Complex Systems: Computer Modelling of Epidemics

Funding: Australian Research Council project Large-scale computational modelling of epidemics in Australia (ARC DP160102742)

Prof. Mikhail Prokopenko

Centre for Complex Systems

Faculty of Engineering

THE UNIVERSITY OF SYDNEY

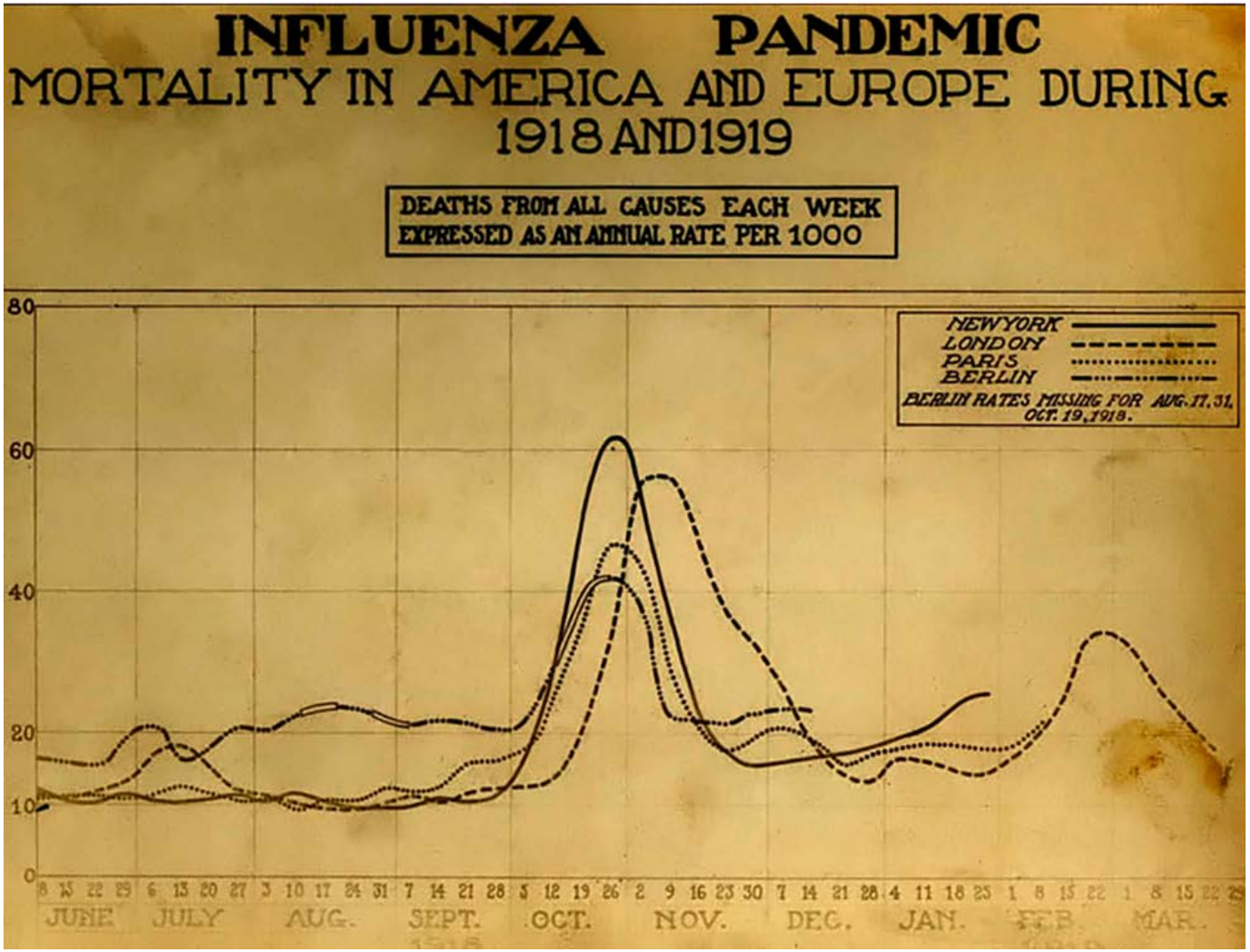
National Science Week and Sydney Science Festival
15 August 2019

THE UNIVERSITY OF SYDNEY

Spanish Flu 1918: 500 million infected, with deaths of three to five percent of the world's population

Soldiers from Fort Riley, Kansas, ill with Spanish influenza at a hospital ward at Camp Funston
Otis Historical Archives Nat'l Museum of Health & Medicine - NCP 1603

Spanish Flu 1918: a chart of deaths in major cities



Pandemic Influenza: The Inside Story. Nicholls H, *PLoS Biology* Vol. 4/2/2006, e50
courtesy of the National Museum of Health and Medicine

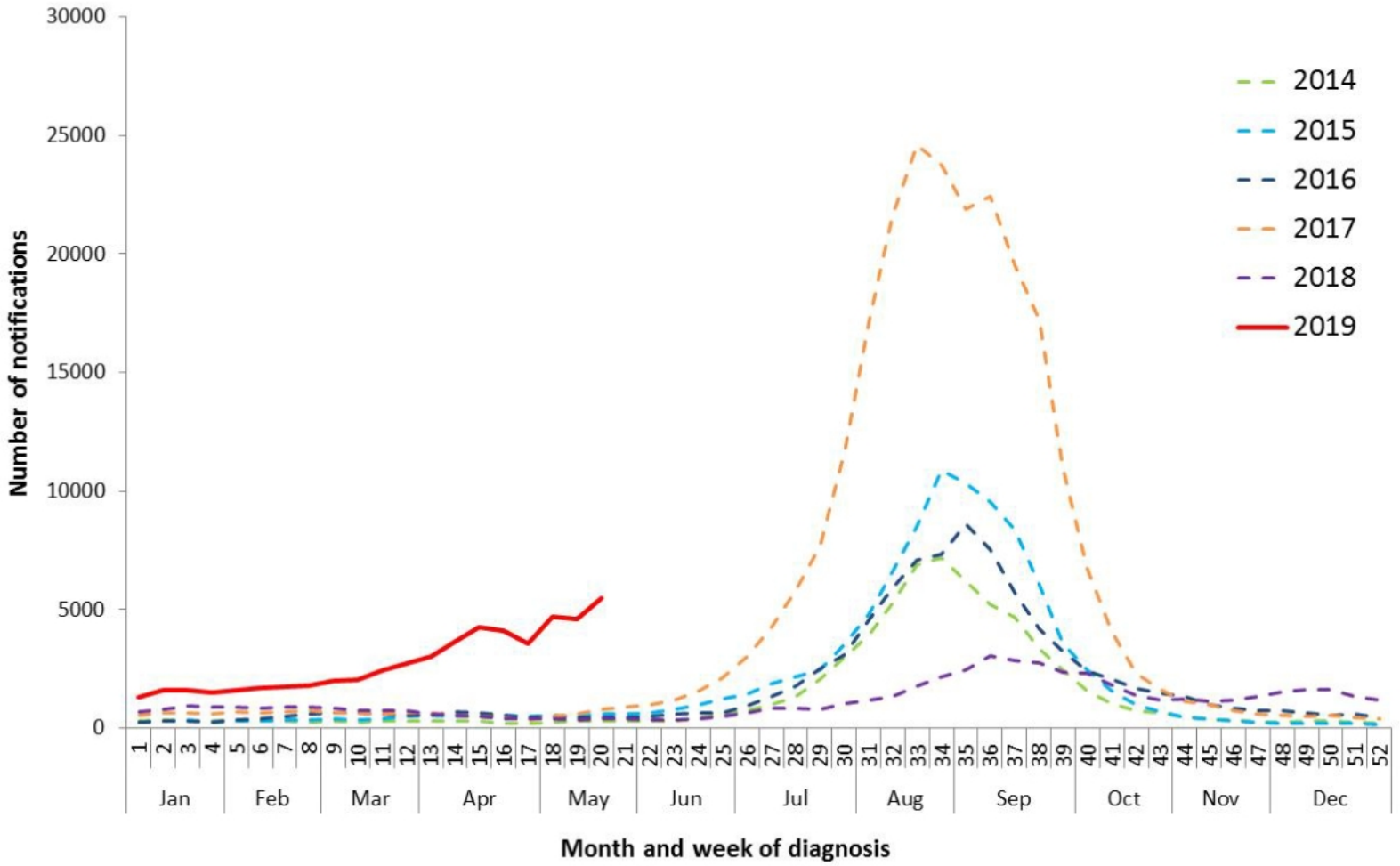
Hundred years later…

"I had hoped that hitting the 100th anniversary of this epidemic (Spanish flu) would spark a lot of discussion about whether we're ready for the next global epidemic. Unfortunately, it didn't, and we still are not ready"

Bill Gates
Chair of Bill & Melinda Gates Foundation
2018

https://www.gatesnotes.com/About-Bill-Gates/Year-in-Review-2018

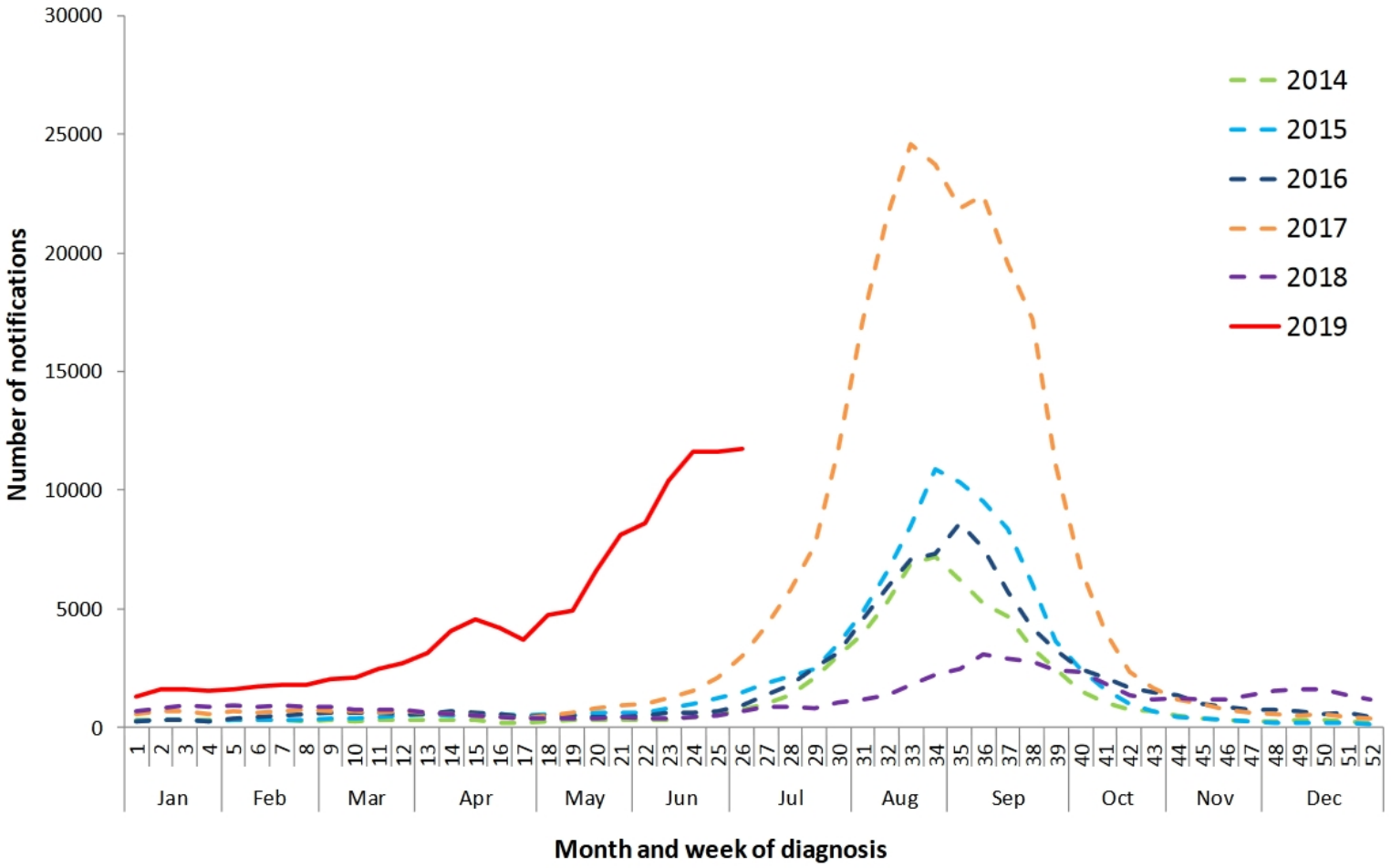
Figure 5. Notifications of laboratory confirmed influenza, Australia, 1 January 2014 to 19 May 2019, by month and week of diagnosis.



