

Acute respiratory virus threats

Jonathan Dushoff, McMaster University

BIO Asia-Taiwan 2025
BioGroup Symposium: A Time to Shine

Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

Why is it flu?

Why is it not flu?

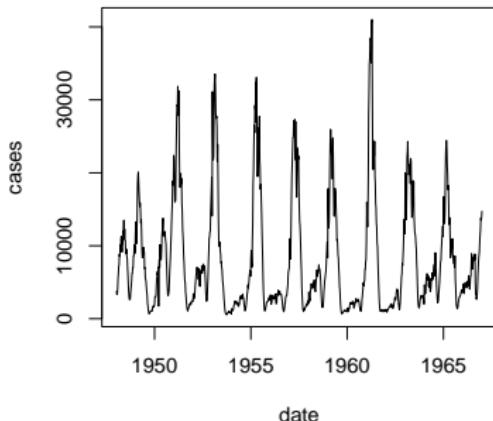
Public-health hybrid strategies

Pharmaceutical hybrid strategies

Dynamical modeling connects scales

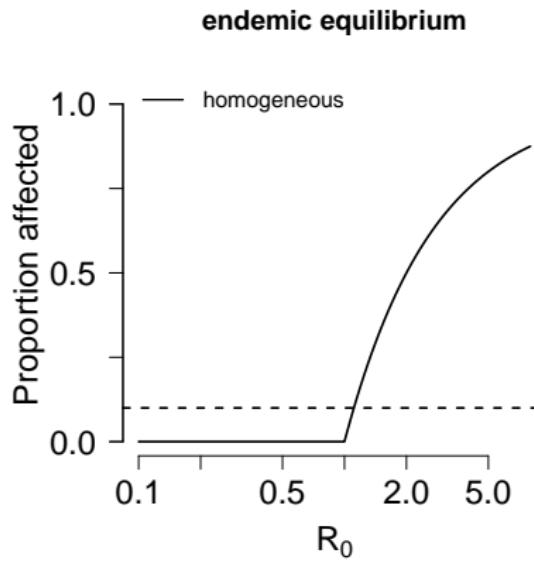


Measles reports from England and Wales

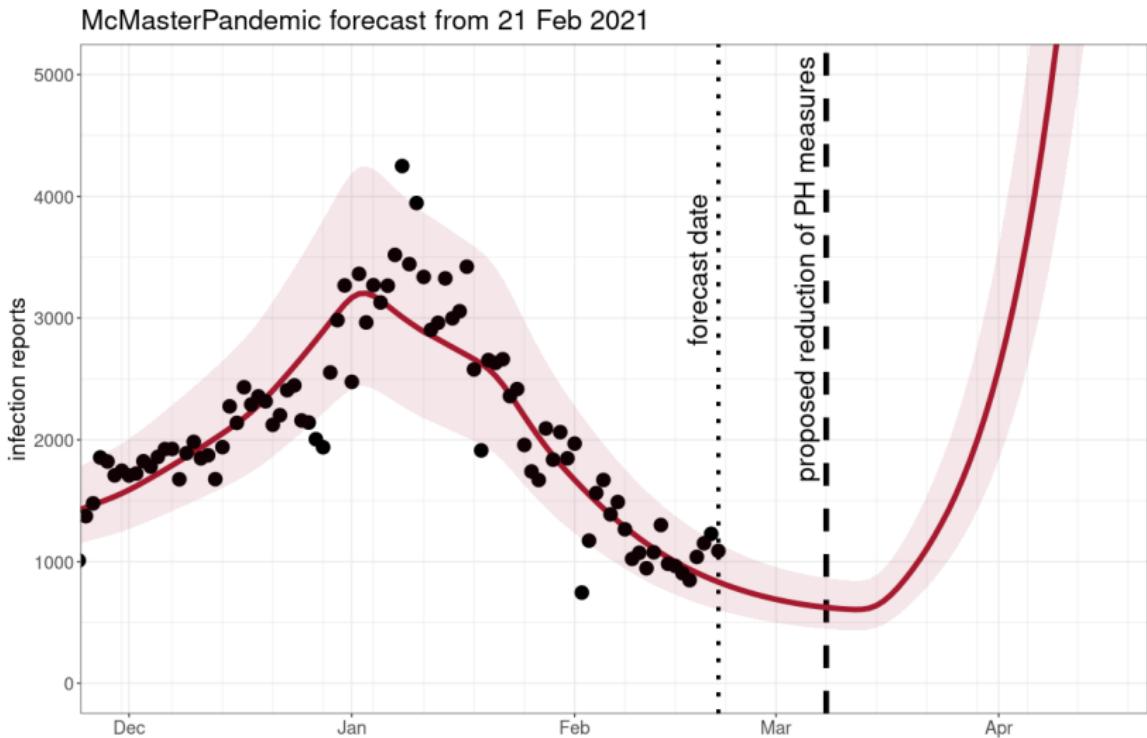


- ▶ Start with rules about how things change in short time steps
 - ▶ Usually based on *individuals*
- ▶ Calculate results over longer time periods
 - ▶ Usually about *populations*
- ▶ Also known as “mechanistic” or “mathematical”

