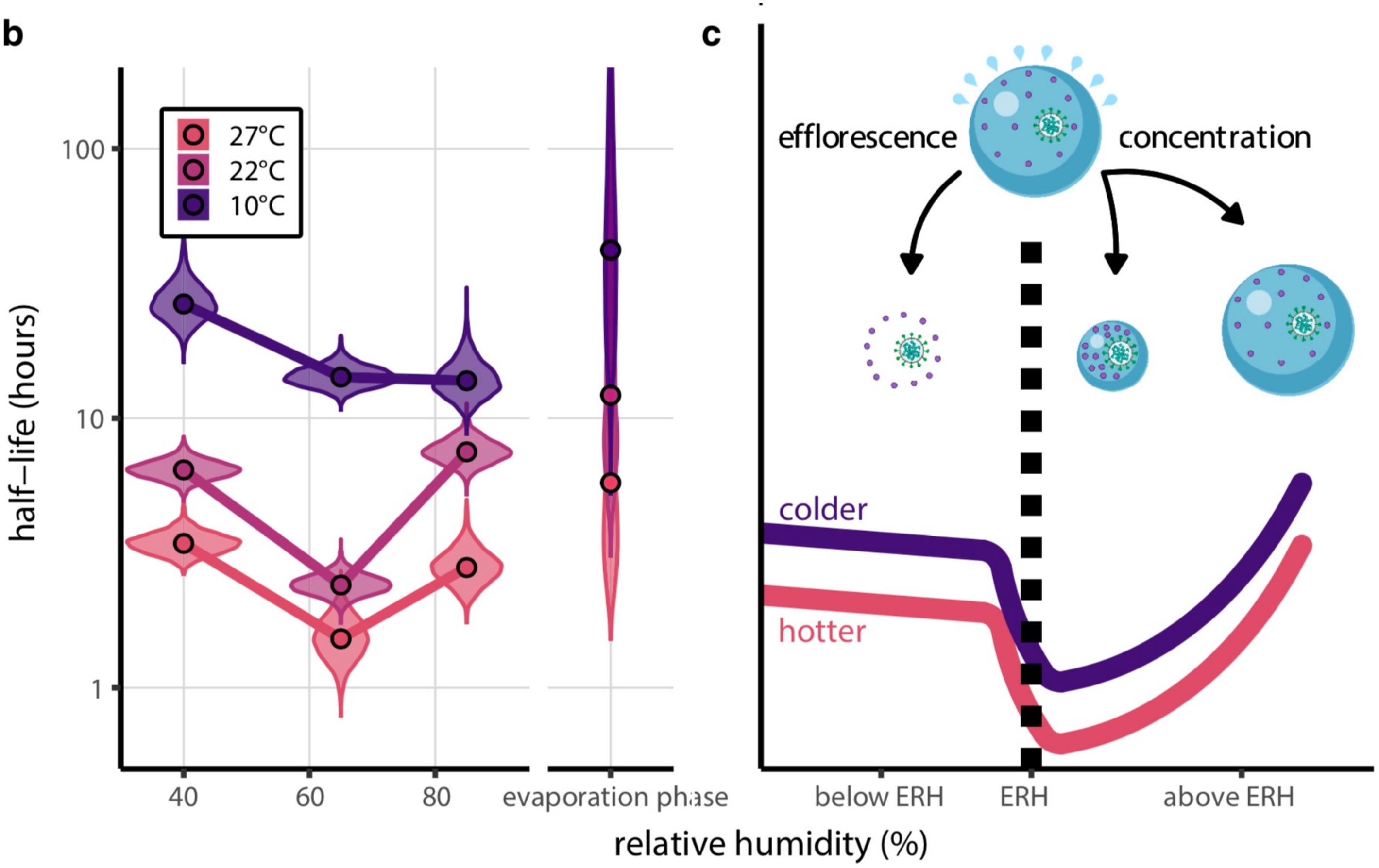
reduced viability, varies with RH

high viability

Yang et al. *PLoS One* 2012

Laboratory studies: SARS-CoV-2/COVID-19

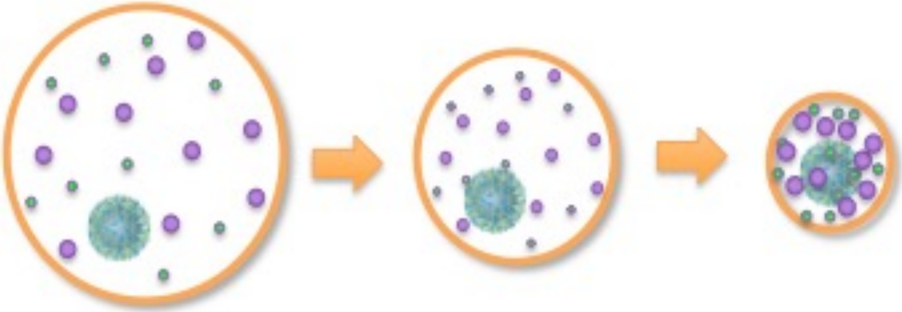
- **Estimated half-life of SARS-CoV-2 on an inert surface vs. Relative Humidity & Temperature** (Morries et al. 2021 *eLife*)



Morries et al. 2021 *eLife*

Potential mechanisms

- ***Why would a virus within a droplet be affected by ambient humidity?***



Relative humidity

Köhler theory

$$\underset{\uparrow}{RH} = \frac{p_\infty}{p_{sat}} \;\overset{\text{Equilibrium}}{\underset{p_\infty = p_d}{=\!=\!=\!=\!=}}\; \frac{p_d}{p_{sat}} = \exp\left(-\frac{6imM_w}{M_s \rho\pi \underset{\uparrow}{d}^3}\right)\exp\left(\frac{4\gamma M_w}{\rho RT\underset{\uparrow}{d}}\right)$$