National Notifiable Diseases Surveillance System

Source: NNDSS

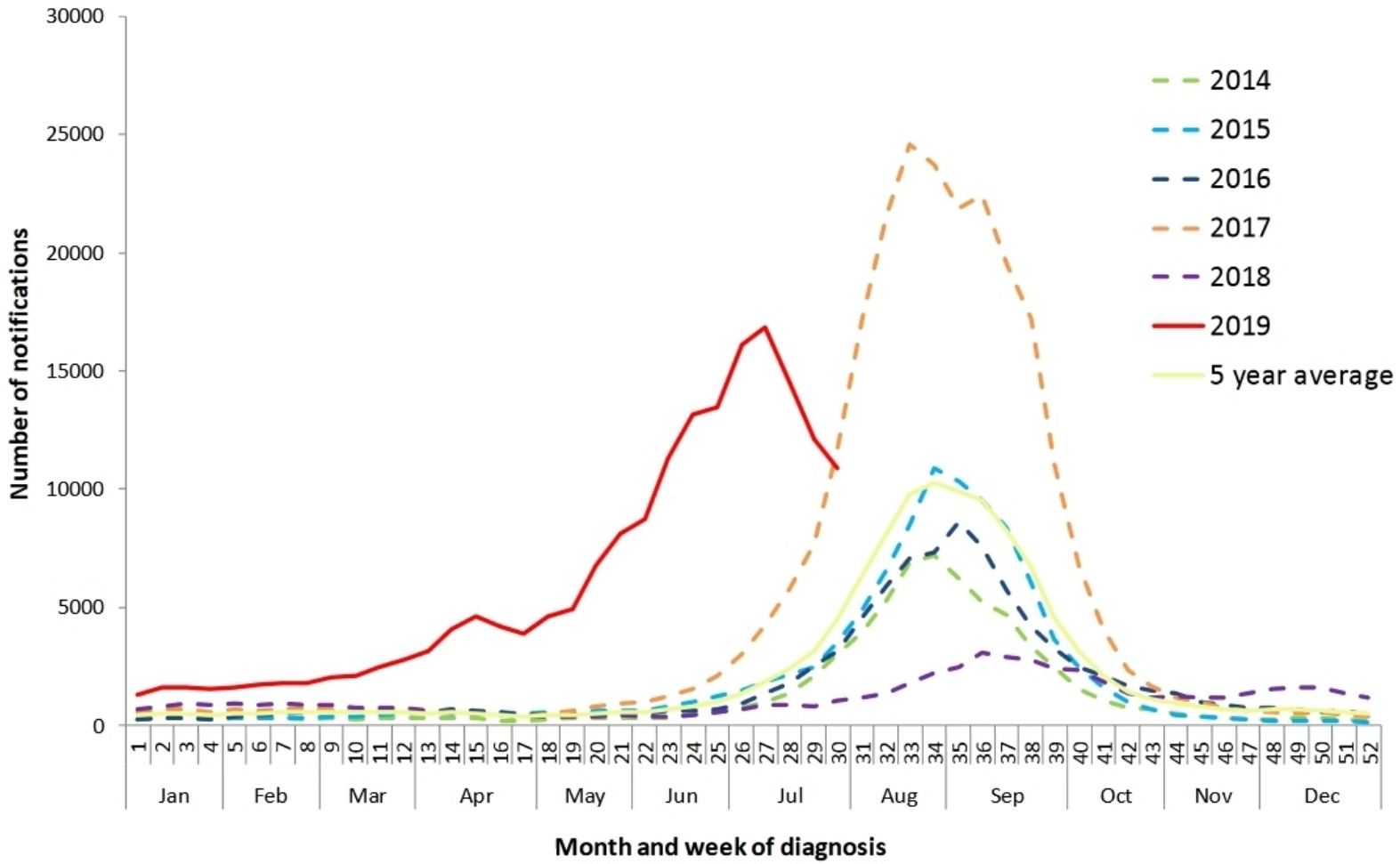
Figure 5. Notifications of laboratory confirmed influenza, Australia, 1 January 2013 to 30 June 2019, by month and week of diagnosis.



National Notifiable Diseases Surveillance System

Source: NNDSS

Figure 5. Notifications of laboratory confirmed influenza, Australia, 1 January 2013 to 28 July 2019, by month and week of diagnosis.*



National Notifiable Diseases Surveillance System

Source: NNDSS

A Contribution to the Mathematical Theory of Epidemics.

By W. O. KERMACK and A. G. MCKENDRICK.

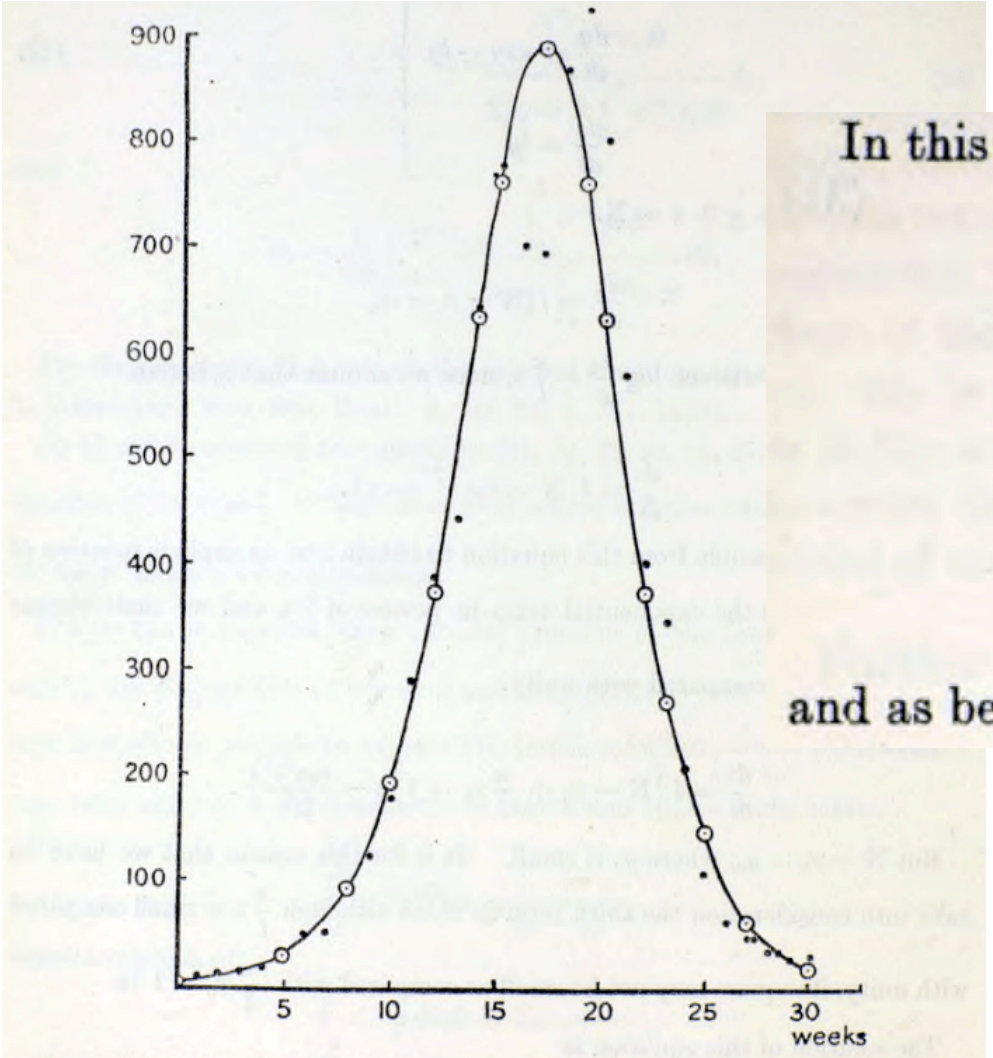
(Communicated by Sir Gilbert Walker, F.R.S.—Received May 13, 1927.)

(From the Laboratory of the Royal College of Physicians, Edinburgh.)

Introduction.

(1) One of the most striking features in the study of epidemics is the difficulty of finding a causal factor which appears to be adequate to account for the magnitude of the frequent epidemics of disease which visit almost every population. It was with a view to obtaining more insight regarding the effects of the various factors which govern the spread of contagious epidemics that the present investigation was undertaken. Reference may here be made to the work of Ross

Compartmental models in epidemiology: Susceptible – Infectious – Recovered



The accompanying chart is based upon figures of deaths from plague in the island of Bombay over the period December 17, 1905, to July 21, 1906. The ordinate represents the number of deaths per week, and the abscissa denotes the time in weeks. As at least

In this case the equations are

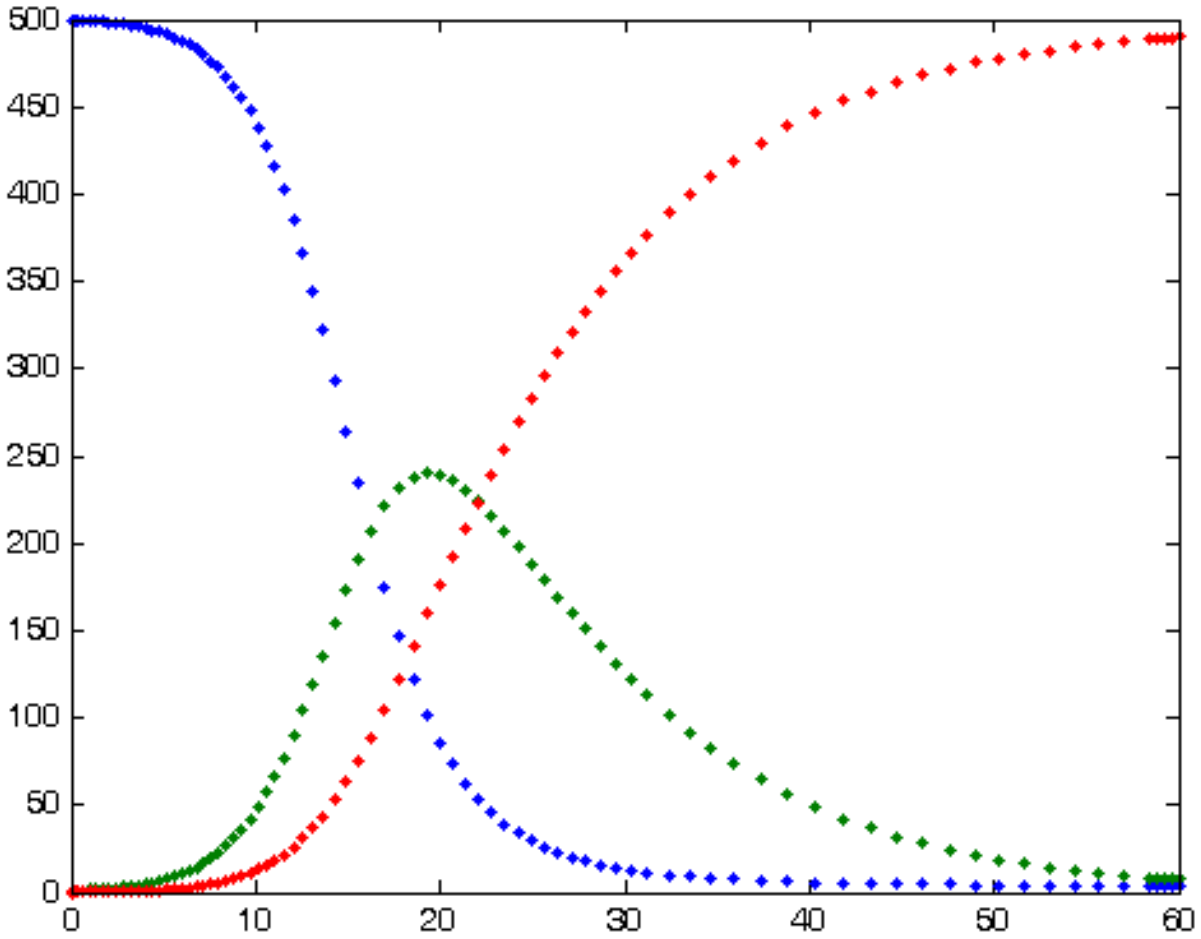
$$\left.\begin{aligned} \frac{dx}{dt} &= -\kappa xy \\ \frac{dy}{dt} &= \kappa xy - ly \\ \frac{dz}{dt} &= ly \end{aligned}\right\}$$

and as before $x + y + z = \mathrm{N}$.