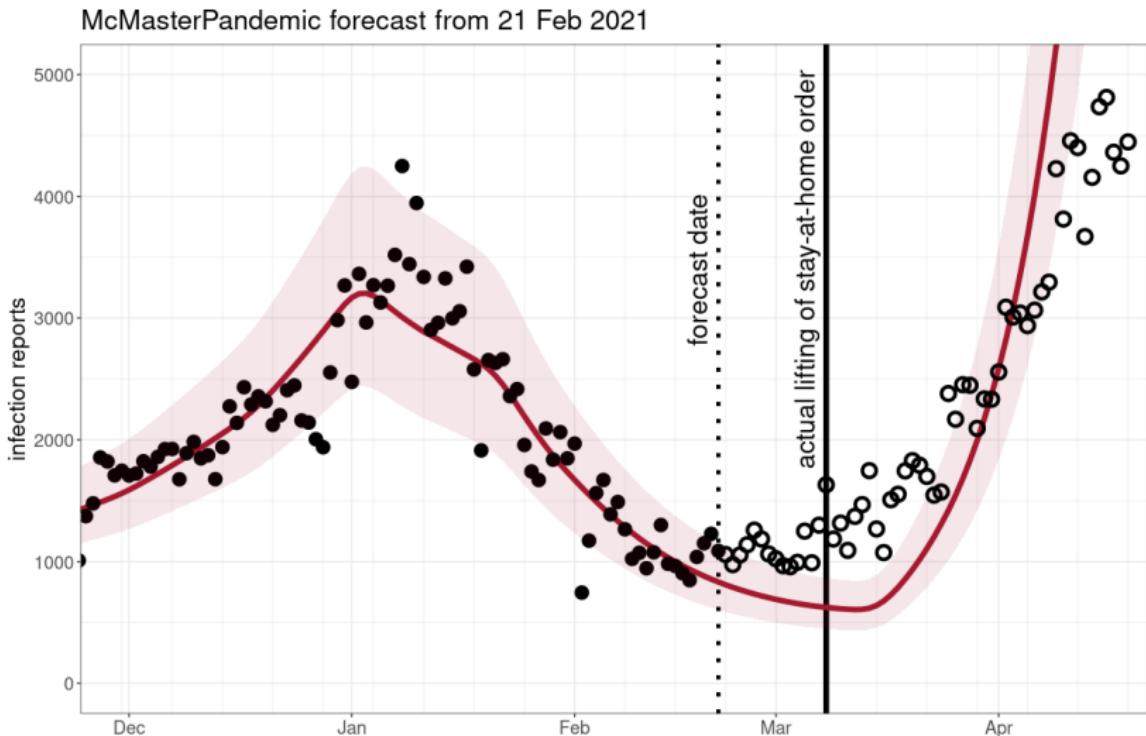
Yellow fever in Panama



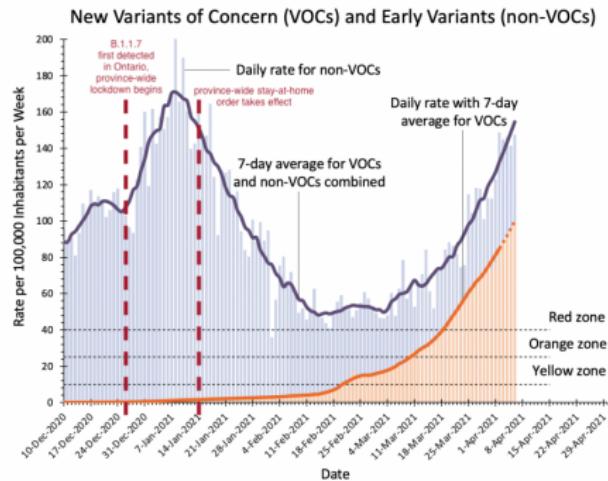
Example: COVID waves



Example: COVID waves



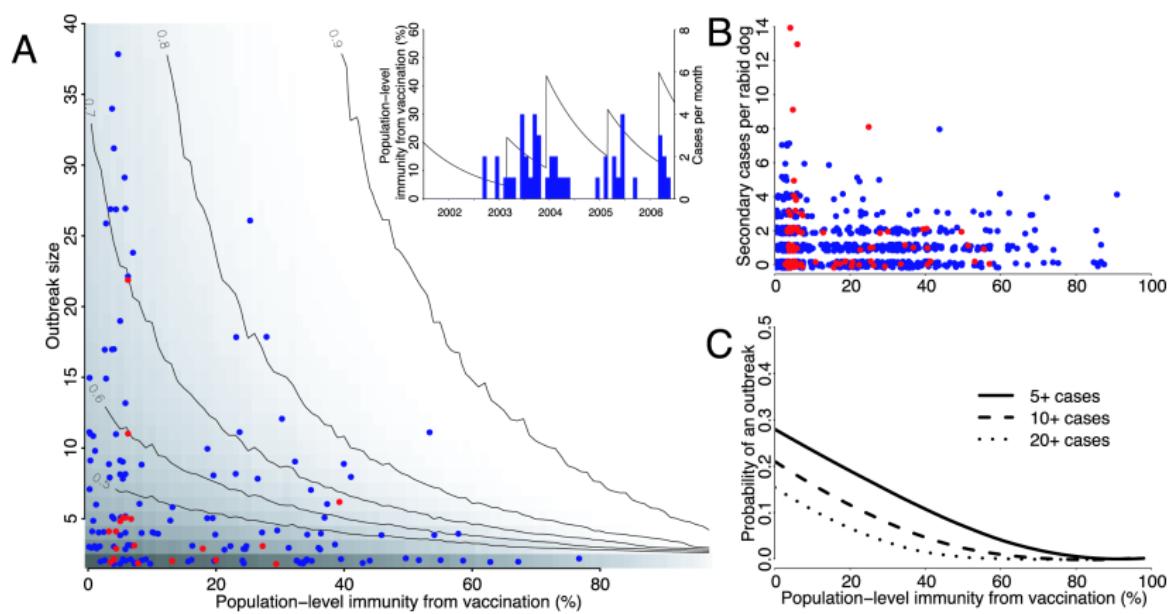
NOW Example: COVID waves



The daily rates of new variants of concern (VOCs) for the last 4 days are predicted.

- ▶ wt was declining
- ▶ alpha was increasing in the background
- ▶ Forecasts need data and dynamics

Example: rabies control



Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

Why is it flu?

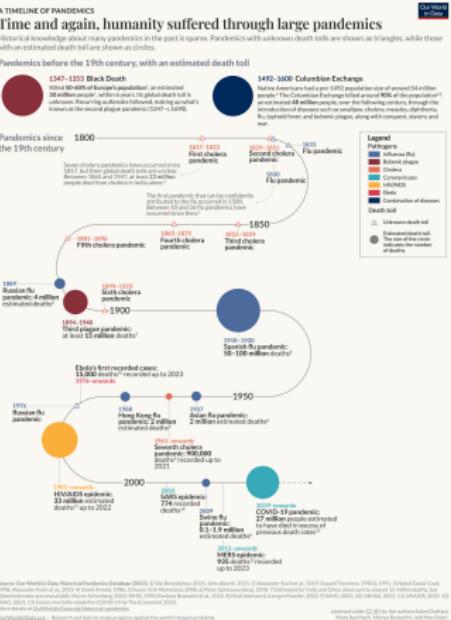
Why is it not flu?

Public-health hybrid strategies

Pharmaceutical hybrid strategies

Pandemics in history

- ▶ Black Death
- ▶ Eurasia meets America
- ▶ Cholera
- ▶ Flu
- ▶ HIV
- ▶ Covid



<https://ourworldindata.org/historical-pandemics>

What has changed?

- ▶ Sanitation, hygiene, clean-water access