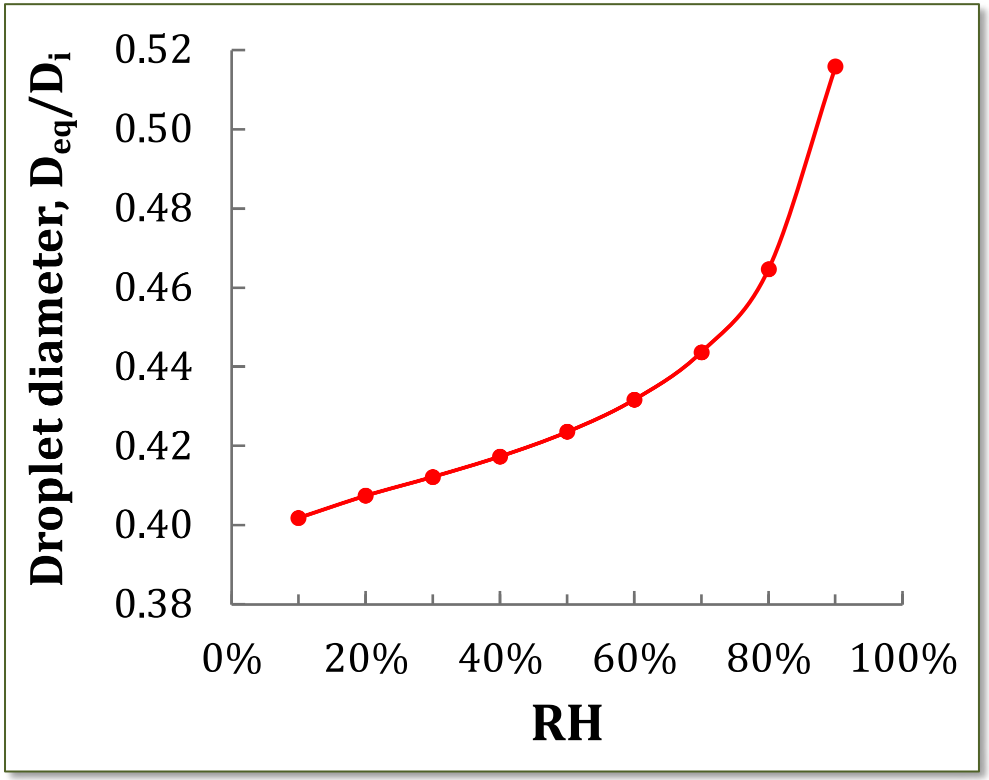
The final droplet/aerosol size depends on ambient humidity

http://www.masterfile.com/stock-photography/image/700-00911645/Bird-Flu-Virus-Under-Magnifying-Glass

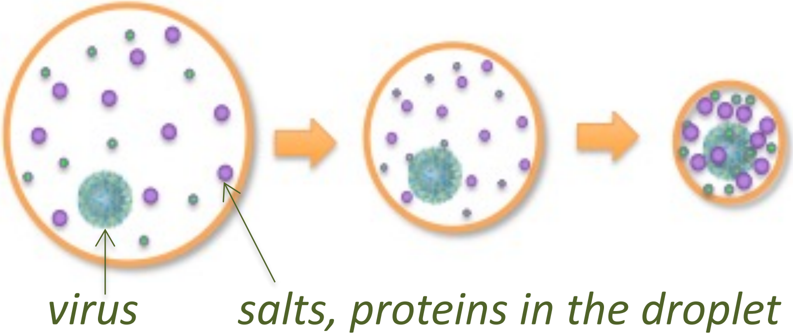
Potential mechanisms

- **Relative humidity v. droplet size (Köhler theory)**

$$RH = \frac{p_\infty}{p_{sat}} \xrightleftharpoons[p_\infty = p_d]{\text{Equilibrium}} \frac{p_d}{p_{sat}} = \exp\left(-\frac{6imM_w}{M_s \rho \pi d^3}\right) \exp\left(\frac{4\gamma M_w}{\rho R T d}\right)$$



Yang et al. 2011 PLoS One



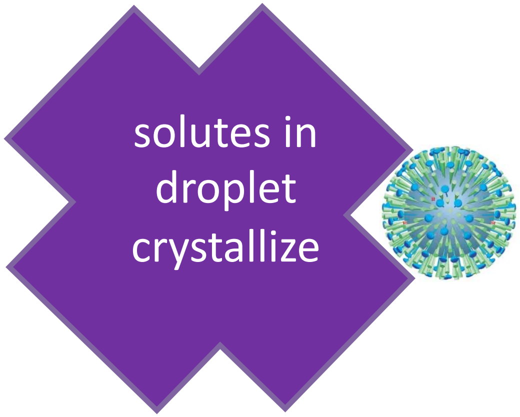
Droplet shrinks by half -->
Concentration increases by 8 times
D--> ½ D
Vol. --> 1/8 Vol.
Conc. --> 8 Conc.

Humidity changes => The micro-environment surrounding the virus changes!

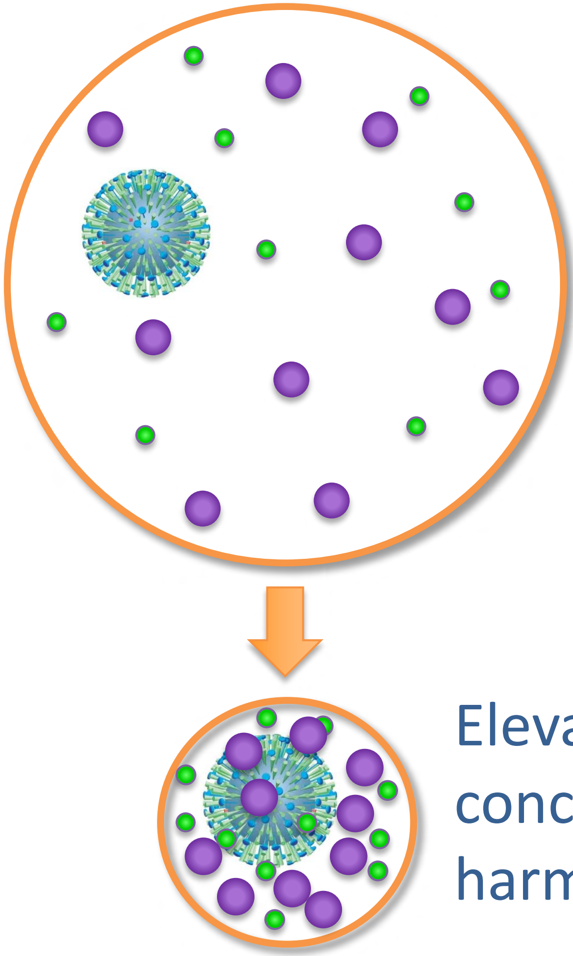
Potential mechanisms: Viability and Three RH Regimes

Low RH (<50%)

