McMaster University

Mathematics and Statistics

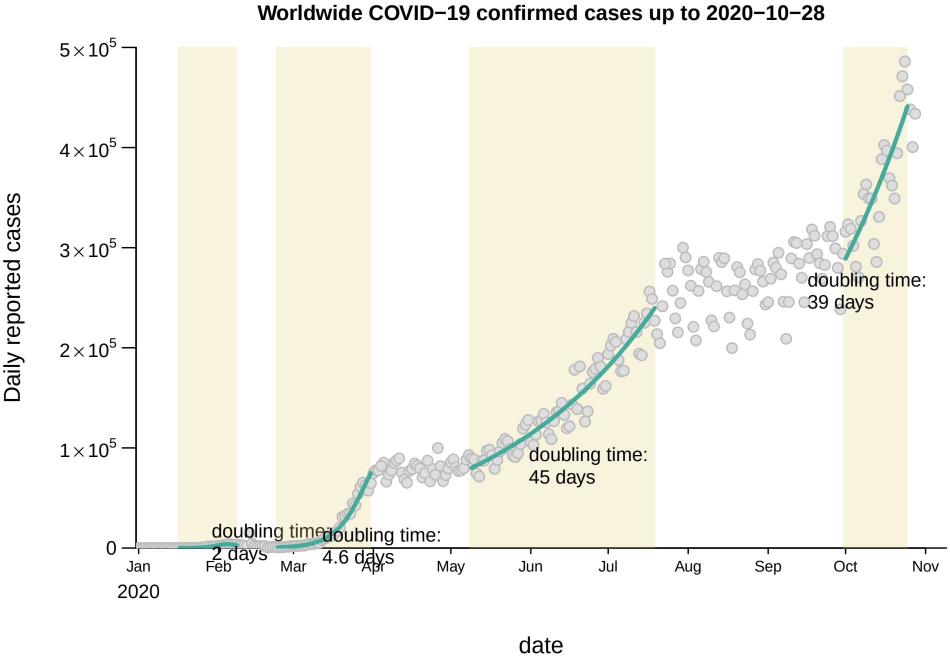
$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 747 / 5GT3
Topics in Mathematical Biology

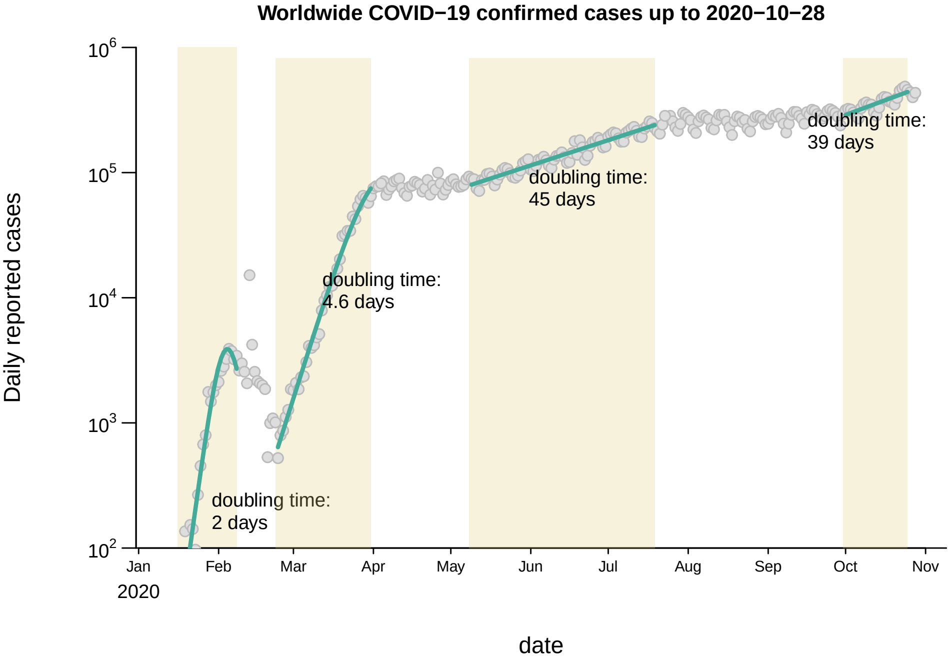
Instructor: David Earn

Lecture 6
Cholera and Influenza Pandemics
Thursday 29 October 2020

COVID-19 status today



Worldwide COVID−19 confirmed cases up to 2020−10−28
Daily reported cases
5×10^5
4×10^5
3×10^5
2×10^5
1×10^5
0
doubling time:
2 days
doubling time:
4.6 days
doubling time:
45 days
doubling time:
39 days
Jan
2020
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
date