- ▶ Germ theory of disease!
- ▶ Antibiotics
- ▶ Vaccines?
- ▶ Antiviral drugs
- ▶ Much of this could collapse, in an apparently unstable world

Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

Why is it flu?

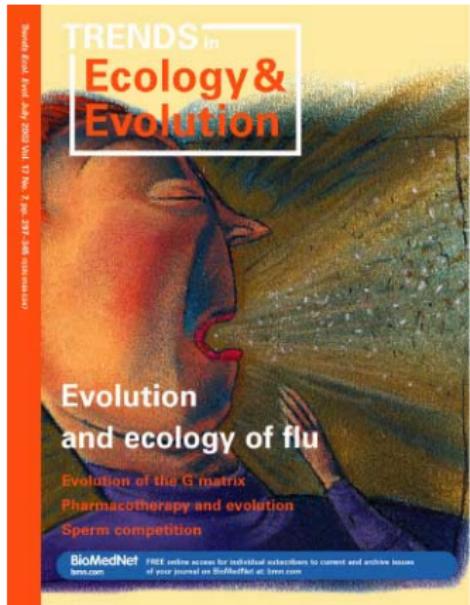
Why is it not flu?

Public-health hybrid strategies

Pharmaceutical hybrid strategies

Acute respiratory viruses (ARVs)

- ▶ Can spread relatively rapidly
 - ▶ Often before characteristic symptoms can be detected
- ▶ Spread through the air
- ▶ Not susceptible to traditional antibiotics



Circulating examples

- ▶ Influenza
- ▶ Coronaviruses
- ▶ RSV and other pneumoviruses
- ▶ Adenoviruses
- ▶ Entero- and rhinoviruses
- ▶ Parainfluenza viruses

Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

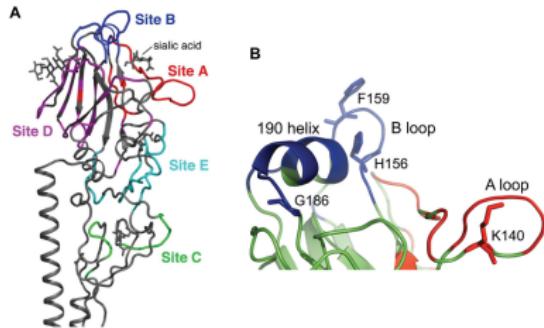
Why is it flu?