Efflorescence occurs ->solutes cannot harm virus -> viability is maintained



Medium RH



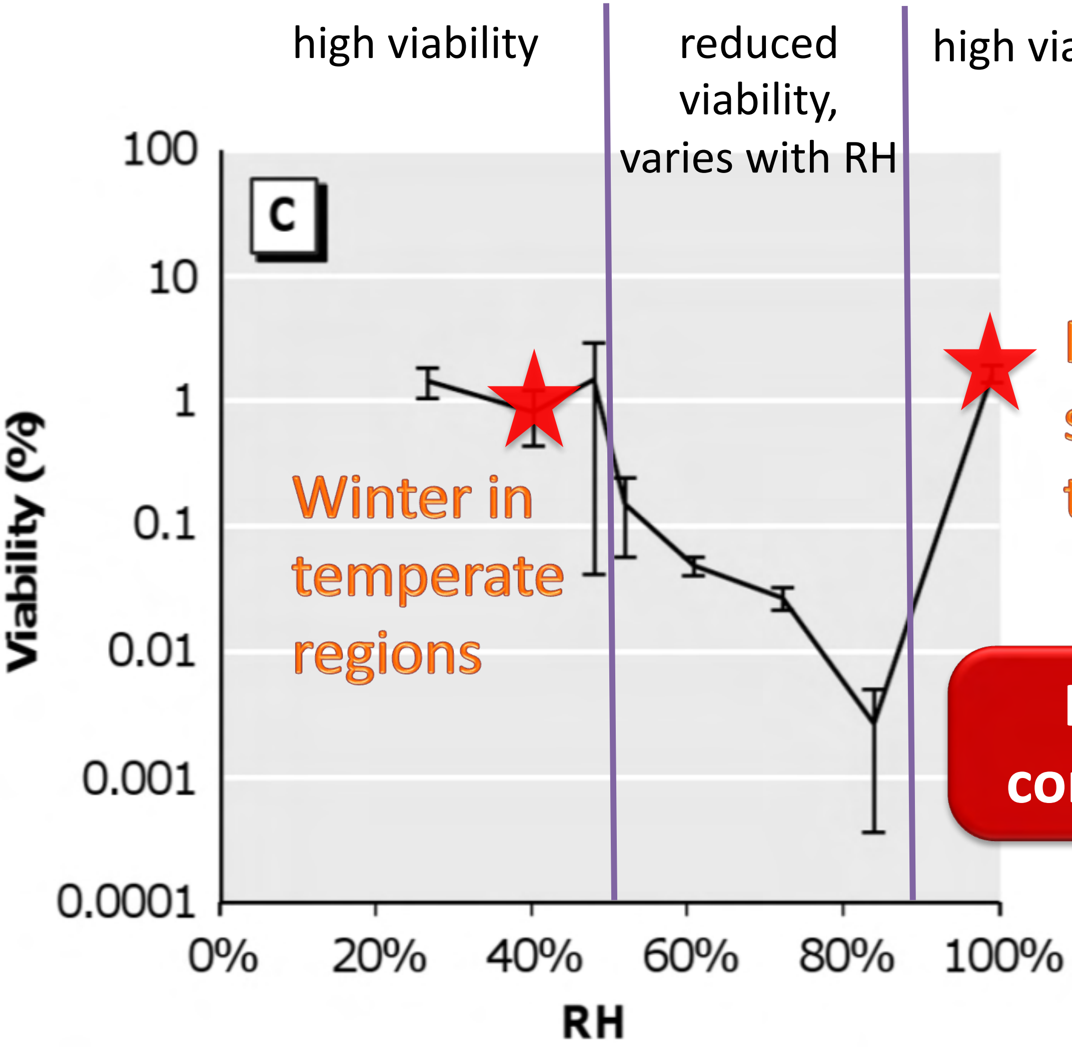
Elevated solute concentrations may harm virus

Very high RH

Minimal evaporation -> physiological conditions are maintained in droplet -> viability is maintained

Slide credit: Linsey Marr; Yang et al., 2012, *PLoS One;* 2012 *AEM*

Potential mechanisms: Viability, Three RH Regimes, and Seasonality



high viability

reduced viability, varies with RH

high viability

Winter in temperate regions

Rainy season in the tropics

It is likely not merely correlation but causation

Yang et al. *PLoS One* 2012

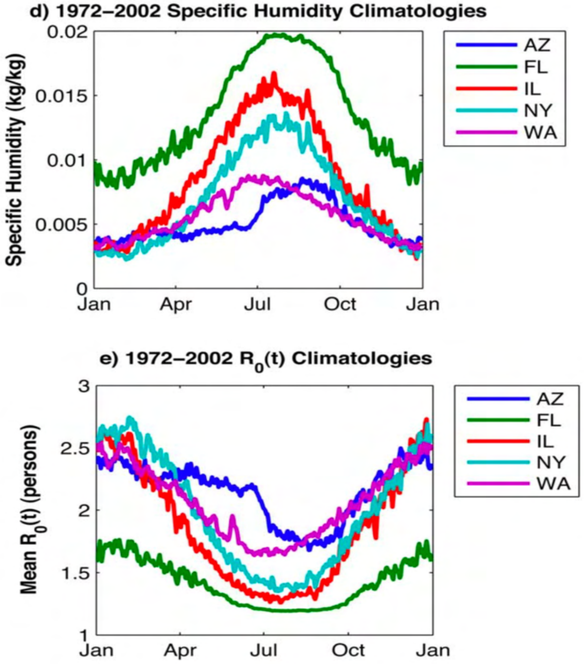
MODEL:
MODELING THE SEASONALITY USING CLIMATE/ENV. CONDITIONS

Temperate regions: A humidity-forced SIRS model for influenza (low humidity -> high transmission)

- **The model:**

$$\frac{dS}{dt} = \frac{N-S-I}{L} - \frac{\beta(t)IS}{N}$$

$$\frac{dI}{dt} = \frac{\boxed{\beta(t)}IS}{N} - \gamma I$$

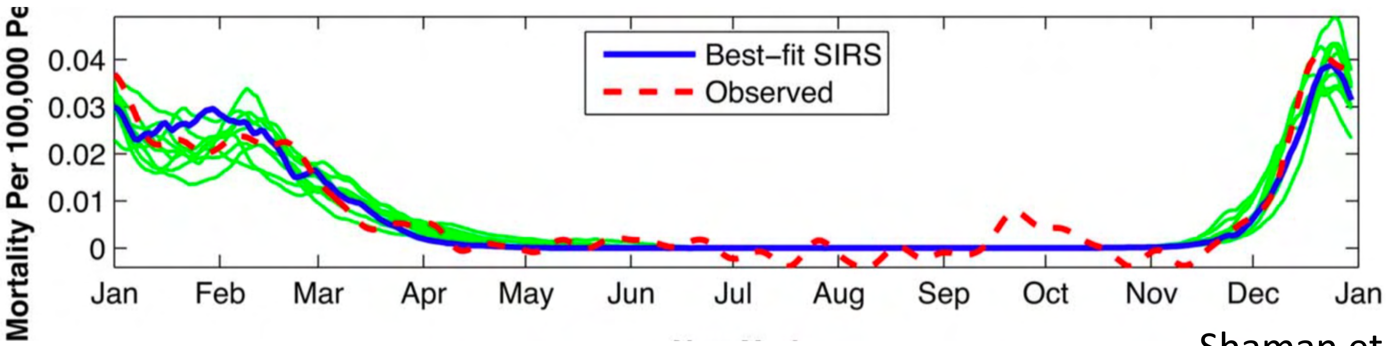


  - ○ *β(t)* is modulated by humidity

$$\beta(t) = (R_{0min} + (R_{0max} - R_{0\min})e^{-180q(t)})\gamma$$

    - ❖ *q(t)*: daily specific humidity
    - ❖ R0min/R0max: min/max bound of R0

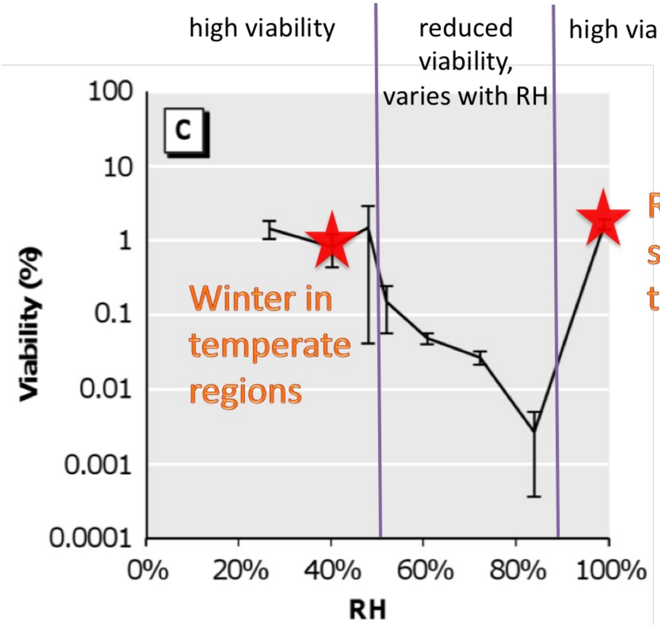
- **Finding: The model is able to recreate the flu epidemic dynamics**



Shaman et al. 2010. PLoS Biol.