THE UNIVERSITY OF SYDNEY

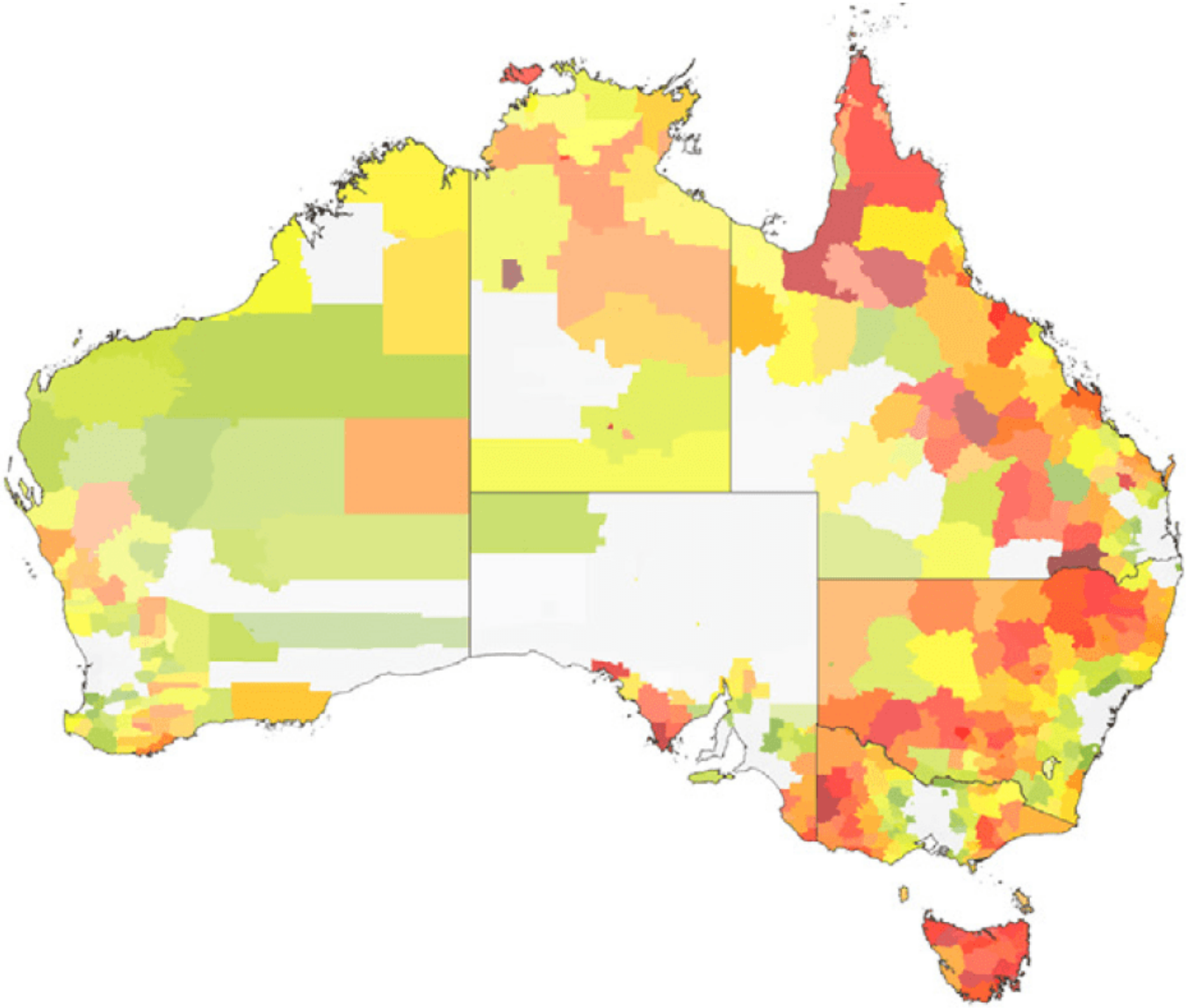
Compartmental models in epidemiology: Susceptible – Infectious – Recovered

Susceptible → Infectious → Recovered



THE UNIVERSITY OF SYDNEY

Different questions: How to “zoom in” ? Where to intervene?



International Journal of Modern Physics C
Vol. 15, No. 1 (2004) 193–201

World Scientific
www.worldscientific.com

LARGE-SCALE MOLECULAR-DYNAMICS SIMULATION OF 19 BILLION PARTICLES

KAI KADAU
Theoretical Division, Los Alamos National Laboratory
MS B262, Los Alamos, New Mexico 87545, USA
kkadau@lanl.gov

TIMOTHY C. GERMANN
Applied Physics Division, Los Alamos National Laboratory
MS F699, Los Alamos, New Mexico 87545, USA
tcg@lanl.gov

PETER S. LOMDAHL
Theoretical Division, Los Alamos National Laboratory
MS B262, Los Alamos, New Mexico 87545, USA
pxl@lanl.gov

Received 8 August 2003
Revised 10 August 2003

SPaSM (Scalable Parallel Short-range Molecular dynamics)

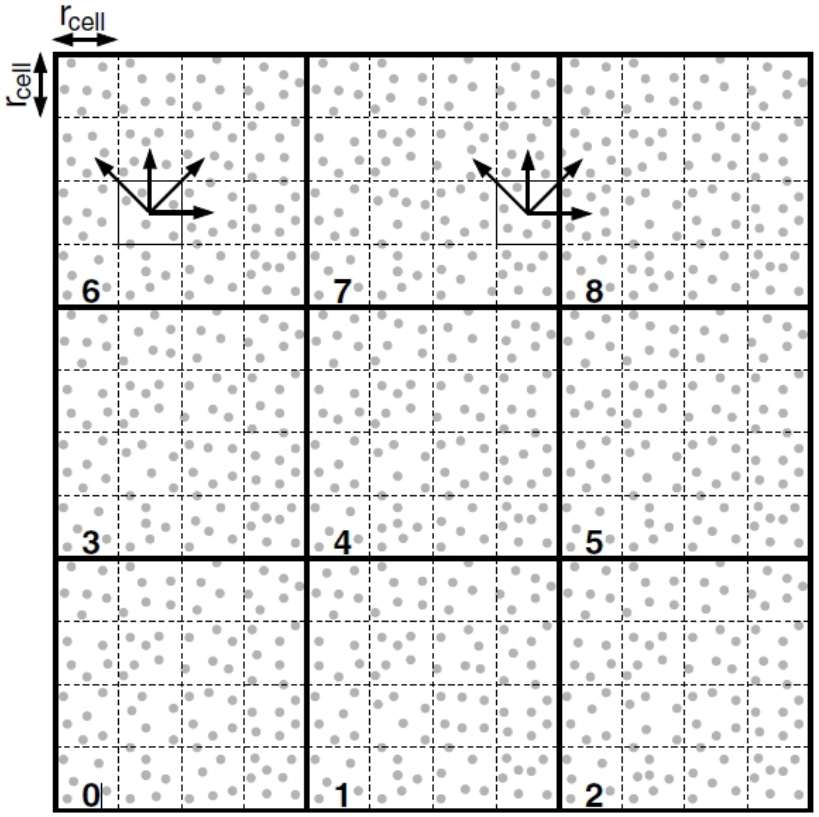


Fig. 1. Schematic of a nine PN (0–8) run with square geometry: A spatial decomposition of the simulation space assigns particles in a rectangle to each PN. The space assigned to each PN is further subdivided into (square) cells with an edge-length r_{cell} slightly larger than the interaction cut-off r_{cut} of the interaction potential. The interaction is calculated only for particles in the same cell and for the eight neighboring cells following an interaction path for each cell that only visits four neighbor cells (see PN 6). If a neighbor cell is located on a different PN (see PN 7), synchronous message passing is applied.

THE UNIVERSITY OF SYDNEY

SPaSM (Scalable Parallel Short-range Molecular dynamics)

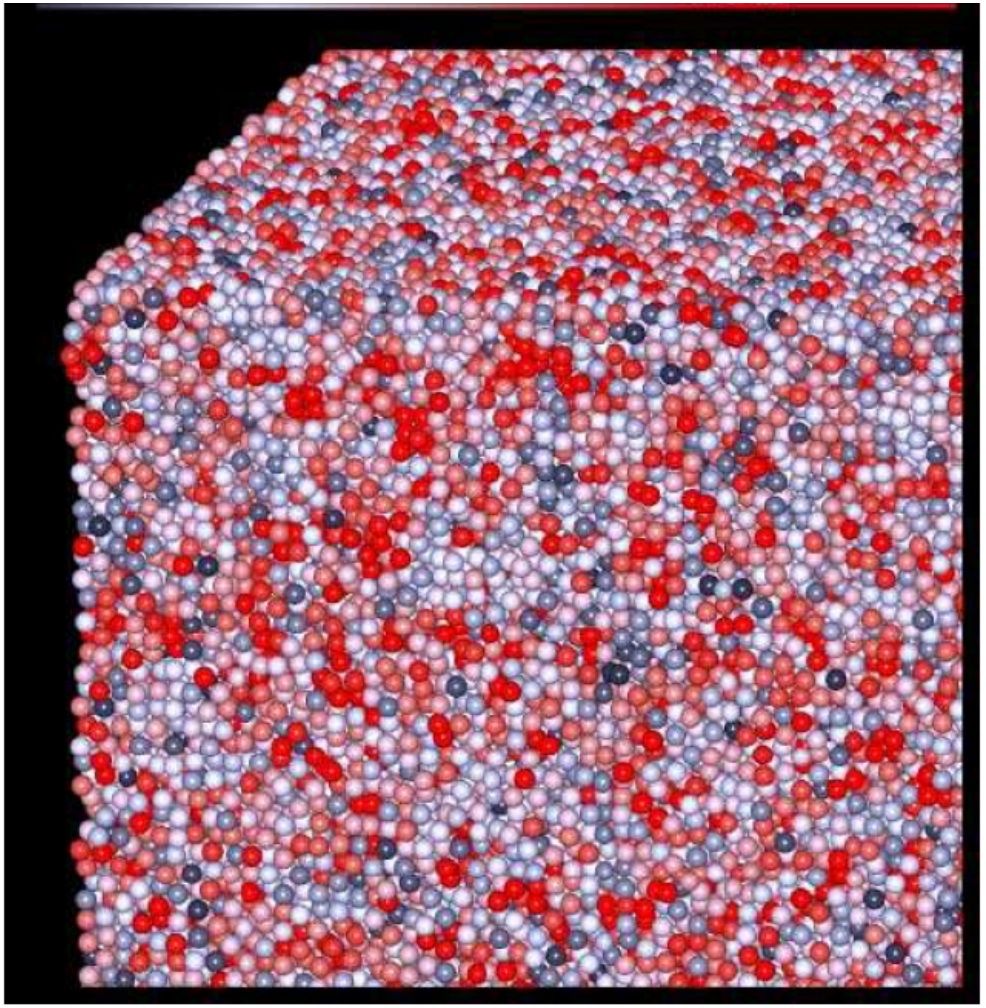


Fig. 3. $\approx$ 37 million particles rendered on four PN with a resolution of 5000 pixel by 5000 pixel (top). The bottom shows a close-up of the same picture file. The grayscale represents the potential energies of the atoms from -6 to -2 (grayscale version of the original color picture).

NAS PNAS

Mitigation strategies for pandemic influenza in the United States

Timothy C. Germann*†, Kai Kadau*, Ira M. Longini, Jr.‡, and Catherine A. Macken*

*Los Alamos National Laboratory, Los Alamos, NM 87545; and ‡Program of Biostatistics and Biomathematics, Fred Hutchinson Cancer Research Center and Department of Biostatistics, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98109

Communicated by G. Balakrish Nair, International Centre for Diarrhoeal Disease Research Bangladesh, Dhaka, Bangladesh, February 16, 2006
(received for review January 10, 2006)

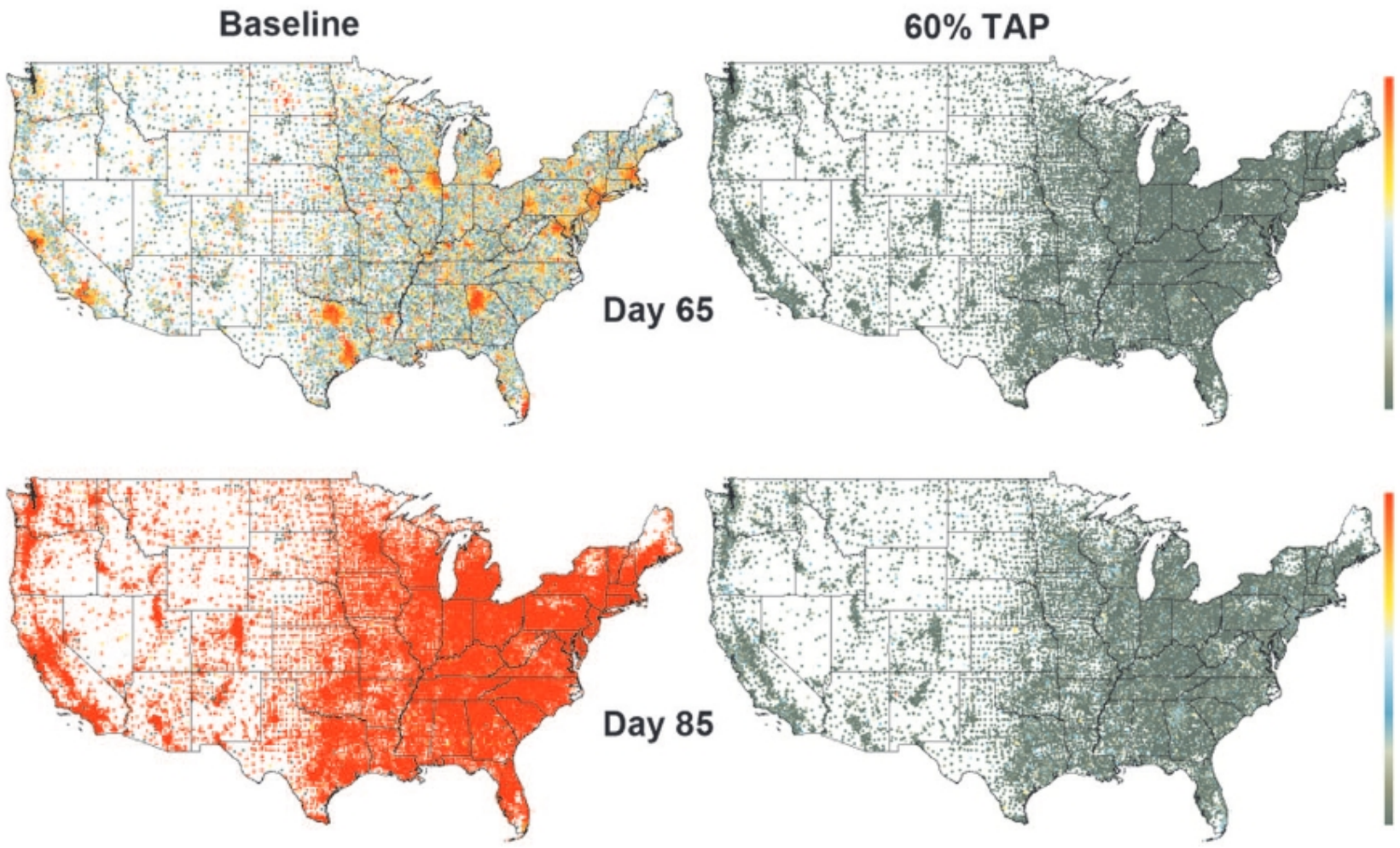
Recent human deaths due to infection by highly pathogenic (H5N1) avian influenza A virus have raised the specter of a devastating pandemic like that of 1917–1918, should this avian virus evolve to become readily transmissible among humans. We introduce and use a large-scale stochastic simulation model to investigate the spread of a pandemic strain of influenza virus through the U.S. population of 281 million individuals for R_0 (the basic reproductive number) from 1.6 to 2.4. We model the impact that a variety of