Why is it not flu?

Public-health hybrid strategies

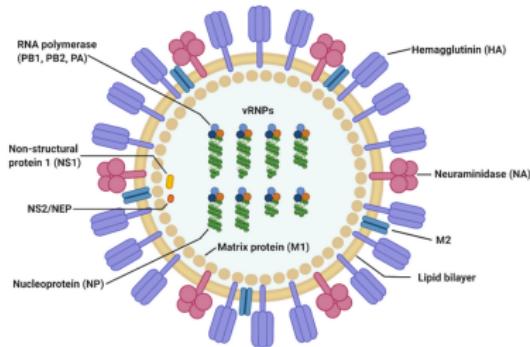
Pharmaceutical hybrid strategies

Flu is highly effective at evolving



Popova et al. 2012

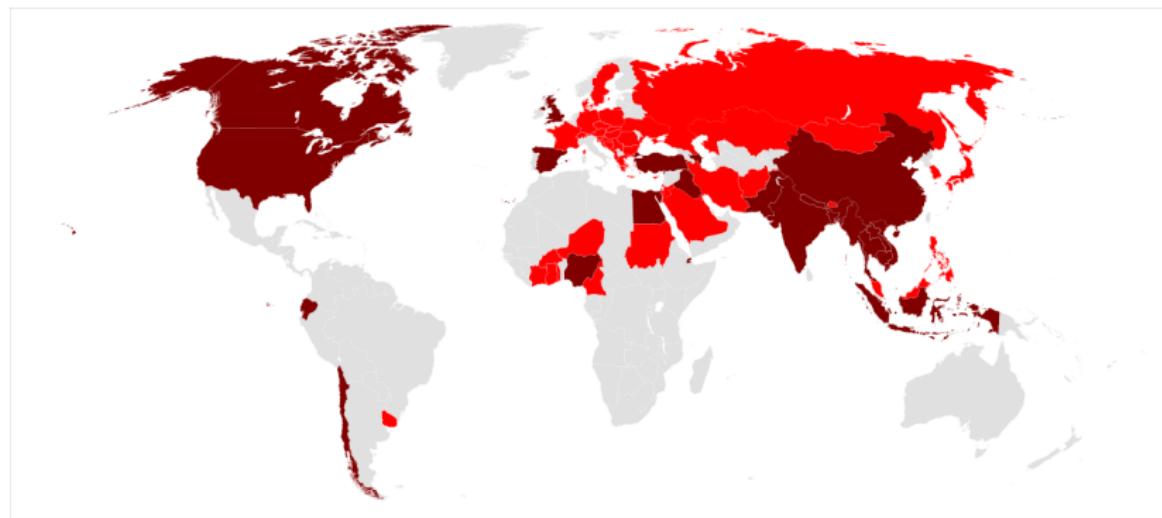
- ▶ Gradual drift
 - ▶ Antigenic loops
- Influenza antigenic loops



Hi Eun Jung and Heung Kyu Lee

- ▶ Dramatic shifts
- ▶ Effective reassortment

Flu is spreading in new species

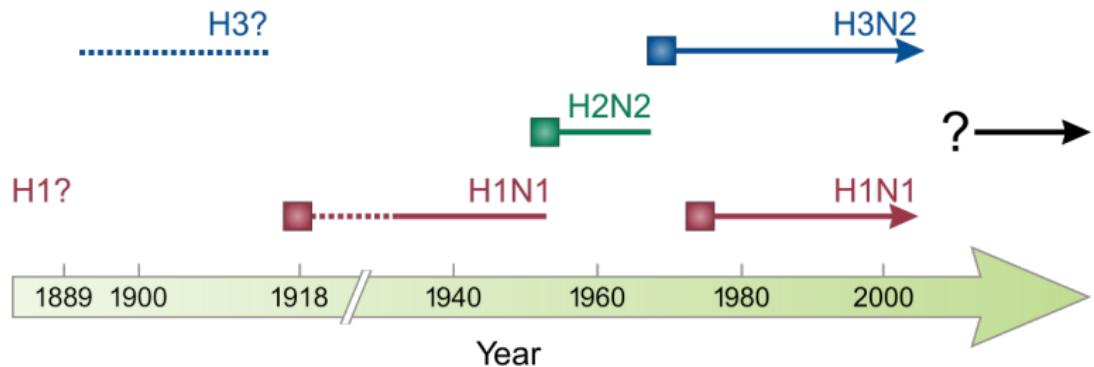


Credit: *IHaveBecauseOfLocks*

- ▶ foxes, sea lions, bears
- ▶ cows, goats, (chickens)