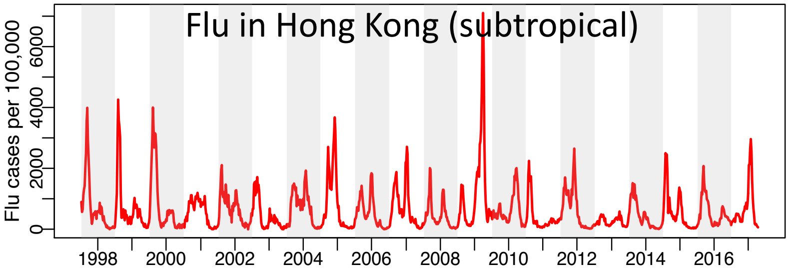
What about the (sub)tropics?

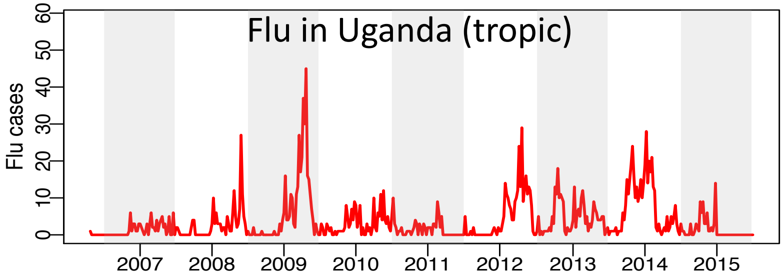
- **Differences vs. temperate climates**
  - (Sub)tropics: Flu can occur year round
  - Humidity: response is not monotonic
    - Recall: viability is high at both very low and very high humidity



Winter in temperate regions

Rainy season in the tropics


Flu in Hong Kong (subtropical)


Flu in Uganda (tropic)

  - Temperature: Also play a key role

Yang et al. 2012 Plos One;
Yang et al. 2018a *Epidemics*;
Yang et al. 2018b *IRV*;
Yang et al. 2020 *PLoS Comput Biol*

A unified climate forced model (influenza)

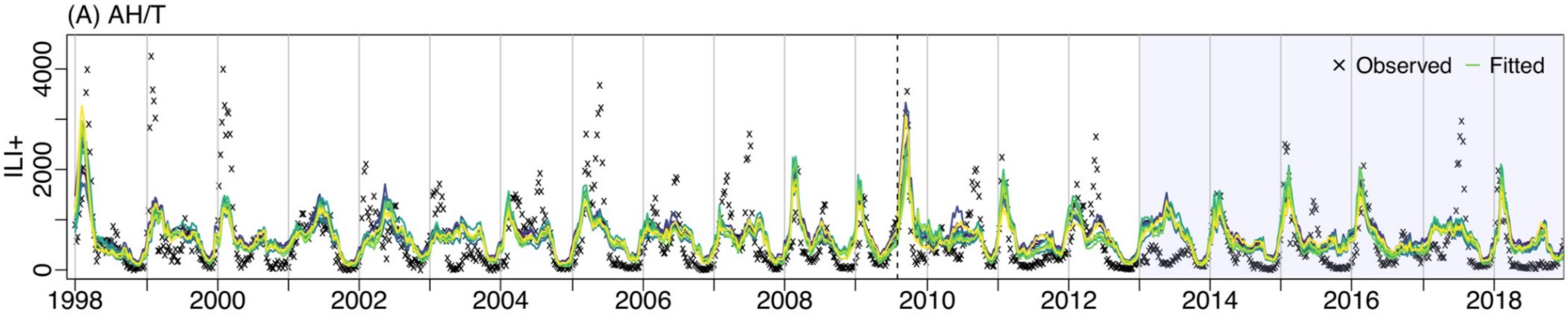
- **Model:** $R_0(t) = \underbrace{[aq^2(t) + bq(t) + c]}_{\text{Bimodal response to humidity, q(t)}}\underbrace{[\frac{T_c}{T(t)}]^{T_{exp}}}_{\text{Include the impact of temperature, T(t)}}$

  Bimodal response to humidity, q(t)

  Include the impact of temperature, T(t)

- **Model testing and parameter estimation:**
  - Combined with an SIRS model, tested using flu incidence data in Hong Kong (subtropical) over ~20 years