resources to minimize the impact of the outbreak? Precise planning is hampered by several unknowns, most critically the eventual human-to-human transmissibility of the human-adapted avian strain (characterized by the basic reproductive number R_0, the average number of secondary infections caused by a single typical infected individual among a completely susceptible population), and the supply of therapeutic agents. Manufacturers of neuraminidase inhibitors, such as oseltamivir,

THE UNIVERSITY OF SYDNEY

Pandemic influenza: agent-based modelling (Germann et al., 2006)

PNAS



Our research (since 2016)

- Modelling influenza pandemics with large-scale high-fidelity agent-based models
  - *demographics*: from census based data to agents
  - *mobility*: travel patterns including long-distance
  - *infection*: disease transmission and natural history models
  - ACEMod – Australian Census-based Epidemic Model

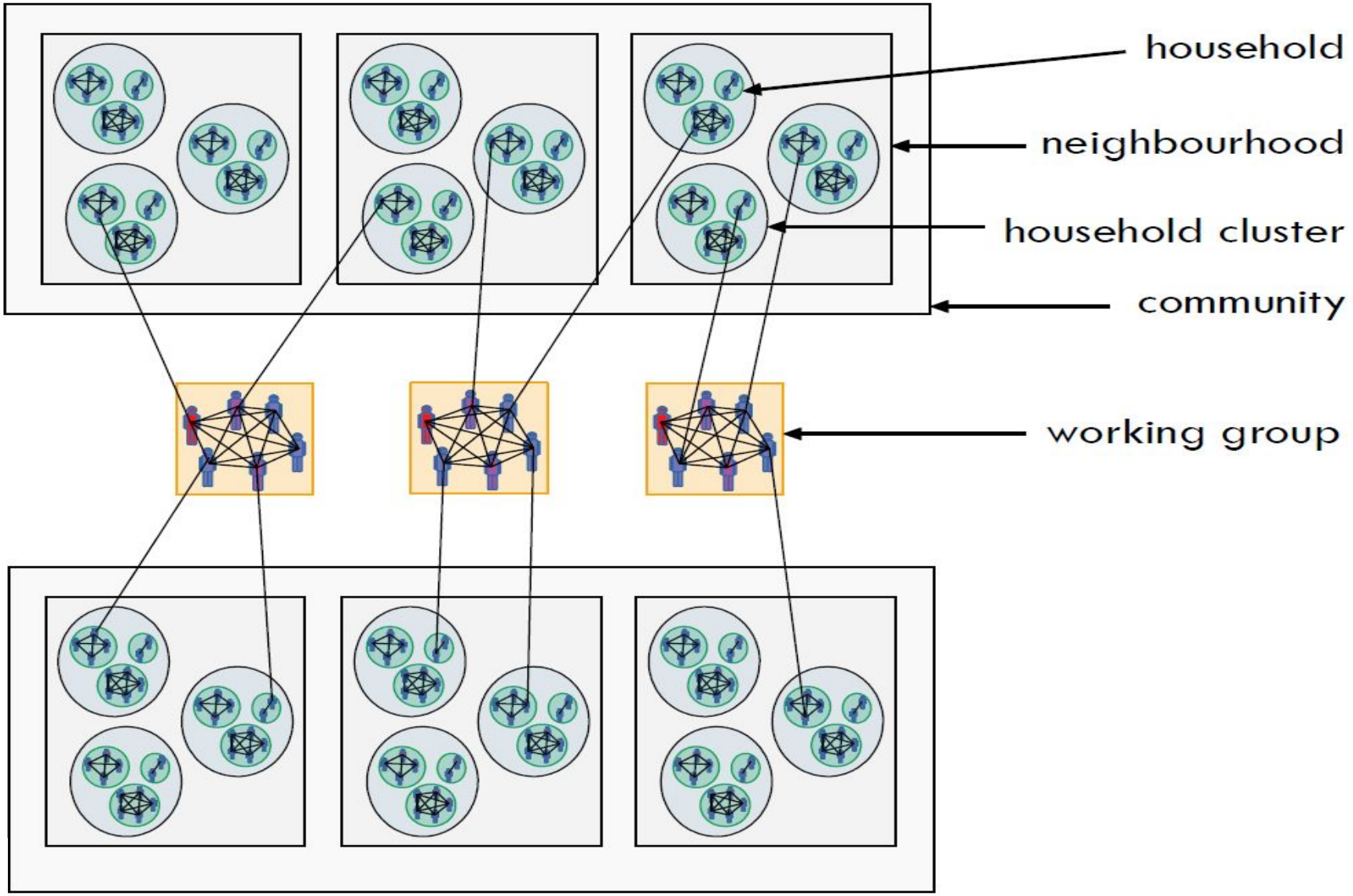
- Influenza pandemics: effects of urbanisation
  - pandemic trends (peaks, prevalence, bimodality)
  - key factors: counter-factual analysis

- Interventions: comparison
  - efficiency of interventions

Agent-based modelling (ABM)

https://www.bankofengland.co.uk/quarterly-bulletin/2016/q4/agent-based-models-understanding-the-economy-from-the-bottom-up

Mixing contexts in our ABM



ABM of influenza epidemics

- anonymous individual (census based) → agents with attributes (e.g., age, gender, occupation, susceptibility and immunity to diseases)
- local agent interactions: contacts and disease transmission over about 20M agents, grouped in social “contexts” (households, workplaces, schools, classrooms, etc.)
- H1N1 virus (and strains)
- outbreak modelling of pandemic scenarios (international air traffic)
- varying sources and intensity of infection, as well as artificial population sets
- calibration to known data on reproductive ratio R_0, attack rates (across “contexts”) and dynamics

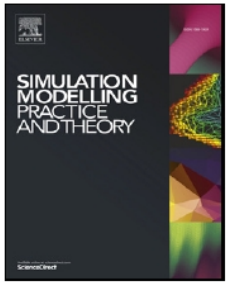
Australian Census-based Epidemic Model: ACEMod

Simulation Modelling Practice and Theory 87 (2018) 412–431

Contents lists available at ScienceDirect

Simulation Modelling Practice and Theory

journal homepage: www.elsevier.com/locate/simpat

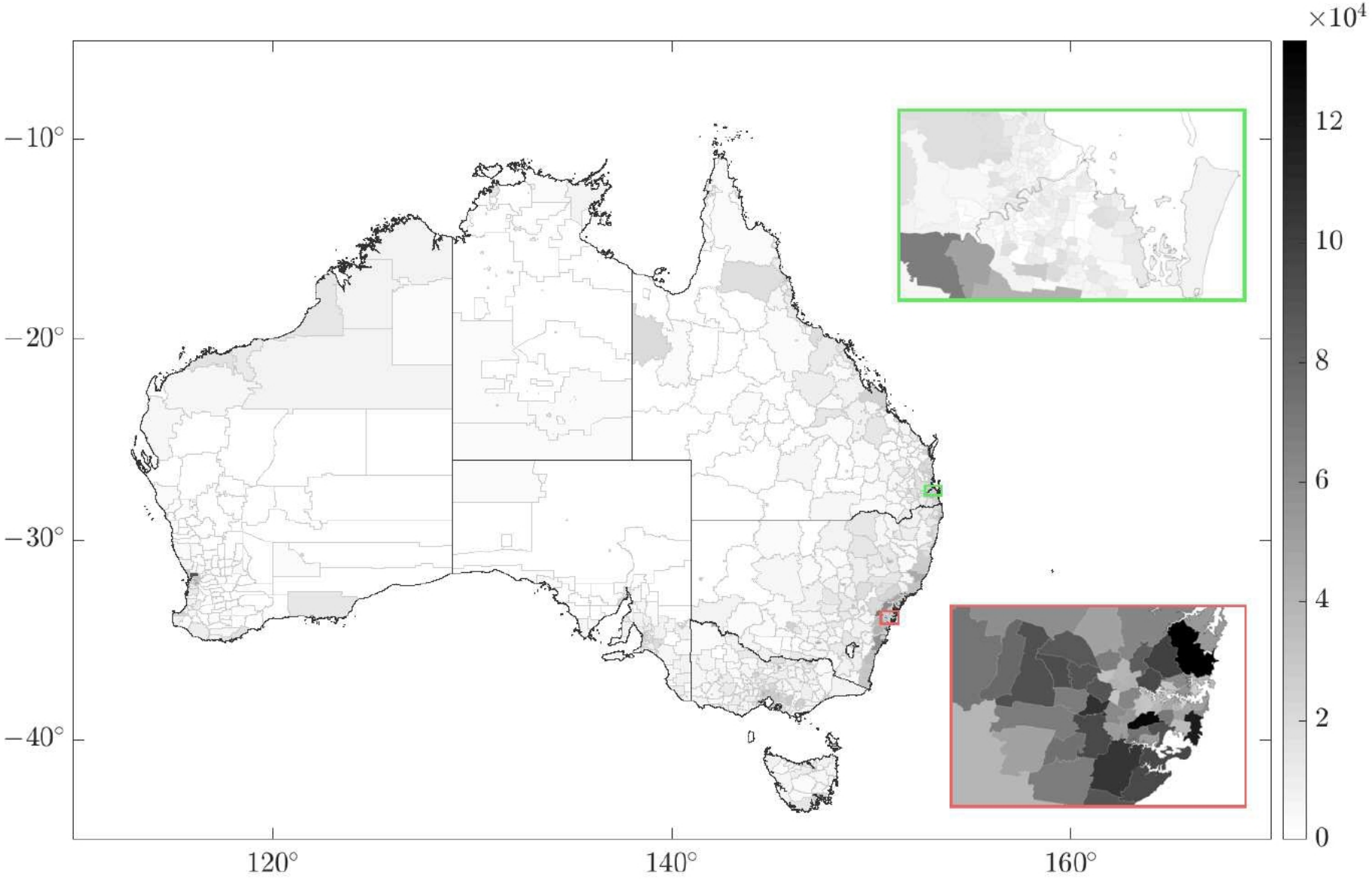


Investigating spatiotemporal dynamics and synchrony of influenza epidemics in Australia: An agent-based modelling approach

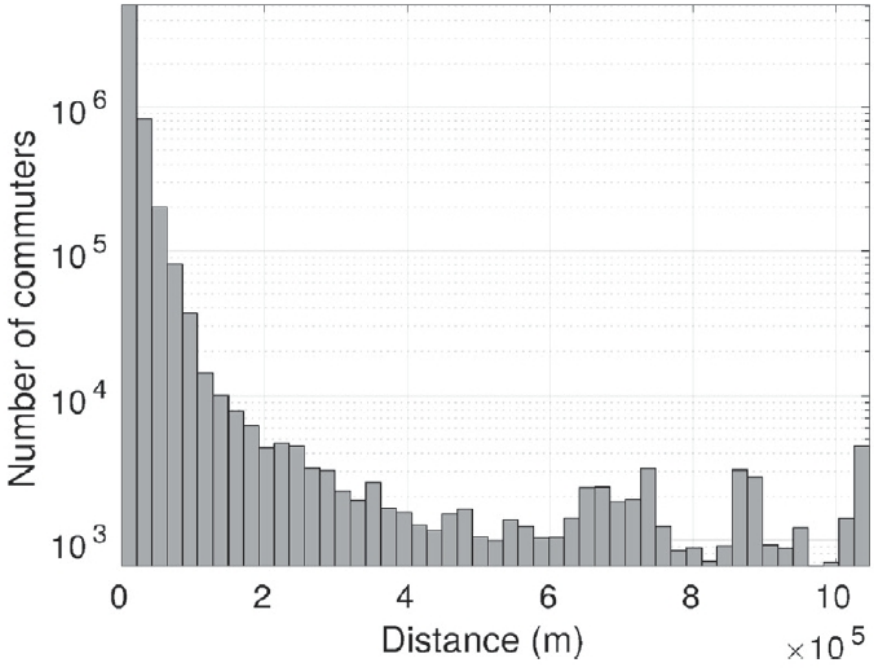
Oliver M. Cliff[*,a], Nathan Harding[a], Mahendra Piraveenan[a], E. Yagmur Erten[a,b], Manoj Gambhir[c], Mikhail Prokopenko[a,d]