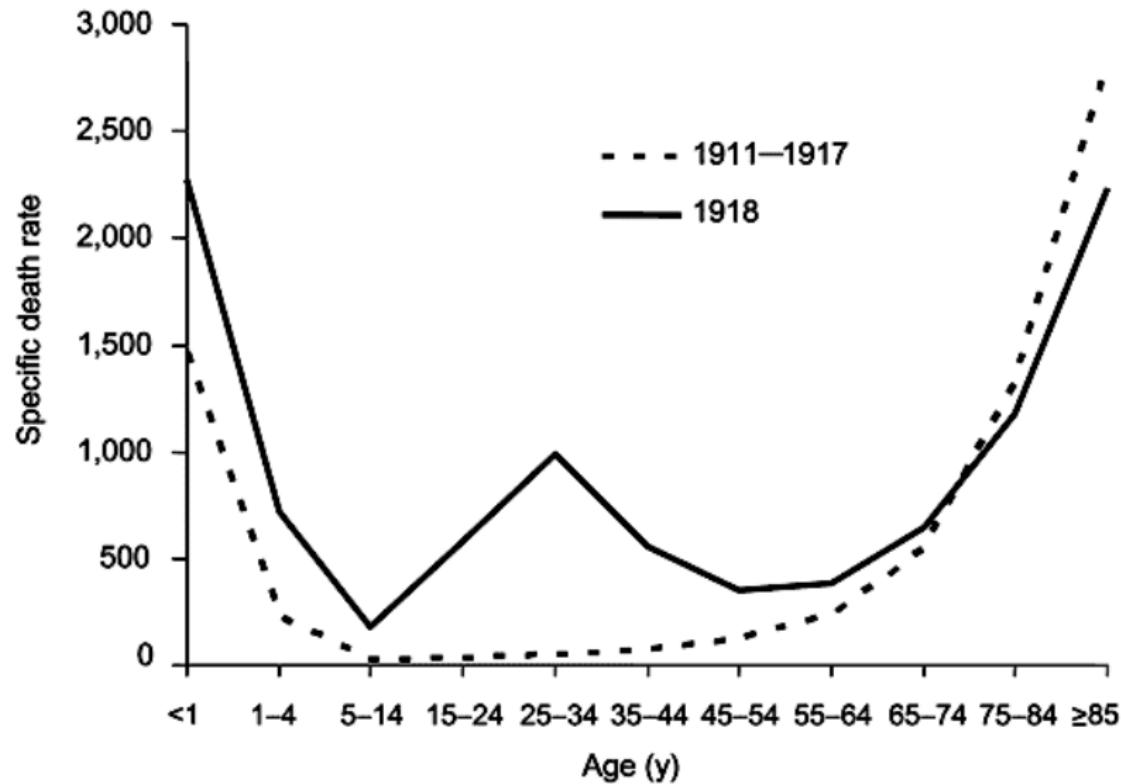
Flu has caused many pandemics in the past

Influenza A virus subtypes in the human population



Credit: Fvasconcellos

Flu caused the deadliest pandemic we know about



Taubenberger and Morens

Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

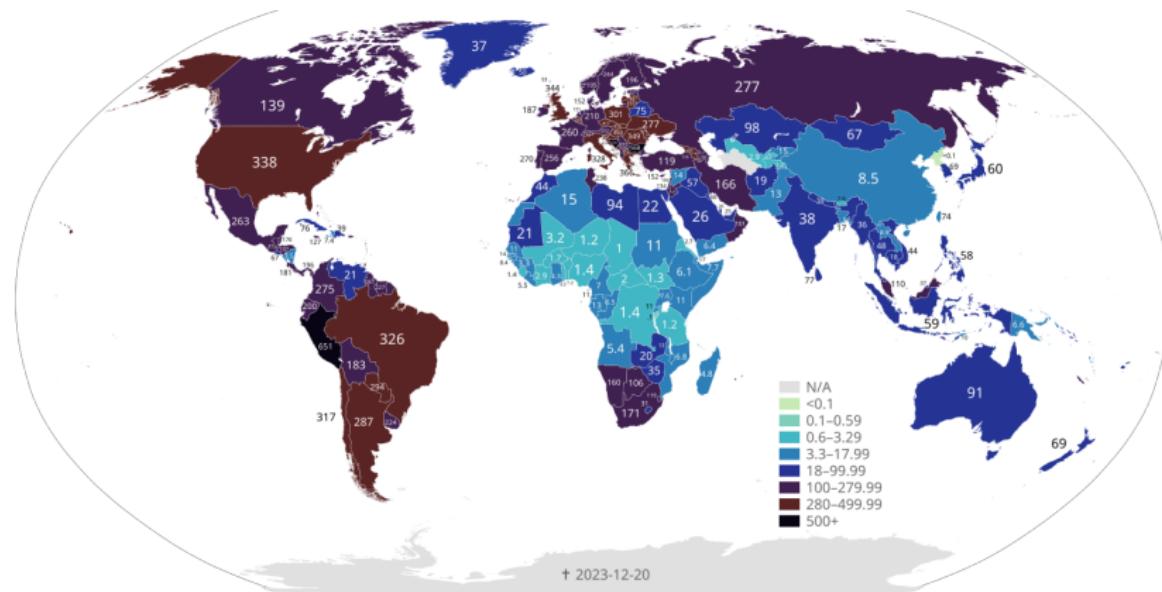
Why is it flu?

Why is it not flu?