- **Results:**
  - Model captures the bimodal epidemics in HK

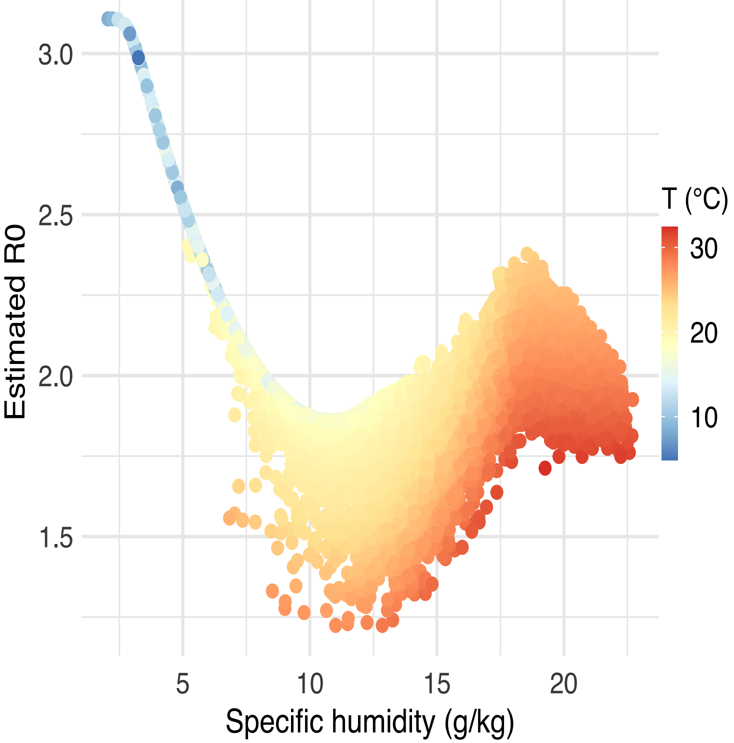


Yuan, Kramer et al. 2021 PLoS Comput Biol

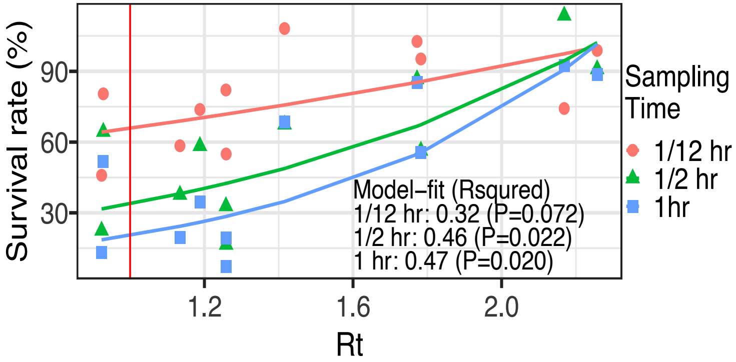
A unified climate forced model (influenza)

- **Model form:** $R_0(t) = [aq^2(t) + bq(t) + c][\frac{T_c}{T(t)}]^{T_{exp}}$
- **Results:**
  - ○ Model captures the bimodal epidemics in HK
  - ○ Covers both (sub)tropical and temperate climate conditions
  - ○ Consistent with lab virus survival/transmission data

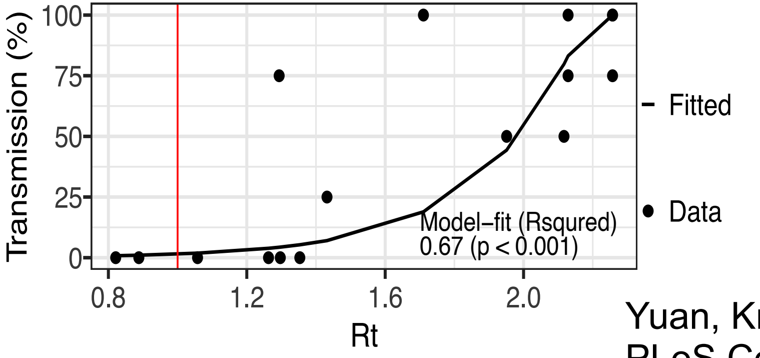
(A) Seasonal R0 vs. Humidity & Temperature



(B) Estimate Rt vs Lab data on viral survival



(C) Estimate Rt vs Lab data on transmission



Yuan, Kramer et al. 2021
PLoS Comput Biol

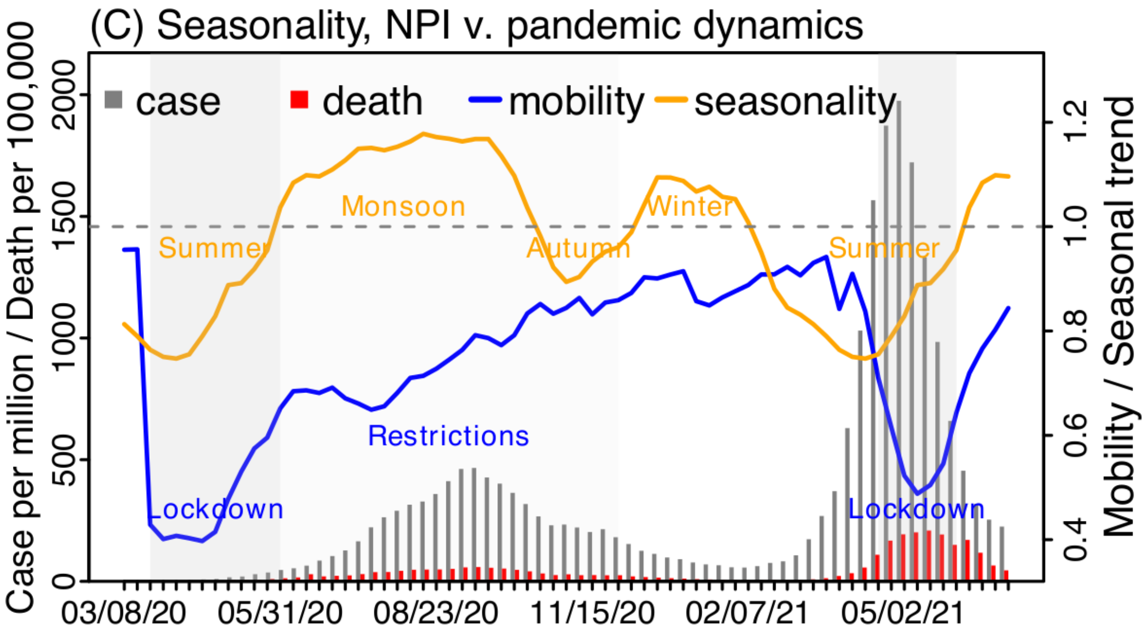
Can we use the model for SARS-CoV-2/COVID-19?

- **Method:** Scale the estimates to the annual average -> extract the seasonal trend
- **Incorporate the seasonal trend into epi-models to account for infection seasonality**