[a] Centre for Complex Systems, Faculty of Engineering and IT, University of Sydney, Sydney, NSW 2006, Australia
[b] Department of Evolutionary Biology and Environmental Studies, University of Zurich, Winterthurerstrasse 190, Zurich, 8057, Switzerland
[c] IBM Research, Melbourne, Australia
[d] Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Westmead, NSW 2145, Australia

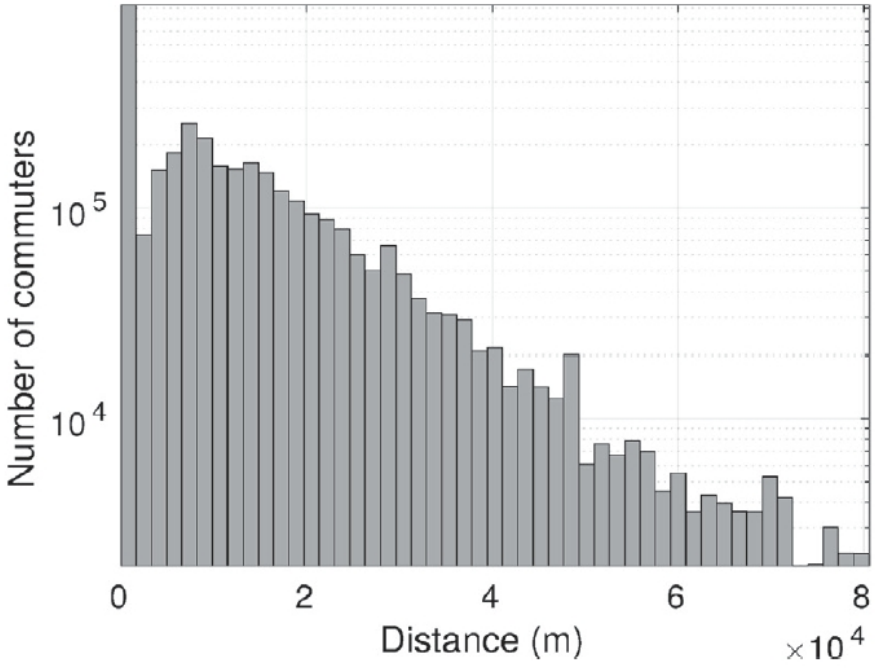
Australian Census based Epidemic Modelling: ACEMod



Australian Census: travel-to-work data (mobility)



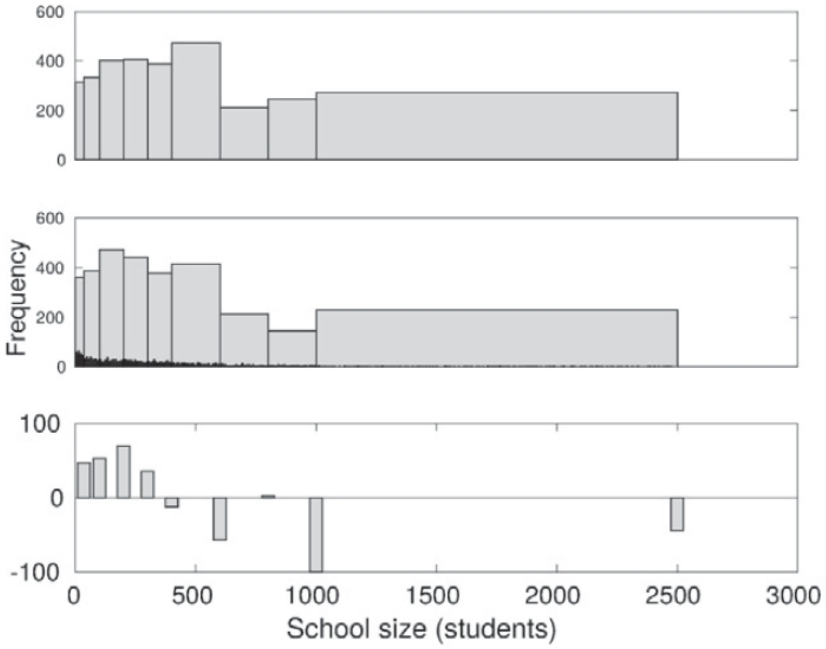
(a) Workers



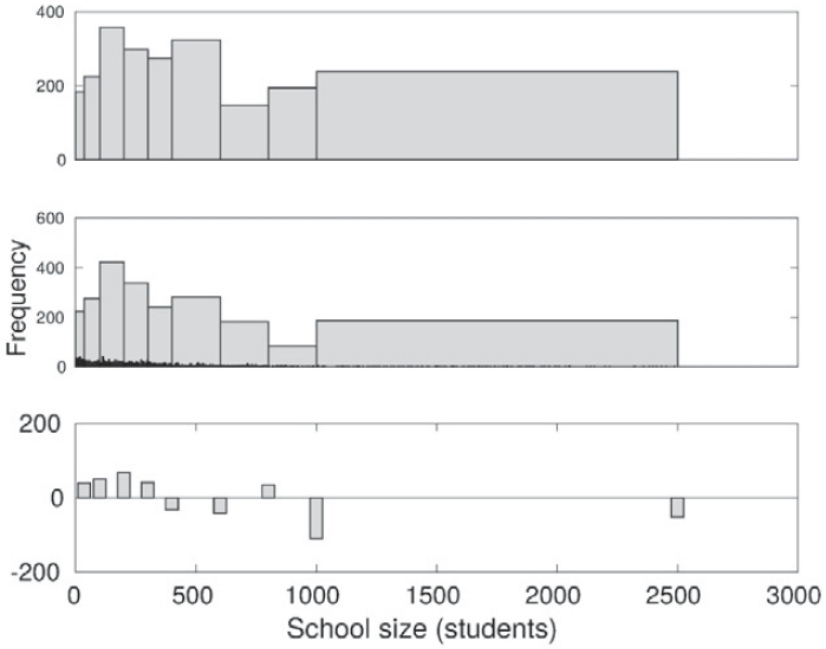
(b) Students

Fig. B1. Commute distance distributions.

Australian Census: schools



(a) NSW



(b) VIC

International air traffic

Airport code	State	City	Passengers
SYD	NSW	Sydney	40884
MEL	VIC	Melbourne	25859
BNE	QLD	Brisbane	14250
PER	WA	Perth	11449
OOL	QLD	Gold Coast	3022
ADL	SA	Adelaide	2214
CNS	QLD	Cairns	1874
DRW	NT	Darwin	597
TSV	QLD	Townsville	105

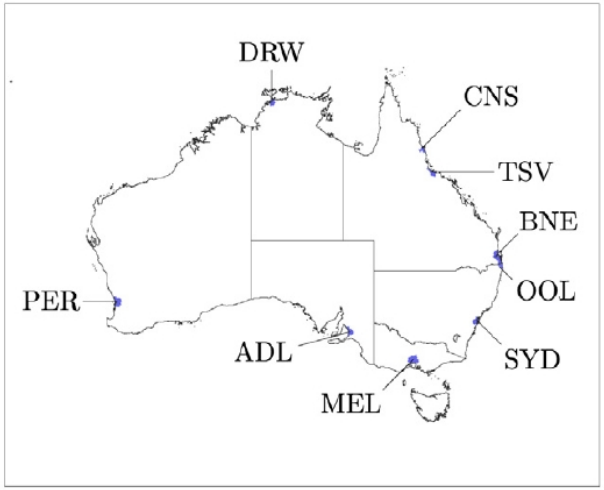


Fig. 3. Daily incoming passengers per Australian international airport obtained from BITRE [30] along with a map detailing the airport locations.

Epidemic modelling: transmission probabilities

Table C2
Daily transmission probabilities $q^g_{j\to i}$ for different contact groups g, obtained by Eq. (4) where $\beta^g_{j\to i}$ are reported by [10].

Contact Group g	Infected Individual j	Susceptible Individual i	Transmission Probability $q^g_{j\to i}$
Household size 2	Any	Child (<19)	0.0933
	Any	Adult (>18)	0.0393
Household size 3	Any	Child (<19)	0.0586
	Any	Adult (>18)	0.0244
Household size 4	Any	Child (<19)	0.0417
	Any	Adult (>18)	0.0173
Household size 5	Any	Child (<19)	0.0321
	Any	Adult (>18)	0.0133
Household size 6	Any	Child (<19)	0.0259
	Any	Adult (>18)	0.0107
School	Child (<19)	Child (<19)	0.000292
Grade	Child (<19)	Child (<19)	0.00158
Class	Child (<19)	Child (<19)	0.035

PNAS

Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza

Simon Cauchemez[a,1], Achuyt Bhattarai[b], Tiffany L. Marchbanks[c], Ryan P. Fagan[b], Stephen Ostroff[c], Neil M. Ferguson[a], David Swerdlow[b], and the Pennsylvania H1N1 working group[b,c,2]

[a]Medical Research Council Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London W2 1PG, United Kingdom; [b]Centers for Disease Control and Prevention, Atlanta, GA 30333; and [c]Pennsylvania Department of Health, Harrisburg, PA 17120-0701

Edited by David Cox, Nuffield College, Oxford, United Kingdom, and approved December 22, 2010 (received for review June 22, 2010)

Evaluating the impact of different social networks on the spread of respiratory diseases has been limited by a lack of detailed data on transmission outside the household setting as well as appropriate statistical methods. Here, from data collected during a H1N1 pandemic (pdm) influenza outbreak that started in an elementary school and spread in a semirural community in Pennsylvania, we quantify how transmission of influenza is affected by social networks. We set up a transmission model for which parameters are estimated from the data via Markov chain Monte Carlo sampling. Sitting next to a case or being the playmate of a case did not significantly increase the risk of infection; but the structuring of

sylvania to investigate how social networks and population structures affect influenza transmission.

Results and Discussion

Outbreak Investigation. Fig. 1 presents the data that were collected during the outbreak investigation. Demographic and clinical information on 370 (81%) students from 295 (81%) households and their 899 household contacts was collected during two rounds of phone interviews (May 16–21 and May 26–June 2). One hundred twenty-nine (35%) students and 141 (16%) household contacts were reported to have had acute re-

Social interactions (Cauchemez et al., 2010)