Public-health hybrid strategies

Pharmaceutical hybrid strategies

COVID



Reported COVID-19 Deaths per 100Kp

Dan Polansky and wikipedia map collaborators

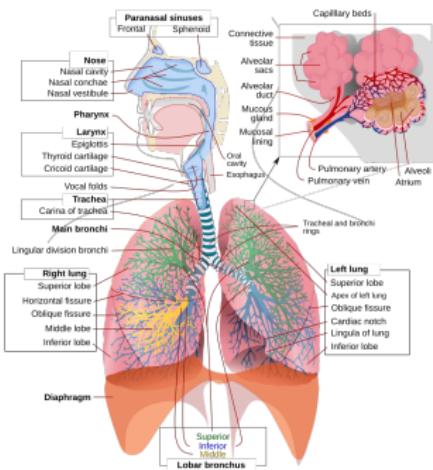
- ▶ COVID was not flu
 - ▶ This caused some early confusion with health guidelines!

How unusual is SARS-CoV-2?

- ▶ The 2019 pandemic was based on
 - ▶ A totally immunologically naive population
 - ▶ A virus not well adapted to the upper respiratory tract
 - ▶ Less spread, but more severe disease
 - ▶ A tightly linked global population
- ▶ Is COVID evolving to be Just Another Seasonal Coronavirus?
- ▶ Could one of the JASCs (common-cold coronaviruses) have caused a similar pandemic if its ancestor had not been introduced until this century?

Tradeoffs

- ▶ Our respiratory tracts look very different to pathogens as we move from the throat down into the lungs
 - ▶ Maybe the result of evolution: the pathogens that spread best are less likely to kill us
- ▶ New ARVs (not specifically adapted to humans) may generally cause more serious disease
 - ▶ When they spread at all



Credit: LadyofHats, Jmarchn

More counterfactuals

- ▶ How deadly would the Spanish flu be today?
 - ▶ It was far worse than COVID in reality
 - ▶ But a big portion of the deaths were slow and could probably have been prevented by antibiotics
 - ▶ Other deaths could have been prevented by oseltamivir
 - ▶ Disruptions from World War I probably slowed responses

How unusual is influenza?

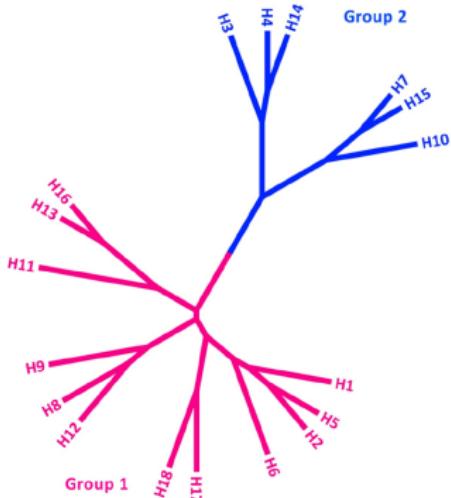
- ▶ If it's possible to be as flexible at evolving as influenza, why aren't there more pathogens that do it?
 - ▶ Maybe there are!
- ▶ SARS-CoV-2 evolved more rapidly than we were expecting
- ▶ Common cold viruses are under-studied, and maybe underestimated
- ▶ Maybe the reason we're more scared of flu is that we know more about it



Dushoff, Pulliam ([xkcd; darwin/cmx](#))

But the pandemics!

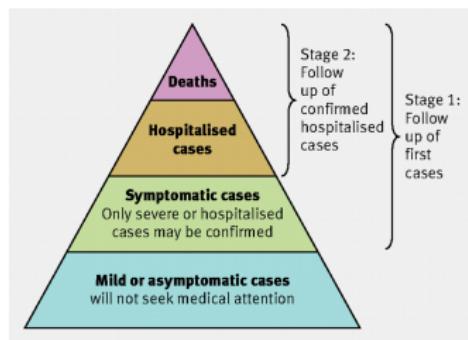
- ▶ Both major branches of H1 have been circulating in the human population for decades
- ▶ H5 has had *many* chances to spread in humans.
 - ▶ Antibodies frequently seen in poultry workers when looked for
 - ▶ Maybe it is not well suited for that particular jump.



Ferrara et al. 2015

Syndromic quarantines

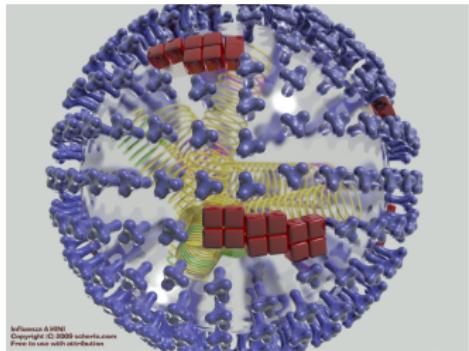
- ▶ The 2009 pandemic response included travel advisories and quarantines for people with fever and cough
 - ▶ This was never going to stop or slow the spread of pH1N1
 - ▶ But did it do something else?
 - ▶ *
- ▶ 2009 flu was *much* less dangerous than people predicted
 - ▶ But this is not necessarily the reason



Garske *et al.* BMJ 2009

Flu infrastructure

- ▶ We have a lot of vaccines against flu
 - ▶ Including various kinds of “universal” vaccines
- ▶ We also have drugs



Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

Why is it flu?