Worldwide COVID−19 confirmed cases up to 2020−10−28
10^6
10^5
10^4
10^3
10^2
Daily reported cases
doubling time:
2 days
doubling time:
4.6 days
doubling time:
45 days
doubling time:
39 days
Jan
2020
Feb
Mar
Apr
May
Jun
Jul
Aug
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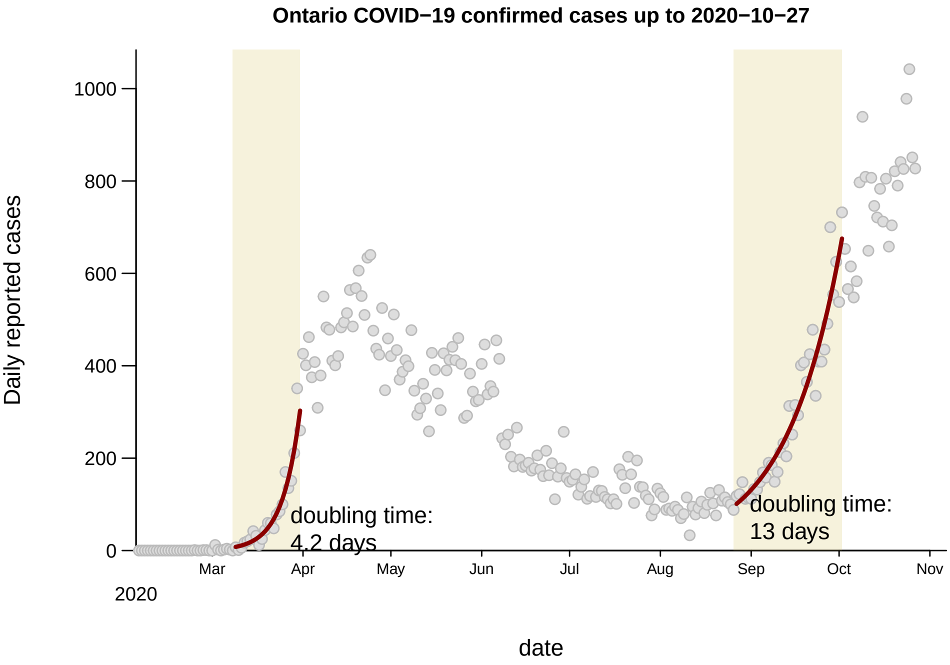
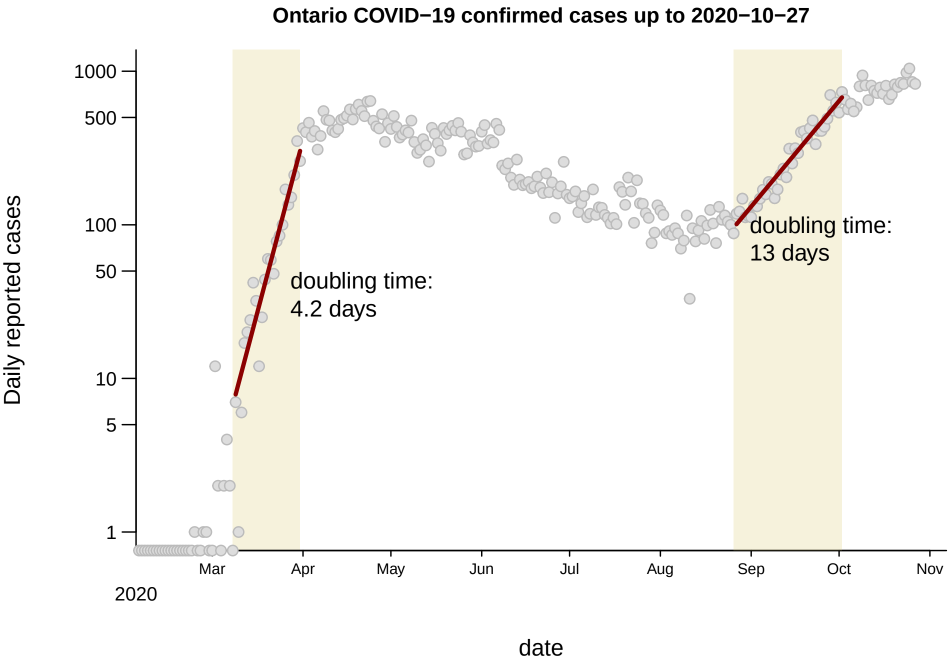
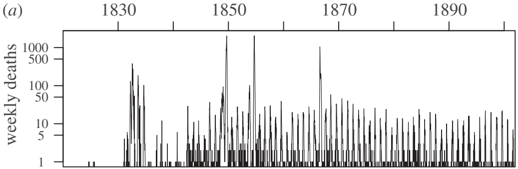
date


Ontario COVID−19 confirmed cases up to 2020−10−27
Daily reported cases
1000
800
600
400
200
0
doubling time:
4.2 days
doubling time:
13 days
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
2020
date


Ontario COVID−19 confirmed cases up to 2020−10−27
Daily reported cases
1000
500
100
50
10
5
1
doubling time:
4.2 days
doubling time:
13 days
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
2020
date

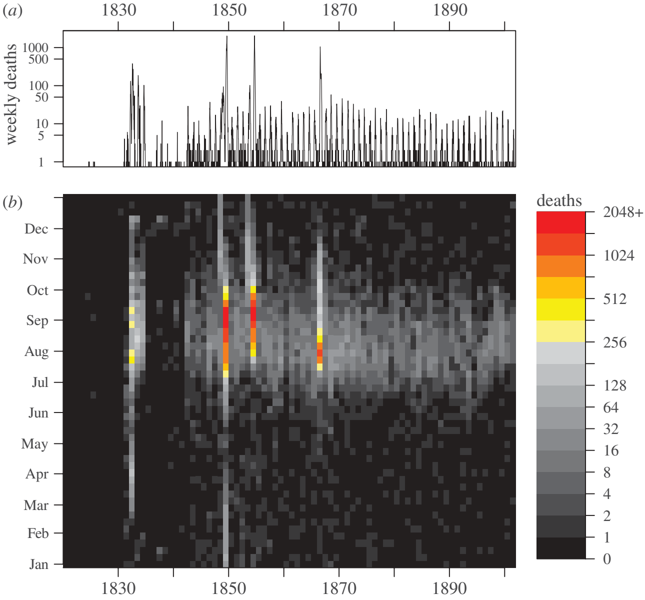
Cholera

19th c. cholera epidemics in London



Tien, Poinar, Fisman, Earn 2011, *J. R. Soc. Interface* **8**:756–760

19th c. cholera epidemics in London



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19th c. cholera epidemics in London

Observations:

- 4 cholera pandemics in the 19th century
- 3/4 were preceded by an out-of-season "Herald Wave"

Hypothesis:

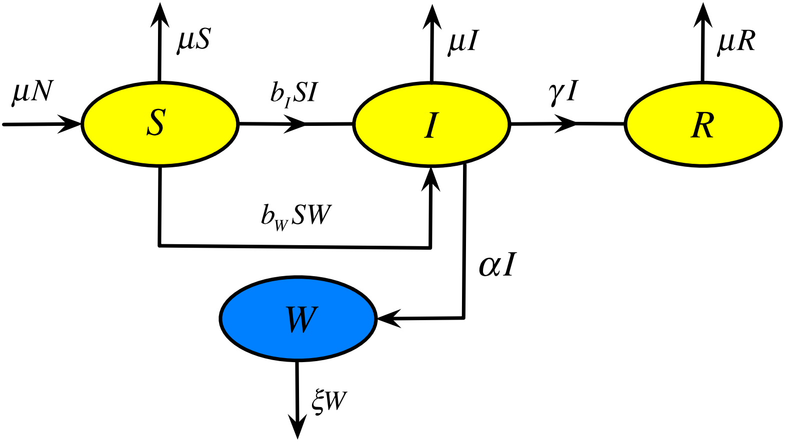
- New strain invaded out-of-season
- Major wave occured in the summer following
- In 1866, new strain happenned to appear in the summer

Mechanistic plausibility:

- Can a sensible dynamical model capture the hypothesized process and the observed two-wave pattern?