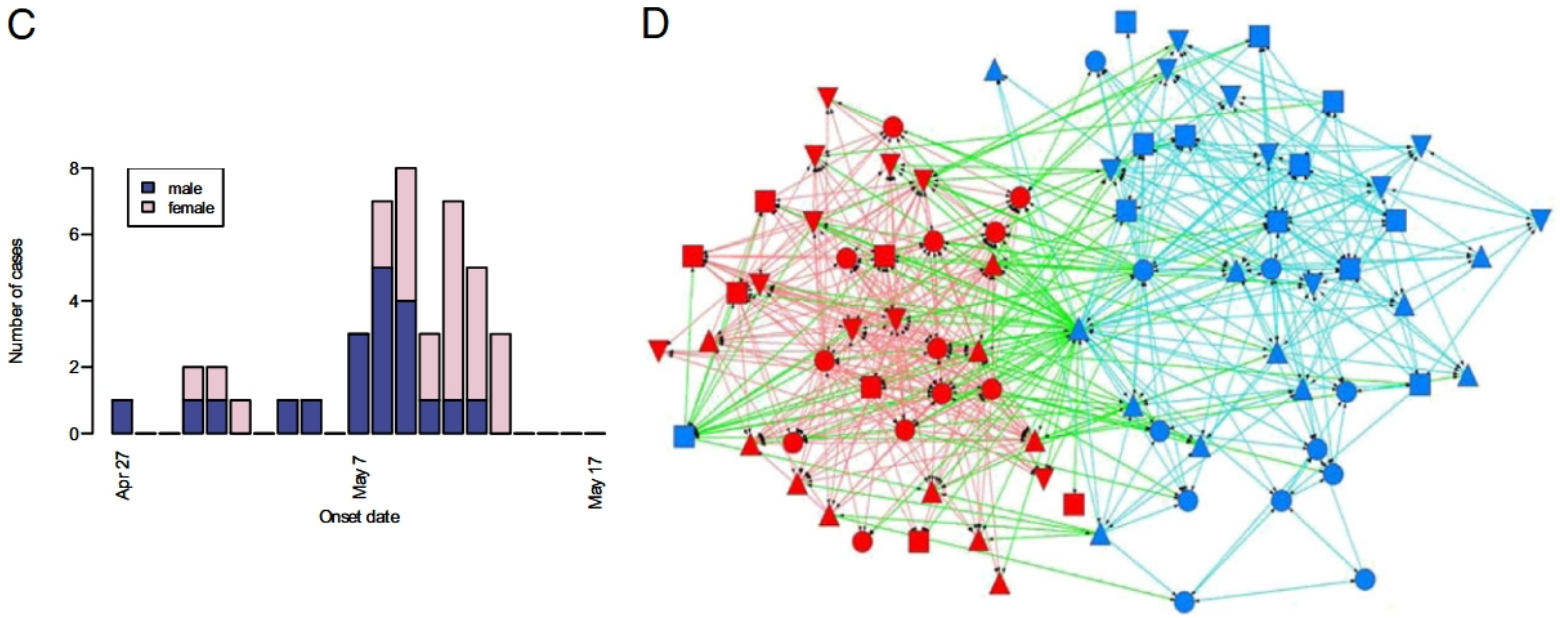


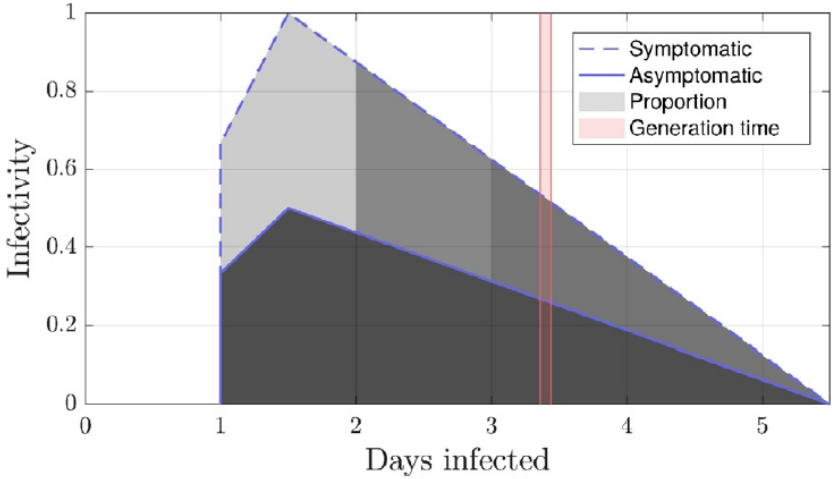
Fig. 1. Epidemiological data collected in the school. (*A*) Number of acute respiratory illness (ARI) cases by date of symptom onset for different types of individuals. (*B–D*) Survey of fourth graders with (*B*) seating charts and diagnosis for ARI in classroom C, (*C*) number of ARI cases by date of symptom onset and sex among fourth graders, and (*D*) social networking among fourth graders based on the question "Who are your playmates?" [color of the nodes, red, female; blue, male; color of the lines, red, girl–girl interaction; cyan, boy–boy interaction; green, boy–girl interaction (one symbol shape per class)]. The algorithm used to draw the network aims at (*i*) distributing nodes evenly, (*ii*) making edge length uniform, (*iii*) minimizing edge crossings, and (*iv*) keeping nodes from coming too close to edges (32, 33) (software: *Netdraw*). It does not use data on sex to position the nodes.

Epidemic modelling: contact rates

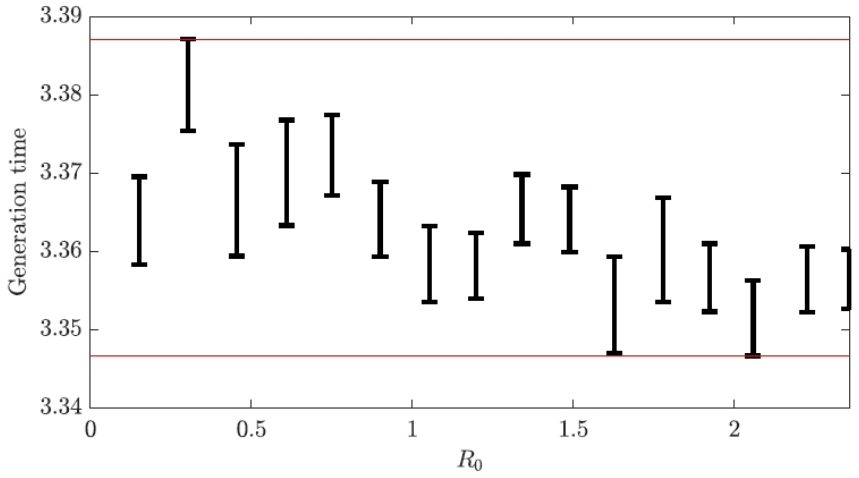
Table C1
Daily contact probabilities $c^{g}_{j\to i}$ for different contact groups g, reported by [22].

Mixing group g	Infected individual j	Susceptible individual i	Contact probability $c^{g}_{j\to i}$
Household cluster	Child (<19)	Child (<19)	0.08
	Child (<19)	Adult (>18)	0.035
	Adult (>18)	Child (<19)	0.025
	Adult (>18)	Adult	0.04
Working Group	Adult (19-64)	Adult (19-64)	0.05
Neighbourhood	Any	Child (0-4)	0.0000435
	Any	Child (5-18)	0.0001305
	Any	Adult (19-64)	0.000348
	Any	Adult (65+)	0.000696
Community	Any	Child (0-4)	0.0000109
	Any	Child (5-18)	0.0000326
	Any	Adult (19-64)	0.000087
	Any	Adult (65+)	0.000174

Epidemic modelling: natural history of the disease



(a) Natural history of the disease.



(b) Simulated generation time.

Fig. 2. Natural history of the disease and corresponding simulated generation time. The disease dynamics are modelled as having a linear increase followed by a linear decrease, as illustrated in Fig. 2 (a). In the figure, the area under the curve is shaded according to the proportion of people *at least* that infectious after disease onset (darker representing a higher proportion). If an agent becomes symptomatic, their infectiousness doubles (dashed blue line) from that day onward. Moreover, 67% of agents become symptomatic; of these agents, 30% start showing symptoms on day 1, 50% on day 2, and the remaining 20% on day 3. We obtain empirical generation times from simulations resulting from this model, shown in 2(b) for a number of R_0 values. The confidence intervals range from 3.35 to 3.39 days (also shown on Fig. 2(a)), depending on R_0 and, in general, the generation time has a slight downward trend as a function of disease severity.

Epidemic modelling: reproductive ratio R_0

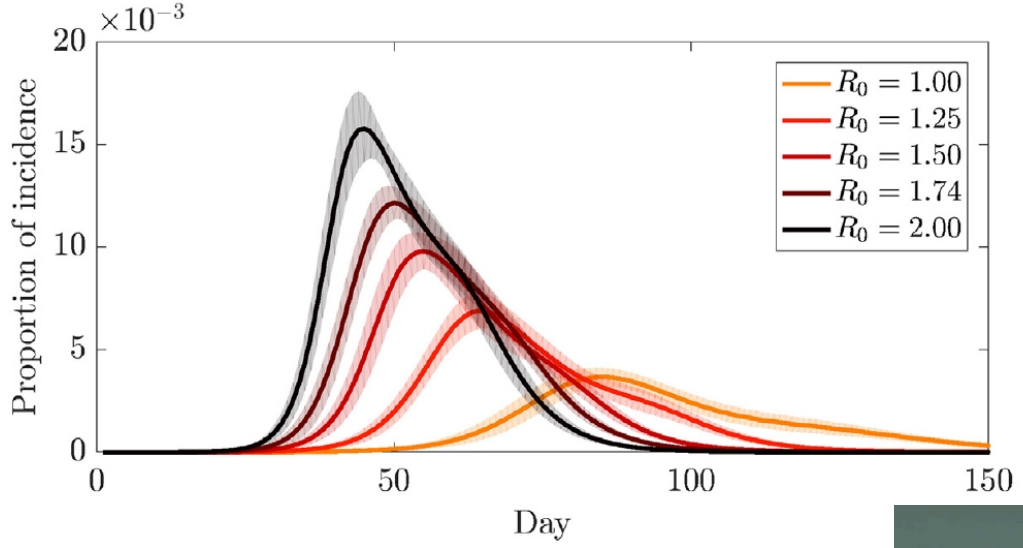
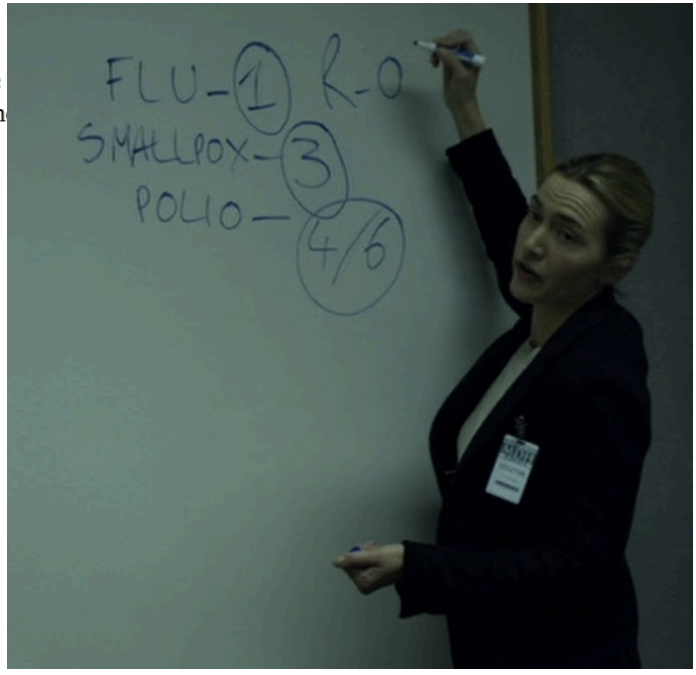


Fig. 5. The epidemic curve illustrates the trajectory of the epidemic by tracing the incidence over time behaviour of the simulated influenza epidemics in Australia with $R_0 = \{1.0, 1.25, 1.5, 1.75, 2.0\}$. We perform plot the mean (solid lines) and standard deviation (shaded area).



"Contagion" (2011)

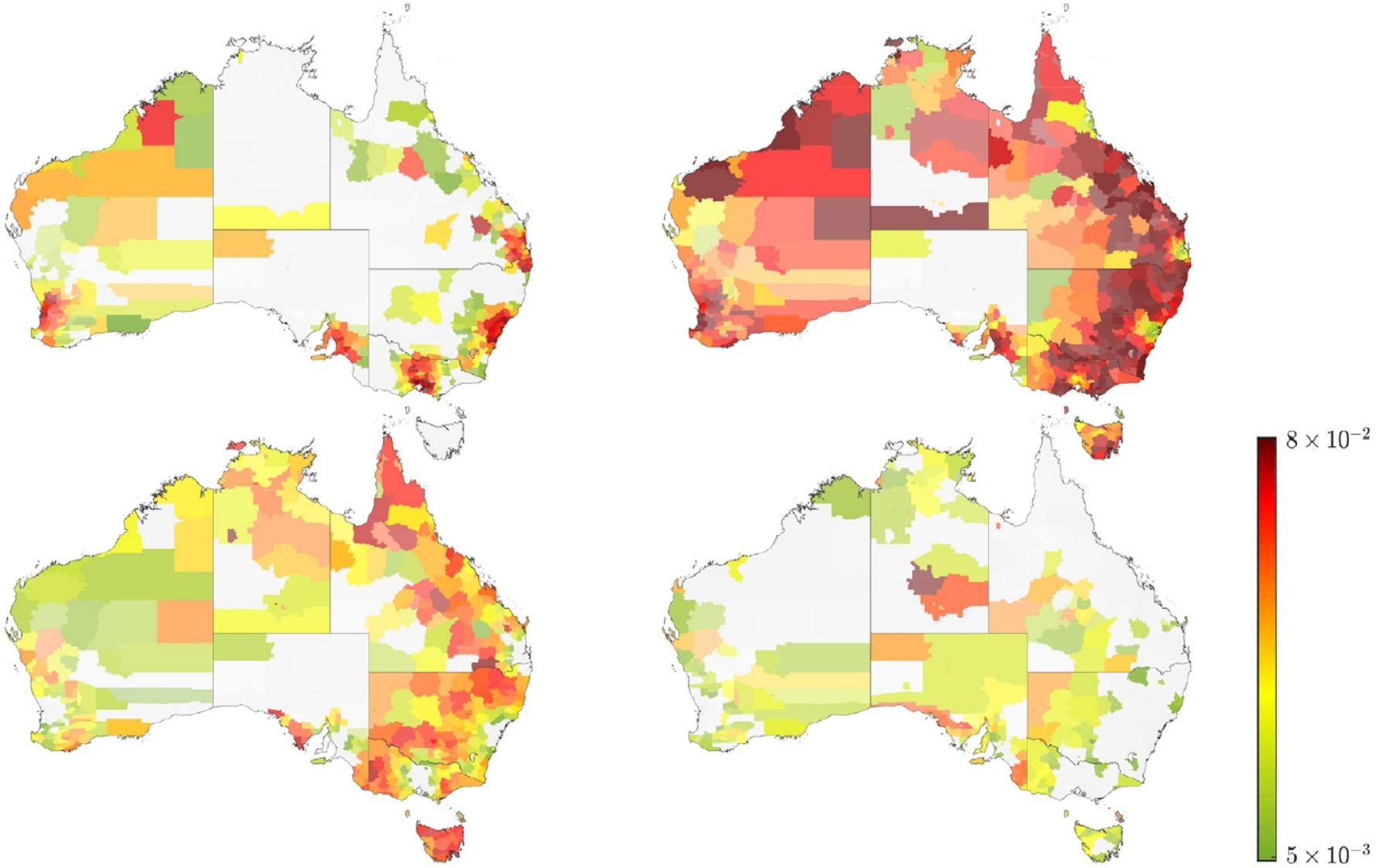
Australian Census based Epidemic Modelling: ACEMod

Table 1
Characteristics of the incidence curves, averaged over 10 trials.