Why is it not flu?

Public-health hybrid strategies

Pharmaceutical hybrid strategies

Public-health hybrid strategies

- ▶ Governments have scaled *down* COVID surveillance programs
 - ▶ but not replaced them with broader programs
- ▶ Readiness will require hybrid programs
 - ▶ Useful against current threats
 - ▶ Help prepare for the next pandemic

Plan

- ▶ Combine data streams
 - ▶ Short-term forecasting of ARVs for healthcare planning
 - ▶ Burden assessments for resource allocation and research prioritization
- ▶ Focus on circulating ARVs
- ▶ Build pipelines and techniques that will be useful for detecting and fighting the next pandemic
- ▶ Leverage dynamical modeling

Obstacles

- ▶ Data sharing and confidentiality
- ▶ Co-operation
 - ▶ International
 - ▶ Intra-national (federal vs. provincial)
 - ▶ Medical and public-health

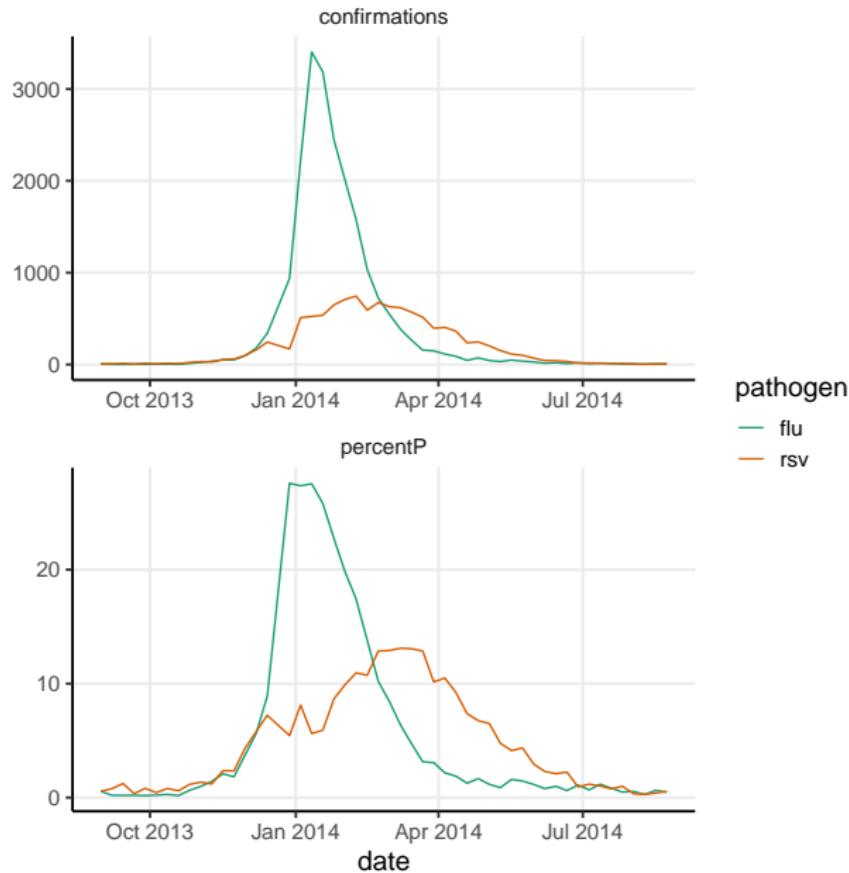
Approaches

- ▶ Build working co-operative relationships
 - ▶ Based on solving short- and medium-term public-health problems now!
- ▶ Better data analysis tools
 - ▶ Principled methods for combining data streams
- ▶ Pipelines
 - ▶ Bring data to modelers: confidentiality agreements, *automated de-identification or data munging*
 - ▶ Bring models to data: models developed on realistic simulated or munged data, packaged in ways that agencies can use
 - ▶ Bayesian tools that can combine standardized model *outputs*

Viral testing data

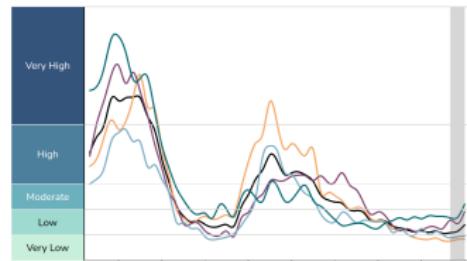
- ▶ How to make sense of testing *patterns* and testing results?
- ▶ What does it mean if influenza tests go up, but not confirmed cases?
 - ▶ Did influenza stay the same or go down?
 - ▶ What factors influence testing rates?
- ▶ How to organize and leverage information on why samples were taken?
 - ▶ And which tests were done on which patient
 - ▶ multiplexing and linkage

Example: Canadian surveillance (2014)



Wastewater data

- ▶ How to standardize samples?
 - ▶ Across sites
 - ▶ Weather and hydrological conditions
 - ▶ Different viruses

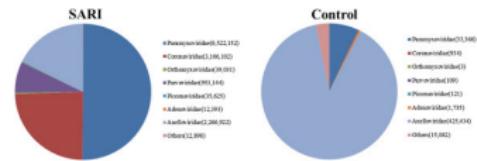


A COVID wastewater dashboard; colors represent different regions of the country
US CDC

Metagenomics

- ▶ How many viruses can we scan for at once, using DNA and RNA?