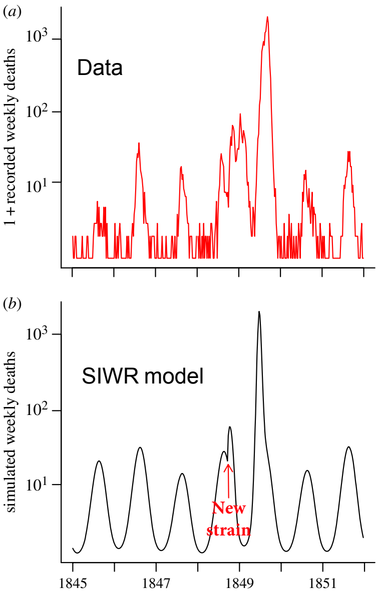
Tien, Poinar, Fisman, Earn 2011, *J. R. Soc. Interface* **8**:756–760

SIWR waterborne pathogen model



Tien & Earn 2010, *Bull. Math. Biol.* **72**:1506–1533

New strain $\Longrightarrow$ herald wave before main in-season wave



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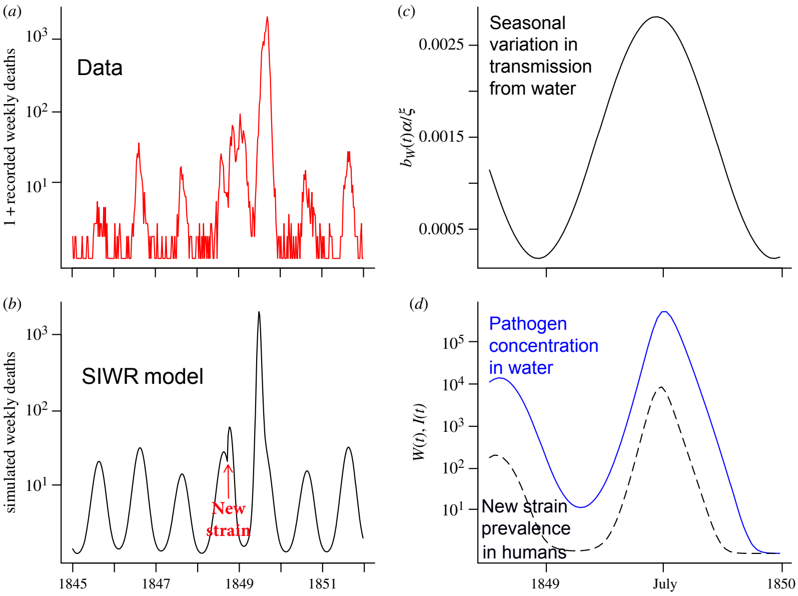
New strain $\implies$ herald wave before main in-season wave



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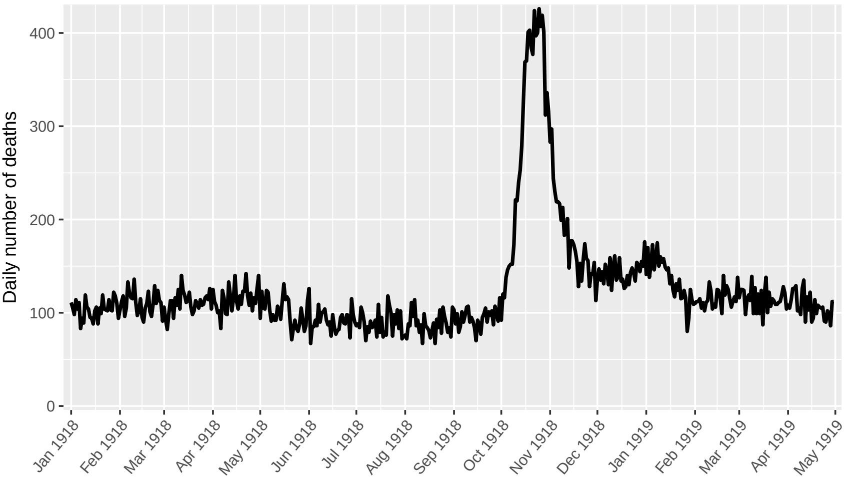
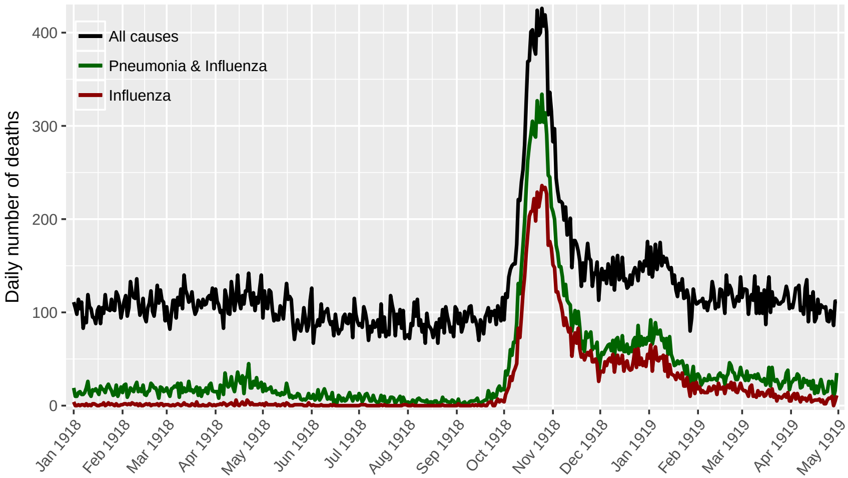
Influenza

102 years ago in Ontario



Earn 2018, "How many people died from influenza in 1918?"
In: *Defining Moments Canada*, ed. J. Lorinc