Basic reproductive number R_0	1.0	1.25	1.5	1.75	2.0
Rate of spread: 1K ill*	29	22	21	18	17
10K ill*	44	33	30	25	24
100K ill*	60	44	39	33	31
1M ill*	80	58	50	42	39
Peak of epidemic*	84	63	59	47	47
Daily number of new cases at peak activity	85.3 K	140 K	189 K	257 K	328 K
Number of days with > 100K ill	44	55	52	51	48
Cumulative number of ill individuals	3.4 M	5.0 M	6.4 M	7.7 M	8.8 M
Synchrony of community epidemic peaks (10^{-3})	1.38	2.67	4.33	6.39	7.70

M – Million; K – Thousand.
* Days after initial introduction.

Australian Census based Epidemic Modelling: ACEMod



(a) $R_0 = 1.5$ (b) $R_0 = 2.0$

Hierarchical spatial spread or wave-like diffusion??

C. Viboud, O.N. Bjørnstad, D.L. Smith, L. Simonsen, M.A. Miller, B.T. Grenfell, Synchrony, waves, and spatial hierarchies in the spread of influenza, *Science* 312 (5772) (2006) 447–451.

The regional spread of infection correlates more closely with rates of movement of people to and from their workplaces (workflows) than with geographical distance.

The hierarchy of spread is immediately apparent: The most populous states exhibit synchronized epidemics, whereas less populated states exhibit more erratic patterns, both relative to each other and to the continental norm.

RESEARCH ARTICLE | SOCIAL SCIENCES

Urbanization affects peak timing, prevalence, and bimodality of influenza pandemics in Australia: Results of a census-calibrated model

Cameron Zachreson[1,*], Kristopher M. Fair[1], Oliver M. Cliff[1], Nathan Harding[1], Mahendra Piraveenan[1] and Mikhail Prokopenko[1,2]

[1]Complex Systems Research Group, School of Civil Engineering, Faculty of Engineering and IT, The University of Sydney, Sydney, NSW 2006, Australia.

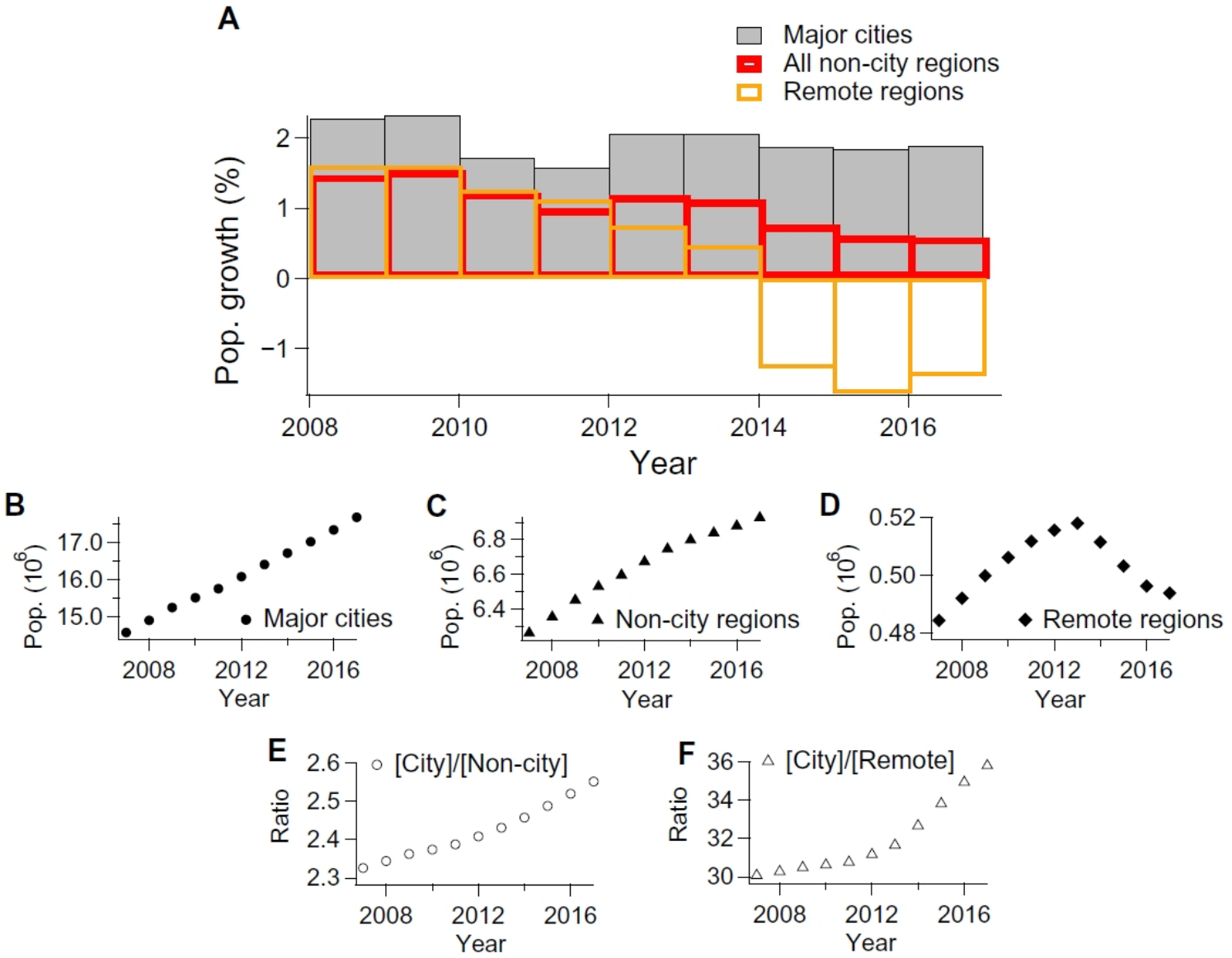
[2]Marie Bashir Institute for Infectious Diseases and Biosecurity, The University of Sydney, Westmead, NSW 2145, Australia.

[*]Corresponding author. Email: cameron.zachreson@sydney.edu.au

– Hide authors and affiliations

Science Advances 12 Dec 2018:
Vol. 4, no. 12, eaau5294
DOI: 10.1126/sciadv.aau5294

Urbanisation

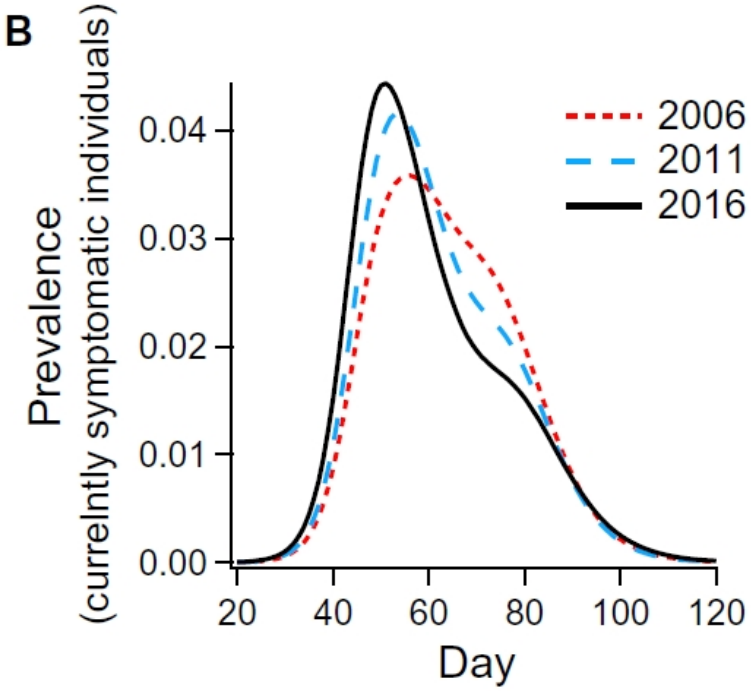


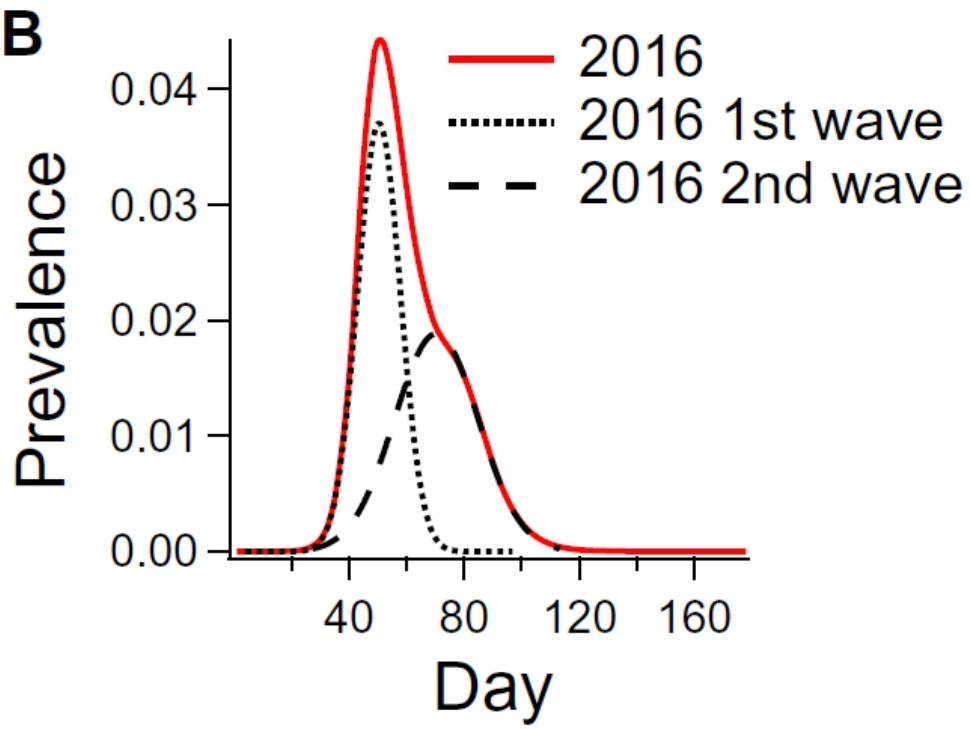
International air traffic

Table 1. Average daily incoming international air traffic.

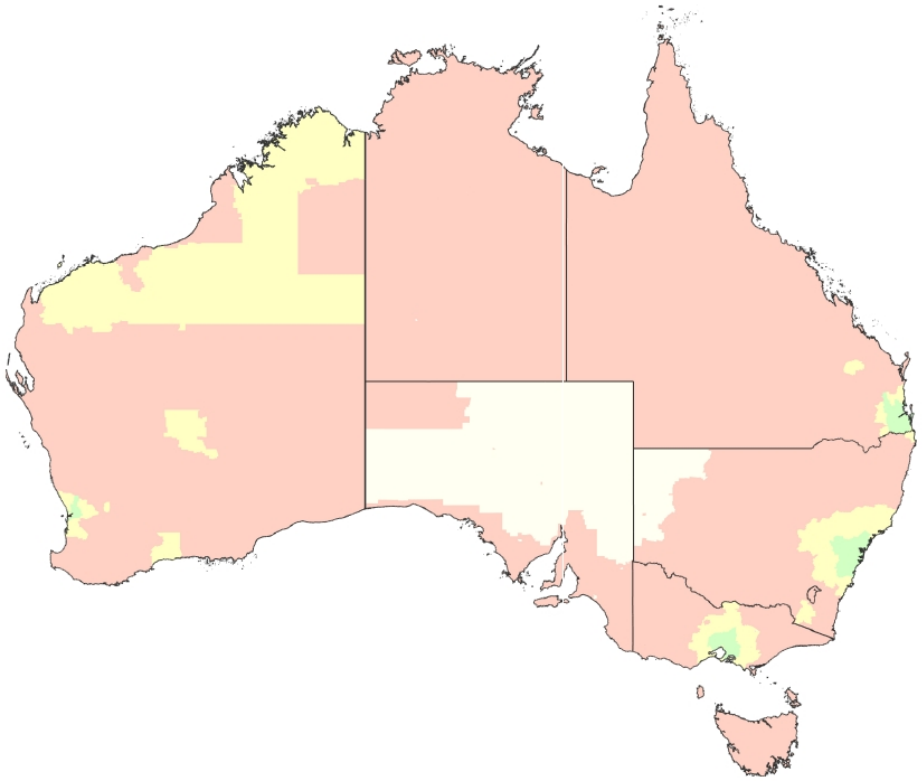
Airport	State	Year		
		2006	2011	2016
Sydney	New South Wales	13,214	15,995	19,991
Melbourne	Victoria	5,923	8,557	12,802
Brisbane	Queensland	5,053	5,946	7,299
Perth	Western Australia	2,766	4,512	5,906
Gold Coast	Queensland	285	1,044	1,435
Adelaide	South Australia	492	766	1,170
Cairns	Queensland	1,186	707	824
Darwin	Northern Territory	160	356	355
Townsville	Queensland	0	11	39