- ▶ Can we find brand-new ones?
 - ▶ in wastewater samples
 - ▶ in samples from respiratory patients?



Virome composition in infected and control children
Wang et al. Clin Microbiol Infect. 2016; PMC7172101

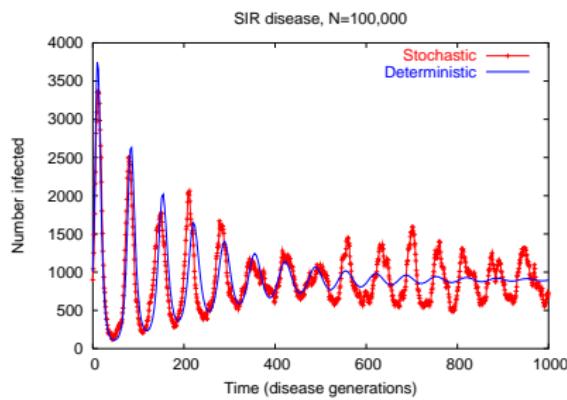
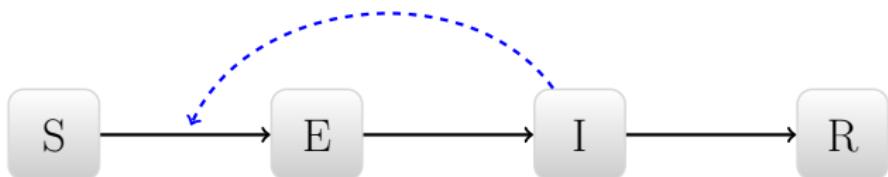
Clinical data

- ▶ Better methods for electronic recording and coding
 - ▶ and textual analysis
- ▶ Comparison between clinical trends and viral trends
 - ▶ Do the viruses we see account for the symptoms we see?



A Civil Defense siren.
Credit: Hssengineering

Dynamical approaches



- ▶ Use dynamical mechanisms to tie things together
- ▶ New infections are caused by infected people

Outline

Dynamical modeling connects scales

Pandemics in history

Acute respiratory viruses (ARVs)

Why is it flu?

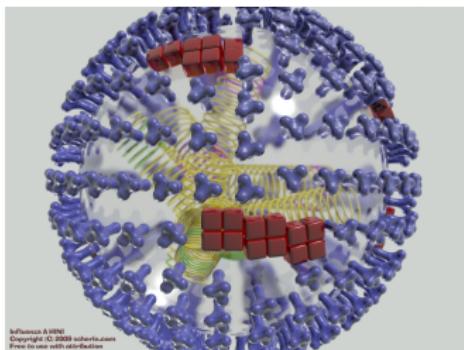
Why is it not flu?

Public-health hybrid strategies

Pharmaceutical hybrid strategies

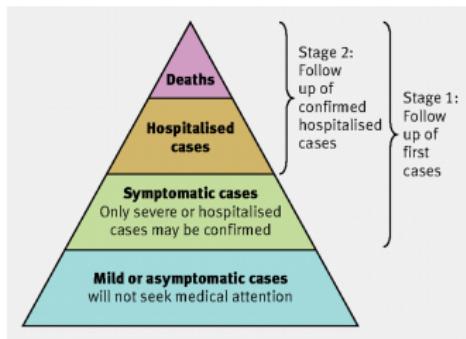
Broader vaccines

- ▶ More emphasis on broader influenza vaccines
- ▶ Can we aim vaccines at all beta coronaviruses
 - ▶ or all coronaviruses
- ▶ Can we aim vaccines at pneumoviruses instead of RSV specifically?
 - ▶ At least 5 species known, including human metapneumovirus
- ▶ Vaccines for other ARVs probably would likely be seen as over-medicalization



Be creative about endpoints

- ▶ Vaccines tend to be least effective at preventing detectable infection
- ▶ As outcomes become more consequential, effectiveness becomes higher
 - ▶ transmission \Rightarrow attended illness \Rightarrow hospitalization \Rightarrow death
- ▶ Do we sometimes want *less* effective broad vaccines for public health?



Garske et al. BMJ 2009

Drugs for the common cold

- ▶ People already take drugs for common cold
 - ▶ symptom suppressors, fever suppressors, anti-biotics
- ▶ These drugs *help* the viruses spread
 - ▶ or help bacteria evolve
- ▶ Should we consider aiming for broad antivirals for entero- and rhinoviruses, for example?
 - ▶ I don't know!

Summary

- ▶ Dynamical questions should be approached dynamically
 - ▶ And statistical questions statistically
- ▶ To leverage public resources, we should think about approaches that can help across scales:
 - ▶ health planning, burden assessment, pandemic readiness
- ▶ We may be under-estimating other low-harm virus families

Thanks

- ▶ Organizers
- ▶ Canadian Institutes for Health Research
- ▶ NTU College of Public Health
- ▶ Audience