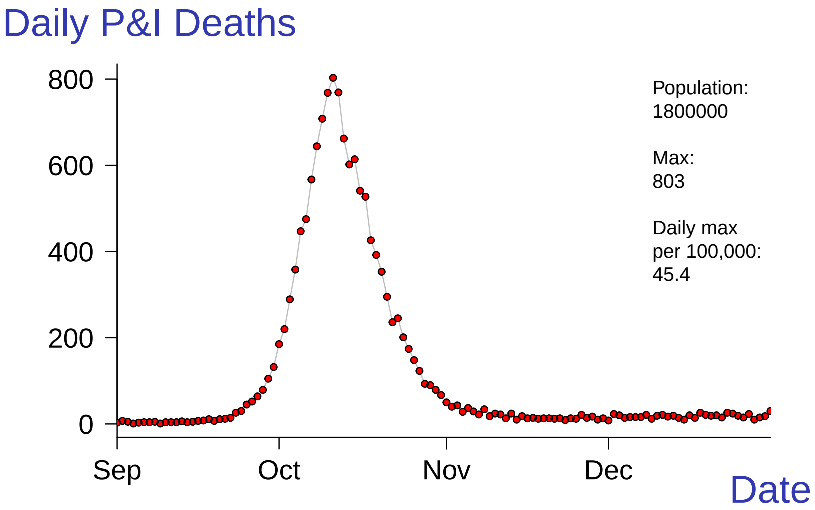
The 1918–1919 Influenza Pandemic in Ontario



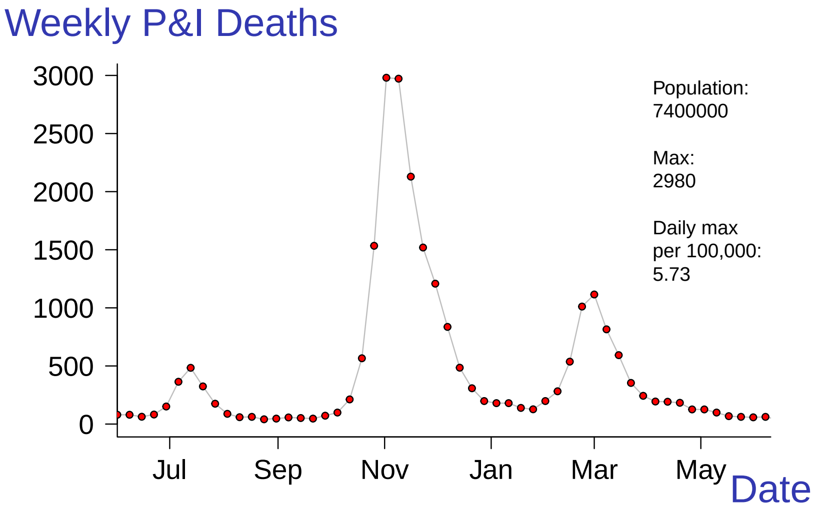
1918 population: 2.8×10^6
Max P&I per 10^5/day: 11.7

Earn 2018, "How many people died from influenza in 1918?"
In: *Defining Moments Canada*, ed. J. Lorinc

Pneumonia & Influenza Mortality, Philadelphia USA, 1918



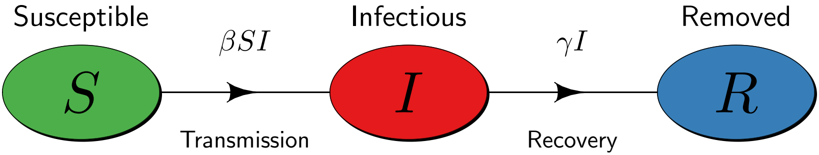
Pneumonia & Influenza Mortality, London England, 1918



He, Dushoff, Day, Ma, Earn 2013, *Proc. R. Soc.* B **280**:20131345

Why were there
three distinct waves
in 1918–19?

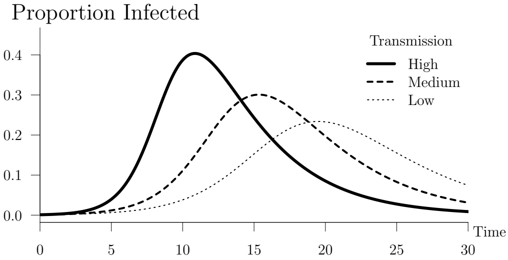
The SIR model



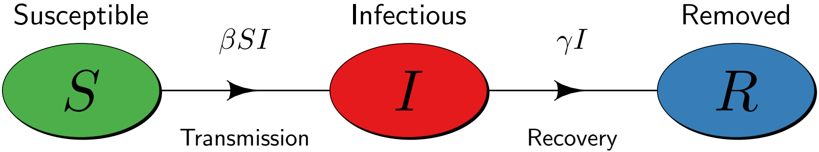
$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$



The SIR model



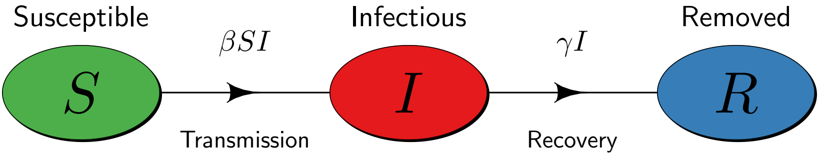
$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

- **Parameters:**
  - Transmission rate β
  - Recovery rate γ

The SIR model



$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

- **Derived Parameters:**
  - Initial growth rate $\beta - \gamma$
  - Mean infectious period $\frac{1}{\gamma}$
  - Basic Reproduction Number

$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$

The SIR model: Effects of Control Measures

- If a proportion (p) of the population is protected from infection (e.g., social distancing, vaccine, ...) then the "effective $\mathcal{R}_0$" is $\mathcal{R}_0(1-p)$.

- $\therefore$ An epidemic will be prevented if $\mathcal{R}_0(1-p) < 1$, *i.e.*,

$$p > p_{\text{crit}} = 1 - \frac{1}{\mathcal{R}_0}$$

- For flu, $\mathcal{R}_0 \simeq 1.5$–$2 \quad \Longrightarrow \quad p_{\text{crit}} \simeq 33$–$50\%$.

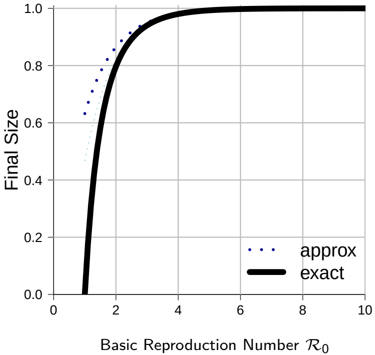
- For COVID-19, $\mathcal{R}_0 \simeq 3$–$6 \quad \Longrightarrow \quad p_{\text{crit}} \simeq 67$–$83\%$.