$$R_0(t) = [aq^2(t) + bq(t) + c][\frac{T_c}{T(t)}]^{T_{exp}}$$

$$b_t = R_0(t)/\overline{R_0(t)}$$

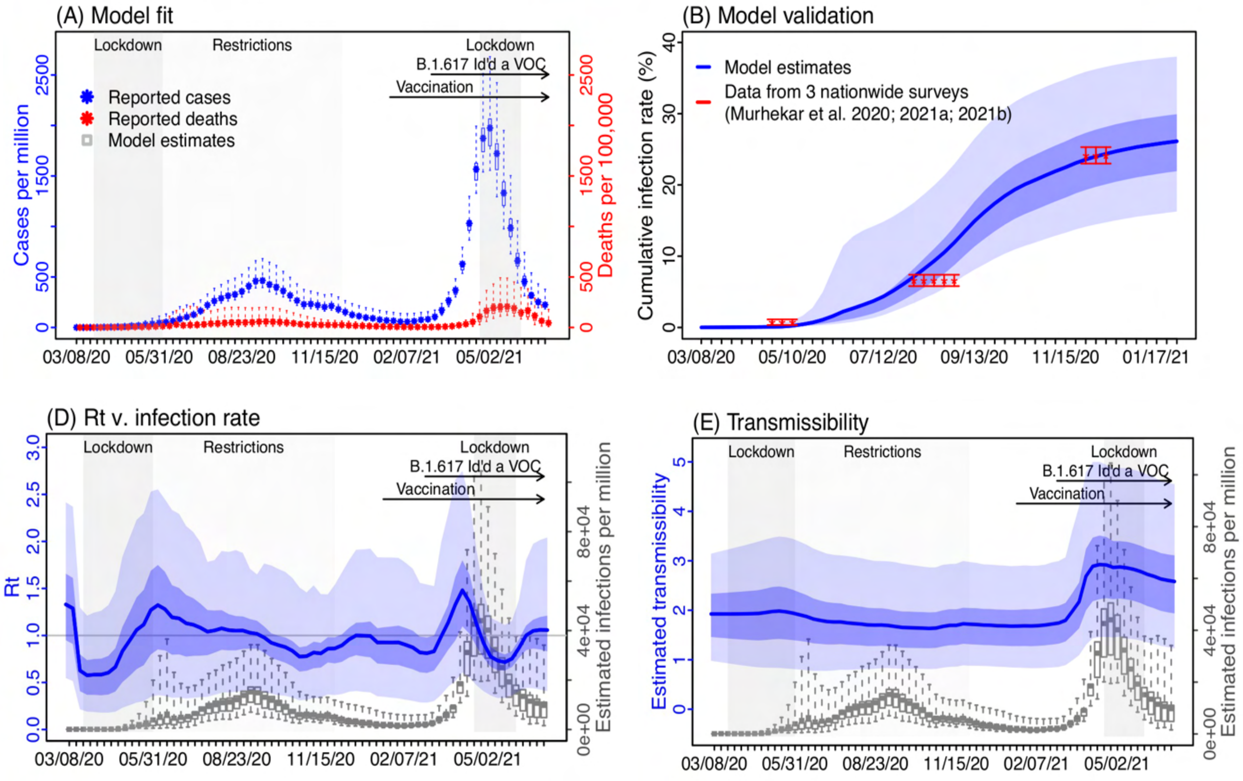
$$\begin{cases} \frac{dS}{dt} = \frac{R}{L_t} - \frac{b_t e_t m_t \beta_t IS}{N} - \varepsilon - v_{1,t} - v_{2,t} \\ \frac{dE}{dt} = \frac{b_t e_t m_t \beta_t IS}{N} - \frac{E}{Z_t} + \varepsilon \\ \frac{dI}{dt} = \frac{E}{Z_t} - \frac{I}{D_t} \\ \frac{dR}{dt} = \frac{I}{D_t} - \frac{R}{L_t} + v_{1,t} + v_{2,t} \end{cases}$$



Example Seasonal trend for India vs. other factors (Yang & Shaman 2022 RSIF)

Example: Modeling COVID-19 in India (monsoon climate)

- **Study:** Combining key transmission determinants and data to model the COVID-19 pandemic in Indian (1^{st} wave and the Delta wave)



Model validation showed the system is able to capture the underlying dynamics

R_t fluctuated over time

vs.

Transmissibility (R_{TX}) ↗ following rise of Delta

By accounting for <u>seasonality</u>, NPIs etc., we can ***estimate variant-specific properties***

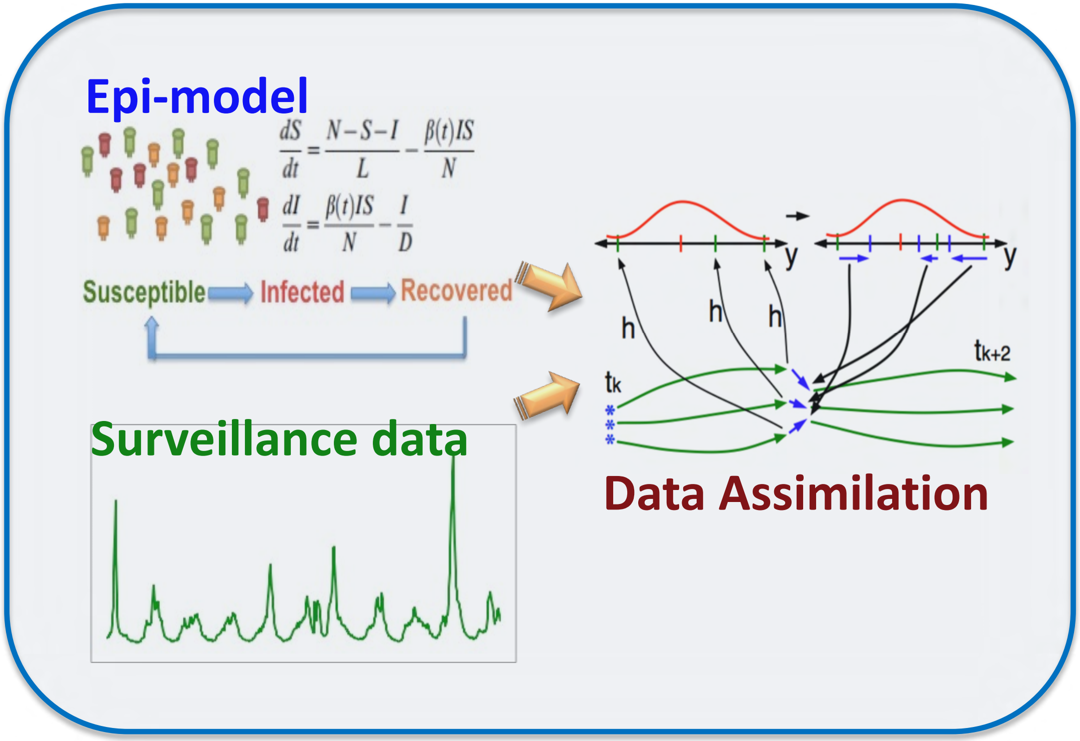
Applicable to diverse climate conditions and variants (Alpha in UK: NH temperate; Beta/Omicron in S Africa: SH temperate; Gamma in Brazil: tropical; Delta in India: monsoon)

Yang & Shaman: 2021 Nature Comm; 2022 RSIF; 2022 eLife

FORECAST: USING THE SEASONALITY MODELS TO IMPROVE FORECAST ACCURACY

Overview of our forecast system

- **3 components: Model + Data + Data Assimilation**
- **2 stages: Training + Forecast**