The SIR model: expected final size (without interventions)

- Final size Z (*final proportion infected*) is determined entirely by $\mathcal{R}_0$:

$$Z = 1 - e^{-\mathcal{R}_0 Z}$$

- Formula derived for SIR model (Kermack & McKendrick, 1927) is valid for much more realistic models (Ma & Earn, 2006; Miller 2012)

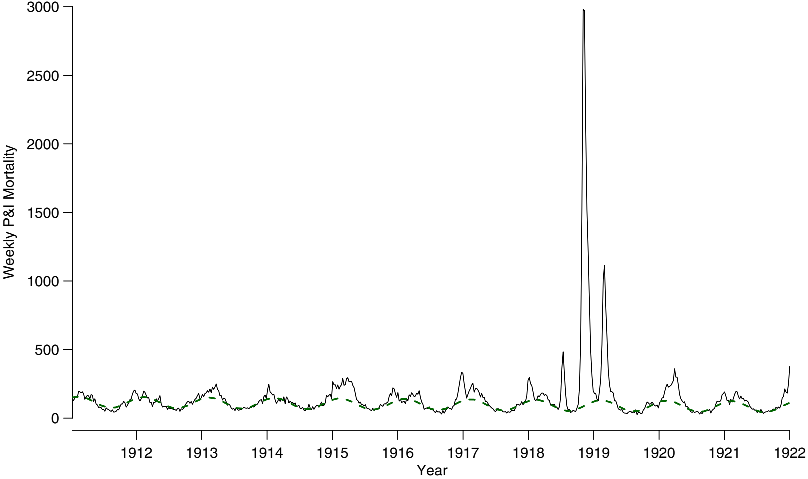


- For 1918 flu: $1.5 \lesssim \mathcal{R}_0 \lesssim 2 \implies$ Proportion of world population infected $\sim$60–80%
- For COVID-19: $\mathcal{R}_0 \simeq$ 3–6 $\implies$ *expected* final size $\sim$ 94–99.7%

Why were there three distinct waves in 1918–19?

- Use compartmental SIR framework as a starting point, but include:
  - Case Fatality Proportion (CFP, ϕ);
  - Rate of decay of immunity (δ).
- Basic model predicts a single epidemic wave.
- Perhaps parameters are time-varying?
  - time-varying transmission rate $\beta(t)$?
  - time-varying recovery rate $\gamma(t)$?
  - time-varying $\delta(t)$ or $\phi(t)$?
- Best model (judged by AICc) has:
  - time-varying β with 12 cubic B-spline basis;
  - constant γ and ϕ;
  - permanent immunity ($\delta = 0$).

Why were there three distinct waves in 1918–19?



He, Dushoff, Day, Ma, Earn 2011, *Theoretical Ecology* **4**:283–288

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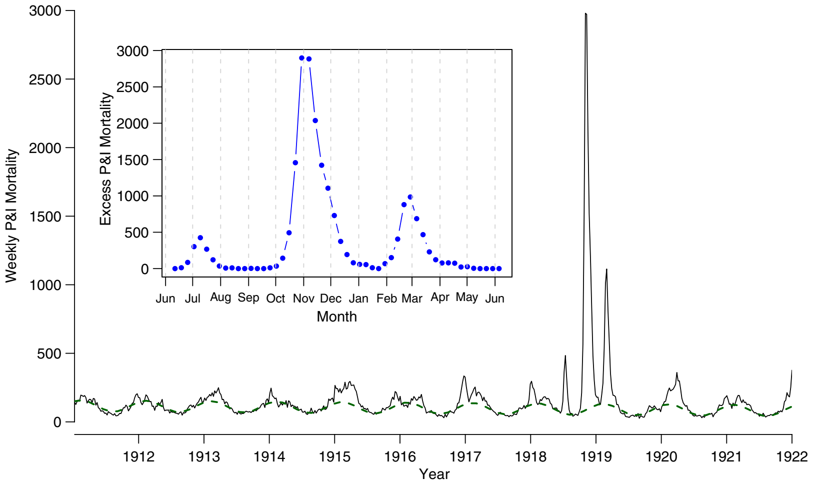

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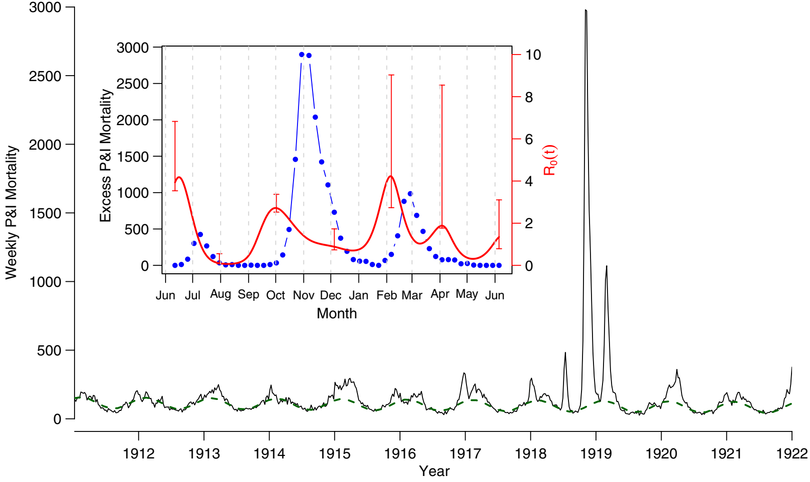

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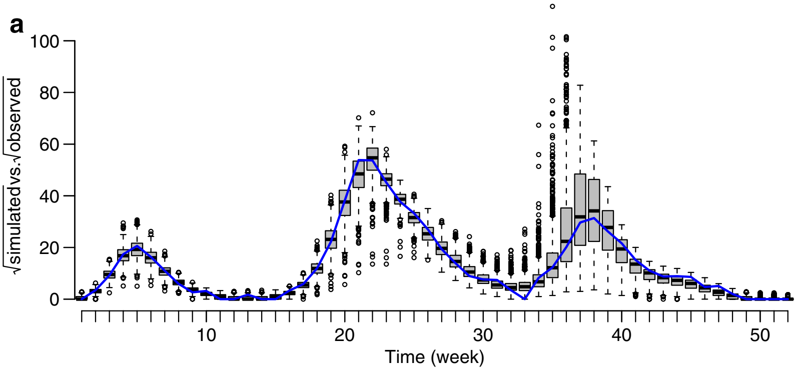

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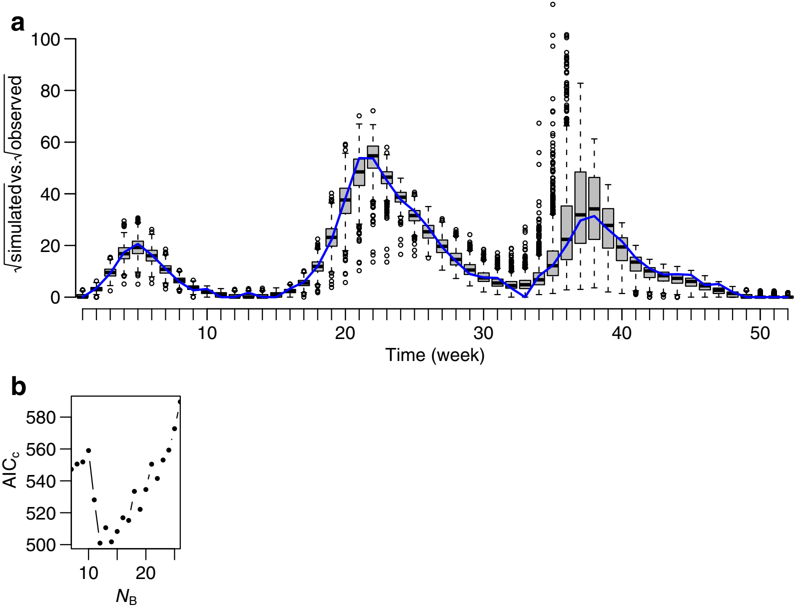

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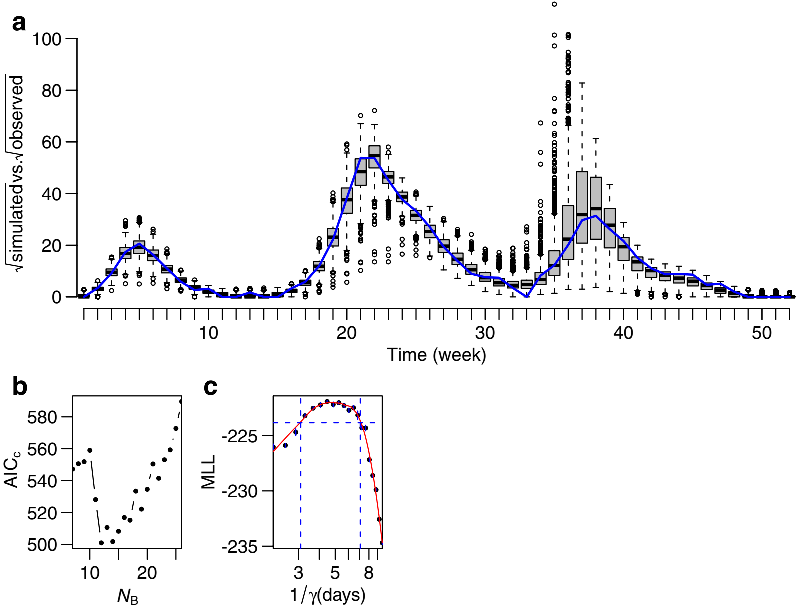

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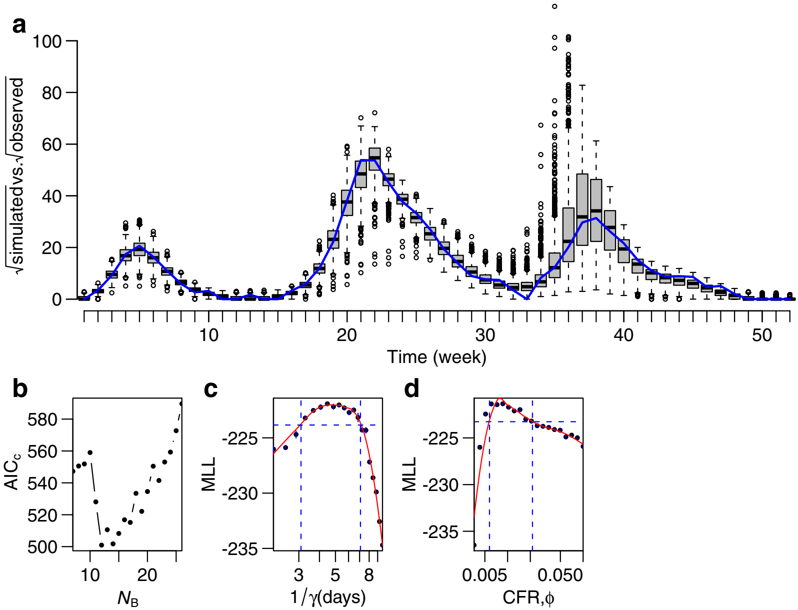

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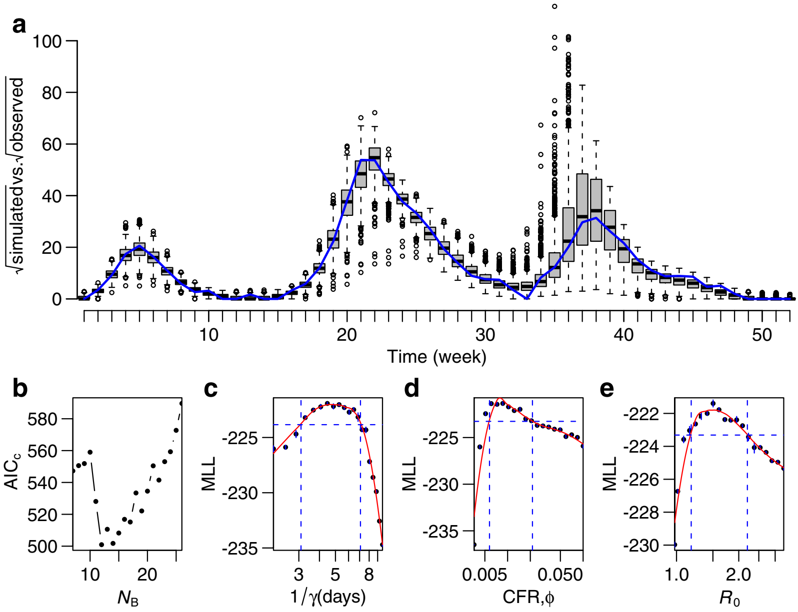
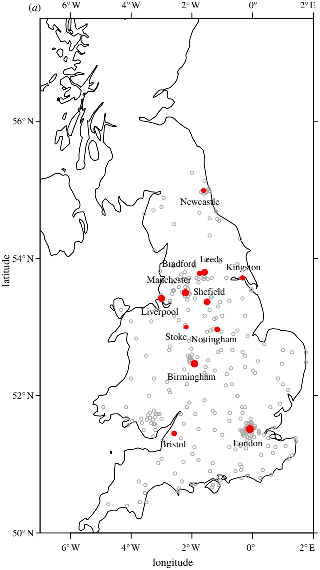


Why were there three distinct waves in 1918–19?