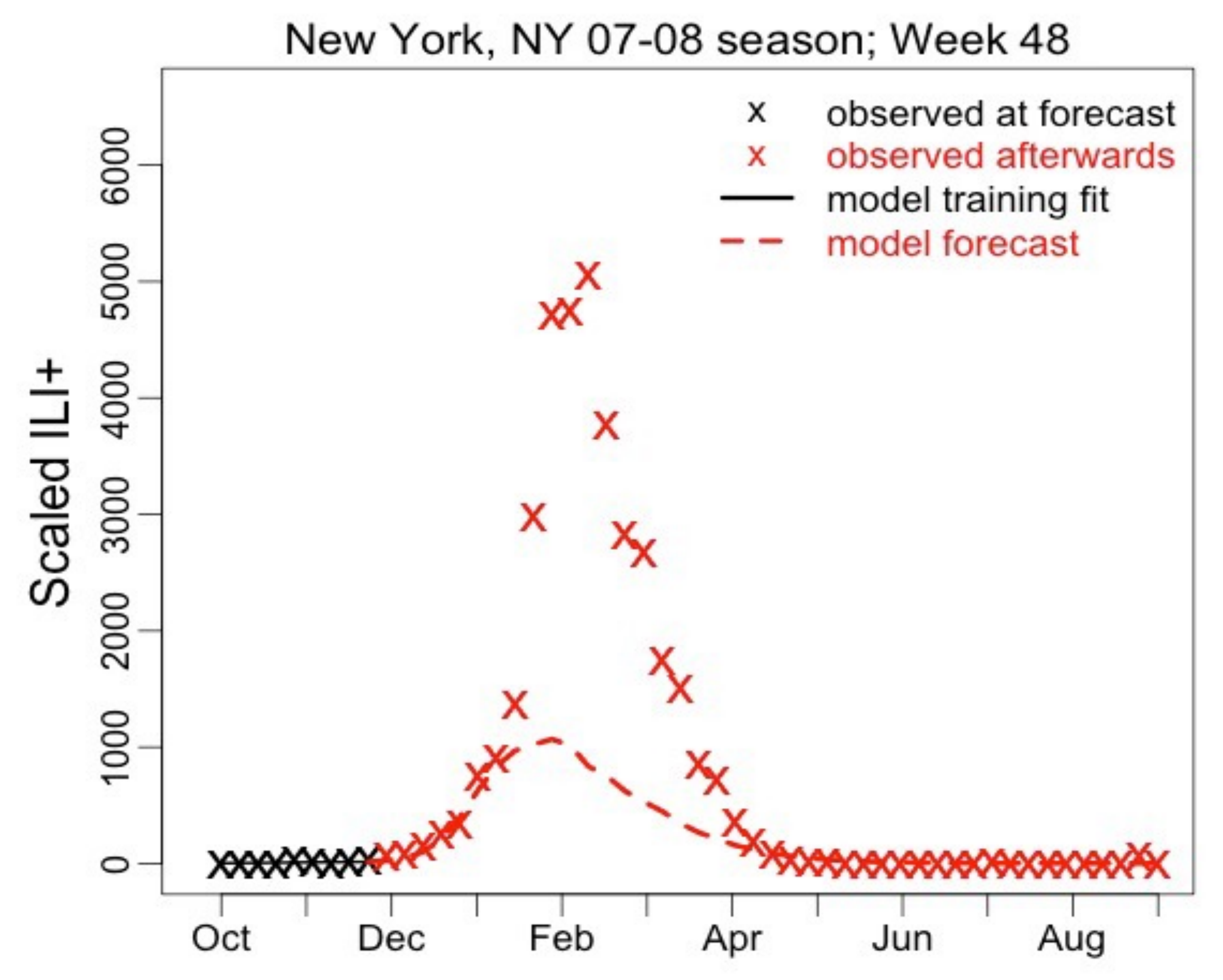
$$\frac{dS}{dt} = \frac{N-S-I}{L} - \frac{\beta(t)IS}{N}$$

$$\frac{dI}{dt} = \frac{\beta(t)IS}{N} - \frac{I}{D}$$

- **Stage1: Training**
  Optimize the model;
  get initial conditions

- **Stage 2: Forecast**
  Predict epi-unfolding

Example forecast



Example retrospective forecast. The forecast is increasingly accurate as more observations are assimilated.

Influenza forecast

- **Study:** Test the forecast accuracy using different settings of humidity forcing vs no humidity included in the model
- **Result:** The inclusion of humidity improves accuracy

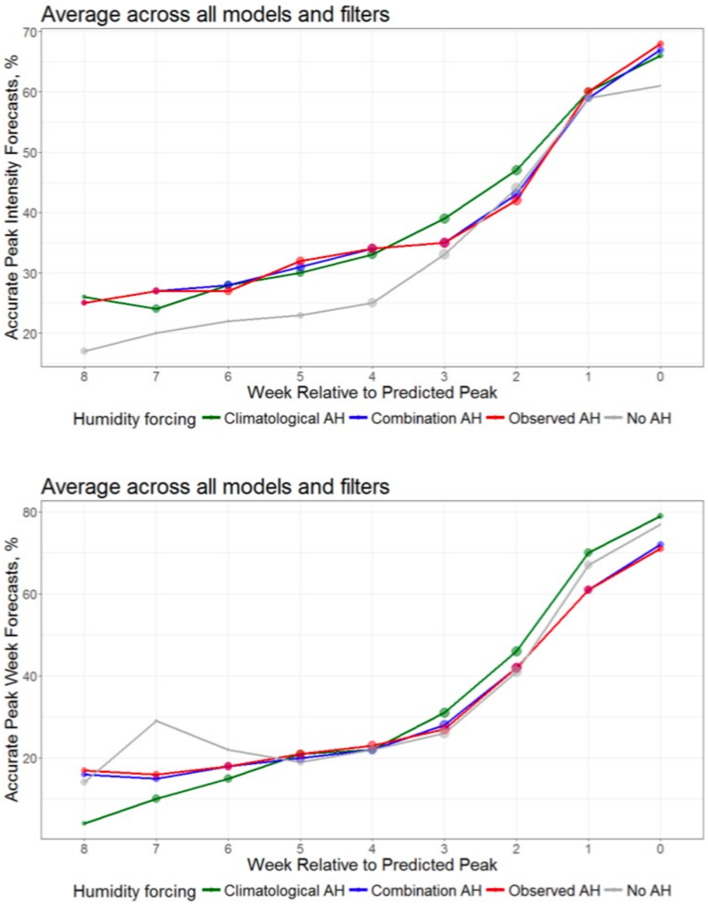
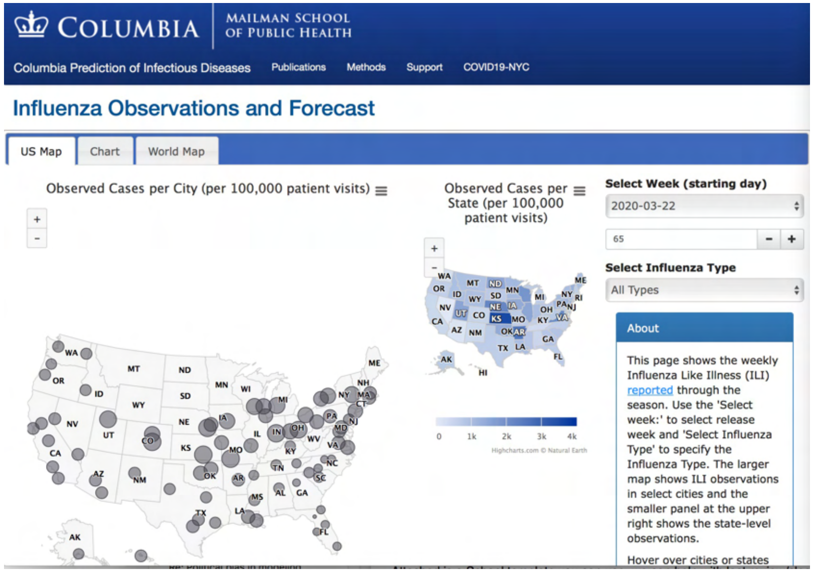


Fig 1. Percentage of forecasts accurate for predictions of peak intensity and peak timing



Influenza Observations and Forecast

Select Week (starting day): 2020-03-22

65

Select Influenza Type: All Types

About

This page shows the weekly Influenza Like Illness (ILI) reported through the season. Use the 'Select week:' to select release week and 'Select Influenza Type' to specify the Influenza Type. The larger map shows ILI observations in select cities and the smaller panel at the upper right shows the state-level observations.