What explains time-varying transmission rate $\beta(t)$?

What *caused* the three distinct waves in 1918–19?



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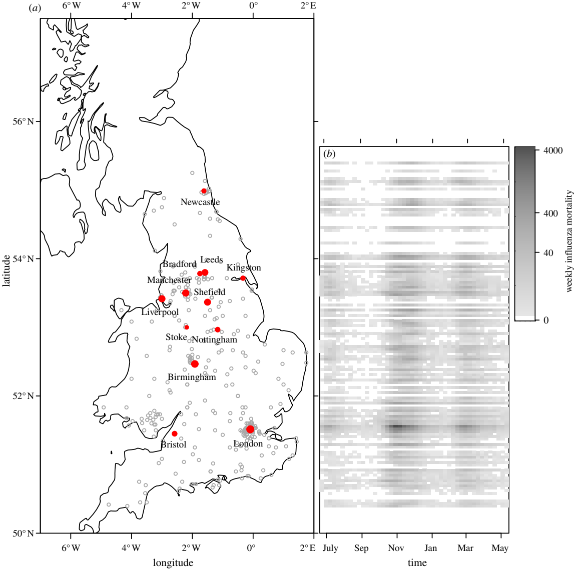

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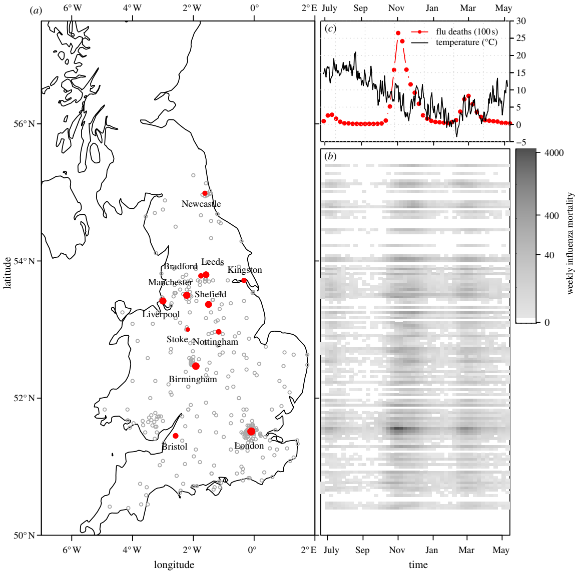

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Expand SIR model

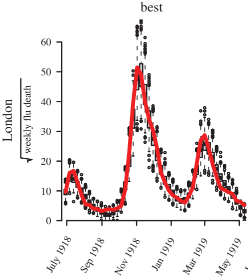
$$dS/dt = -\beta SI \qquad \text{Susceptible}$$
$$dI/dt = \beta SI - \gamma I \qquad \text{Infectious}$$
$$dR/dt = (1-\phi)\gamma I \qquad \text{Recovered}$$
$$dD/dt = \phi\gamma I - gD \qquad \text{Not infectious, will die}$$
$$dM/dt = gD \qquad \text{Died of influenza}$$
$$dP/dt = gD - \lambda P \qquad \text{Public perception of risk}$$

$1/g =$ mean time from loss of infectiousness to death
$1/\lambda =$ mean duration of impact of deaths on public perception

Mechanistic basis of transmission rate variation:

$$\beta(t,P) = \underbrace{\beta_0}_{\text{Baseline}} \cdot \underbrace{\left[e^{-\xi T(t)}\right]}_{\text{Weather}} \cdot \underbrace{\left[1+\alpha H(t)\right]}_{\text{School}} \cdot \underbrace{\left[1-P(t)\right]^{\kappa}}_{\text{Behaviour}}$$

What *caused* the three distinct waves in 1918–19?



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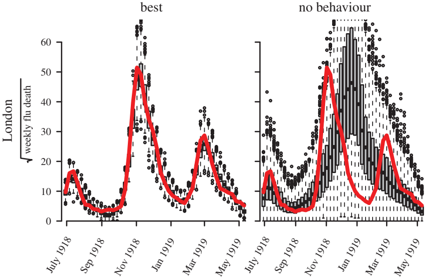

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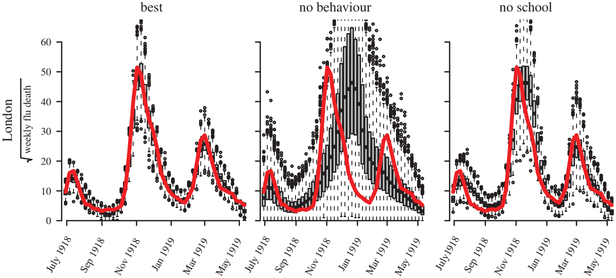

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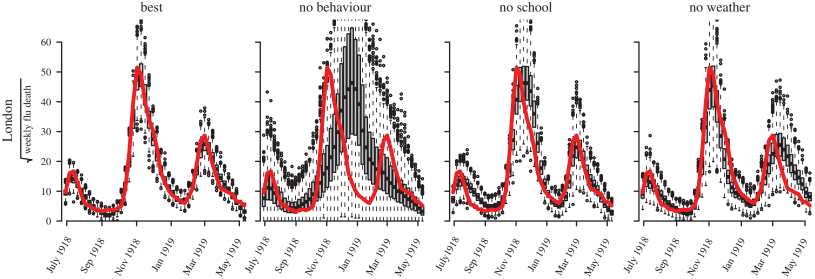

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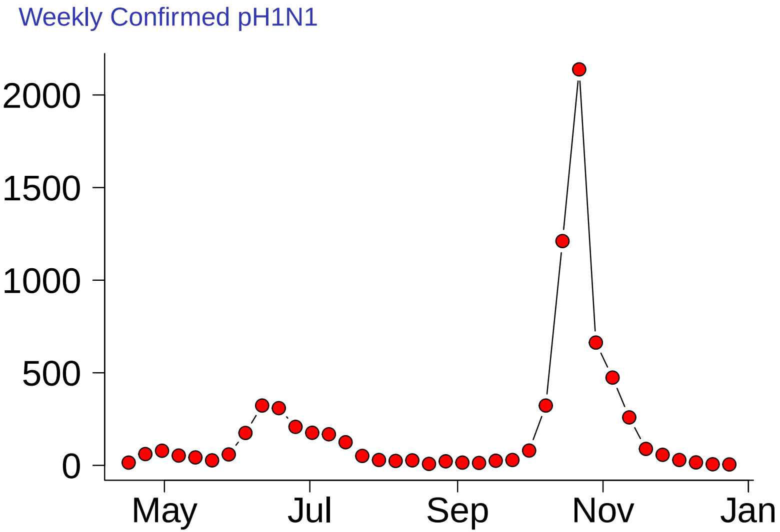
What *caused* the three distinct waves in 1918–19?

- Behavioural response to perception of risk
  - cannot fit three distinct waves without it
- school closing and weather have detectable effects, but much smaller than behaviour change

He, Dushoff, Day, Ma, Earn 2013, *Proc. R. Soc.* B **280**:20131345

Why were there
two distinct waves
in 2009?

2009 Influenza Pandemic in Alberta



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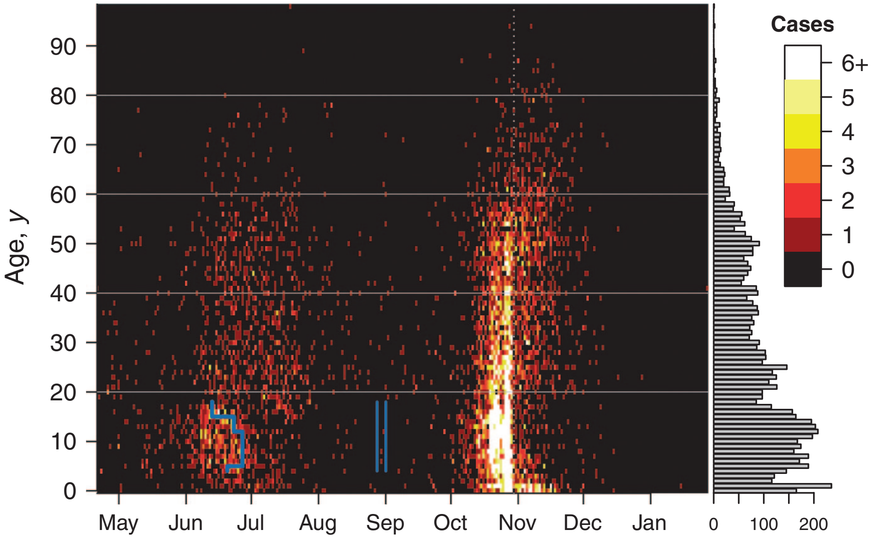

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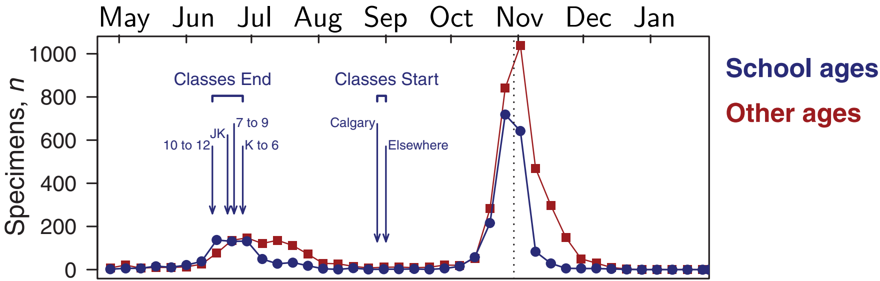

- Cases fell in school ages when schools closed
- Cases fell in other ages 3–4 weeks later
- Second wave began a few weeks after schools re-opened
- Mass vaccination started in late October

- Investigate mechanisms with two-age-class SIR model

Earn, He, Loeb, Fonseca, Lee, Dushoff 2012, *Ann. Int. Med.* **156**, 173–181

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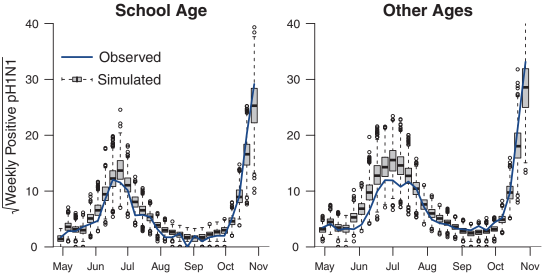

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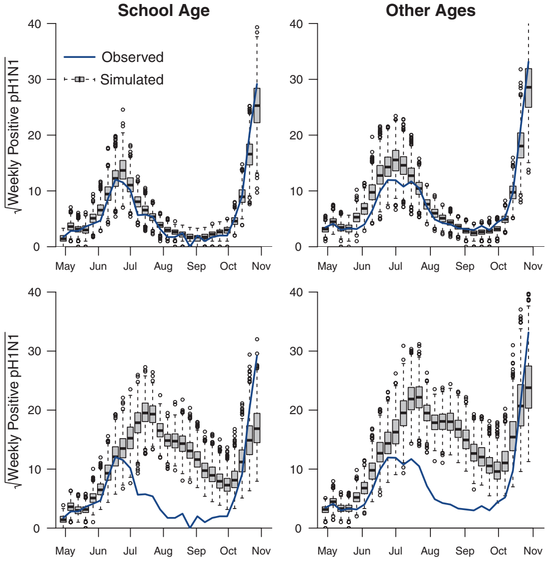

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2009 Influenza Pandemic in Alberta

- Schools closing had a major effect on attenuating the first wave
- Weather also had a detectable effect
- Summer wave would have been much larger if schools had not closed

Earn, He, Loeb, Fonseca, Lee, Dushoff 2012, *Ann. Int. Med.* **156**, 173–181