Hover over cities or states

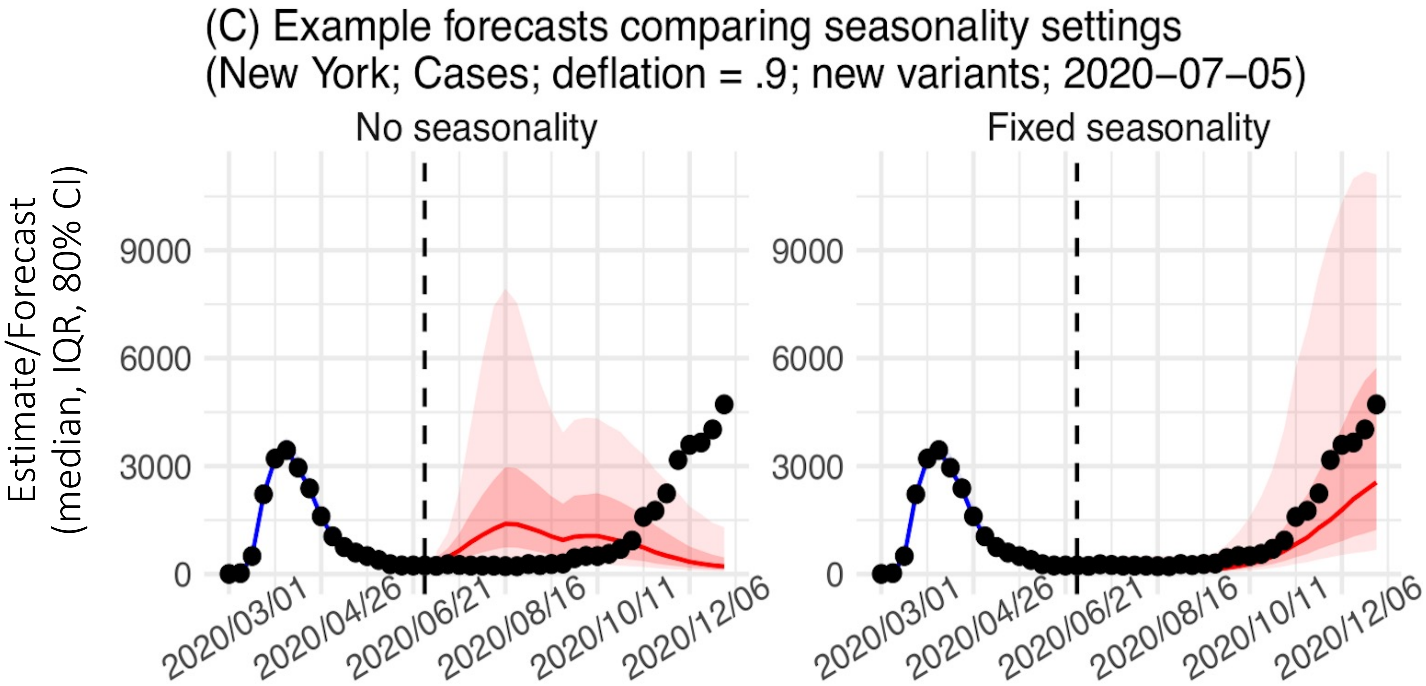
The humidity-forced SIRS model has been used in flu real-time forecast since 2012

Shaman et al.: http://cpid.iri.columbia.edu

Shaman et al. 2017 PLoSCB

COVID-19 forecast

- **Study:** Test multiple strategies to improve long-lead COVID-19 forecast
  - Study period: July 2020 – Sep 2022 (multiple waves)
  - 10 states, one each from the 10 HHS regions -> different seasonality
- **Result:** Including seasonality -> high accuracy in general, more so during the respiratory virus season



Yang & Shaman 2023 PLoS CB

PUBLIC HEALTH ACTION: HOW WOULD BETTER UNDERSTAND SEASONALITY HELP?

How would this help public health?

- **Use the seasonal timing/infection risk to guild vaccination campaign, public health messaging**
- **More accurate epidemiological parameter estimation -> better gauge risk**
- **More accurate forecast -> better aid public health preparation**

- **Example: Modeling and projection of COVID-19 in NYC**
  - Two versions of model-inference systems:
    - With vs. w/o seasonality
  - The system with seasonality predicted the 2nd wave (Fall/winter 2020), 6 months in advance

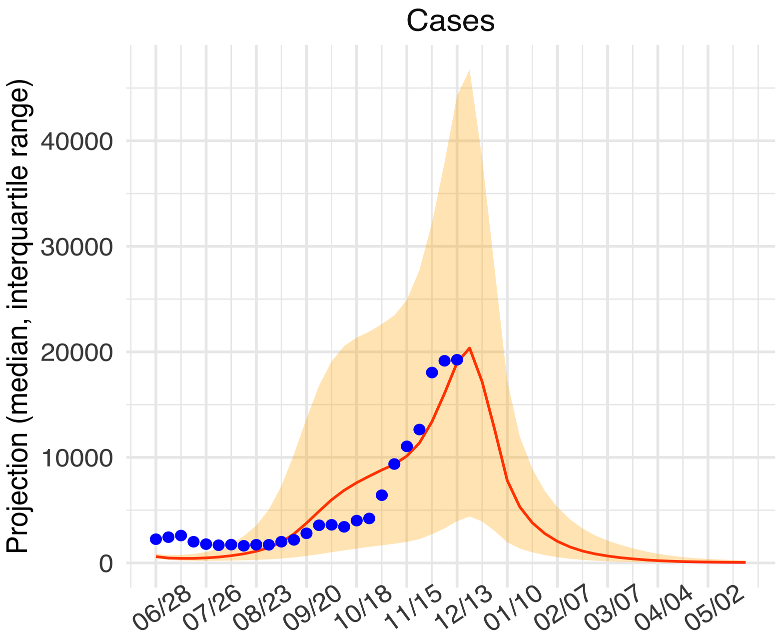


Fig: Model projection vs observations 6 months later
Red line: projection made on 6/30/2020;
surrounding area: projection interquartile range;
blue dots: observed (Yang et al. 2021 RSIF)

Yang et al. 2020 Lancet ID; 2021 RSIF; 2022 Sci Adv

SUMMARY

Summary

- **Infection seasonality plays a key role in epidemic dynamics**
- **Climate/environmental conditions (humidity and temperature) can modulate infection seasonality**
  - This interaction is causal, medicated by several mechanisms
- **Incorporating the response to environmental factors can improve the accuracy of infectious disease models and infectious disease forecasts**
- **The model estimates and forecasts can be used to guild public health action**
- **“Knowledge is power”**

thank you!