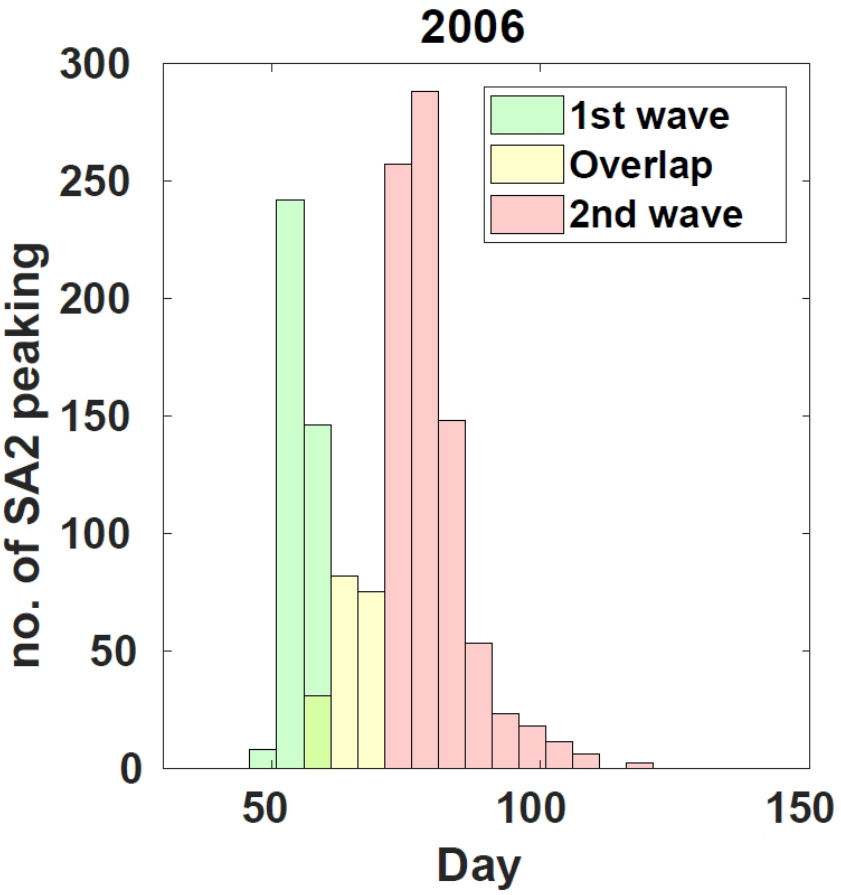
Prevalence and epidemic peak



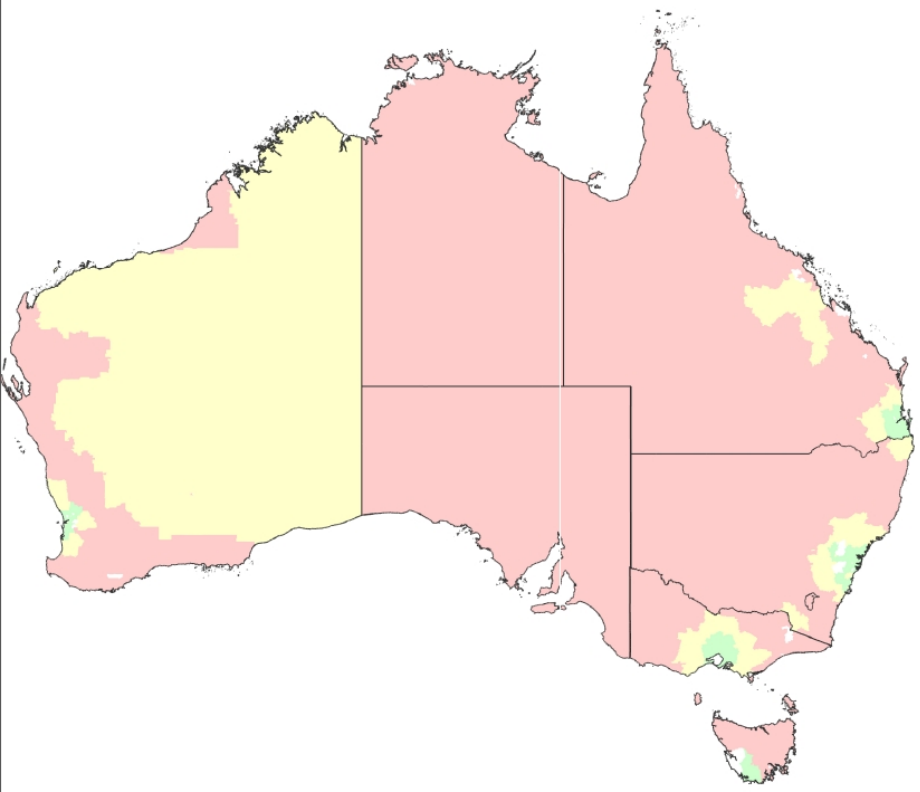


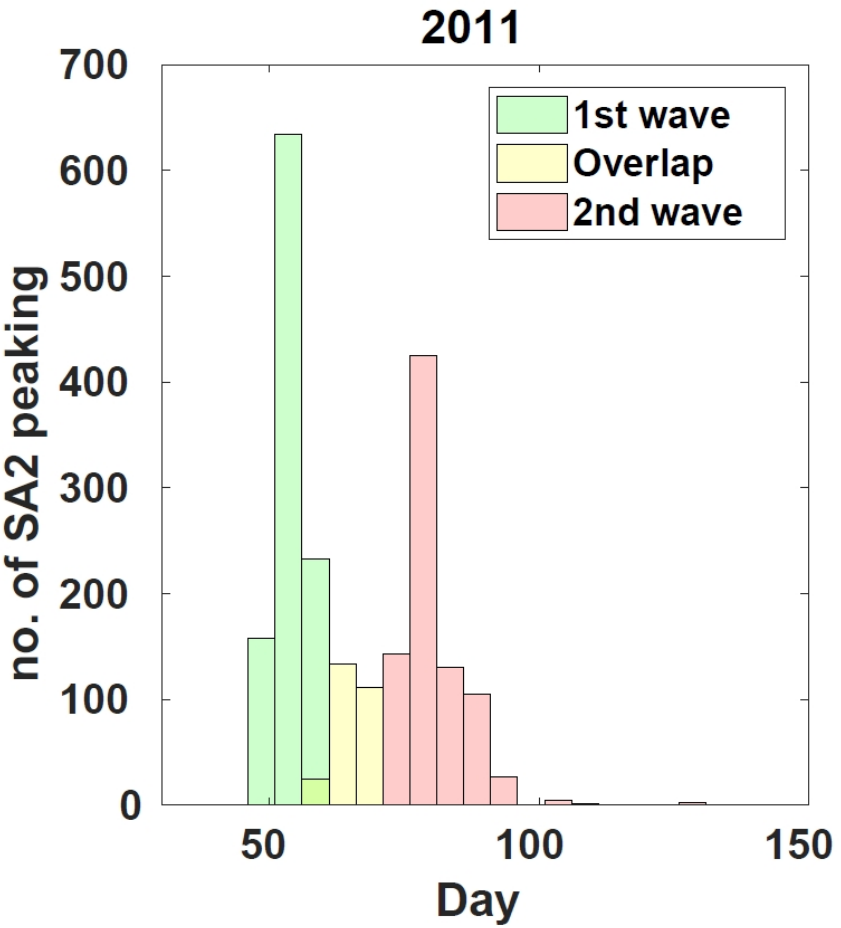
Bimodality: 2006



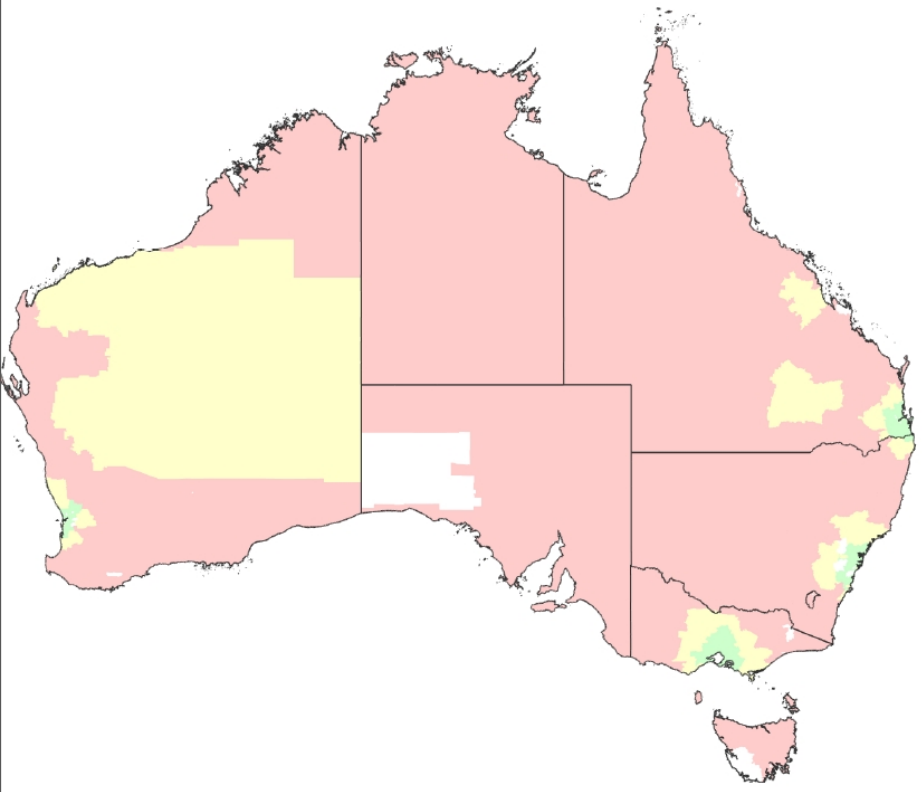


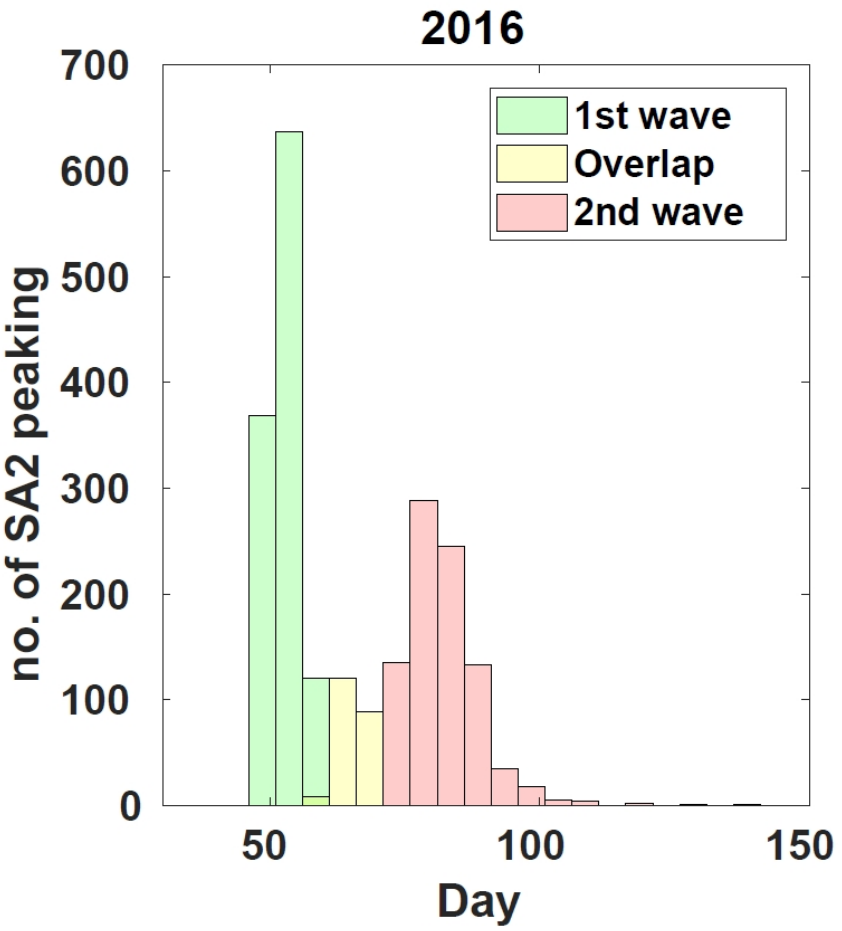
Bimodality: 2011



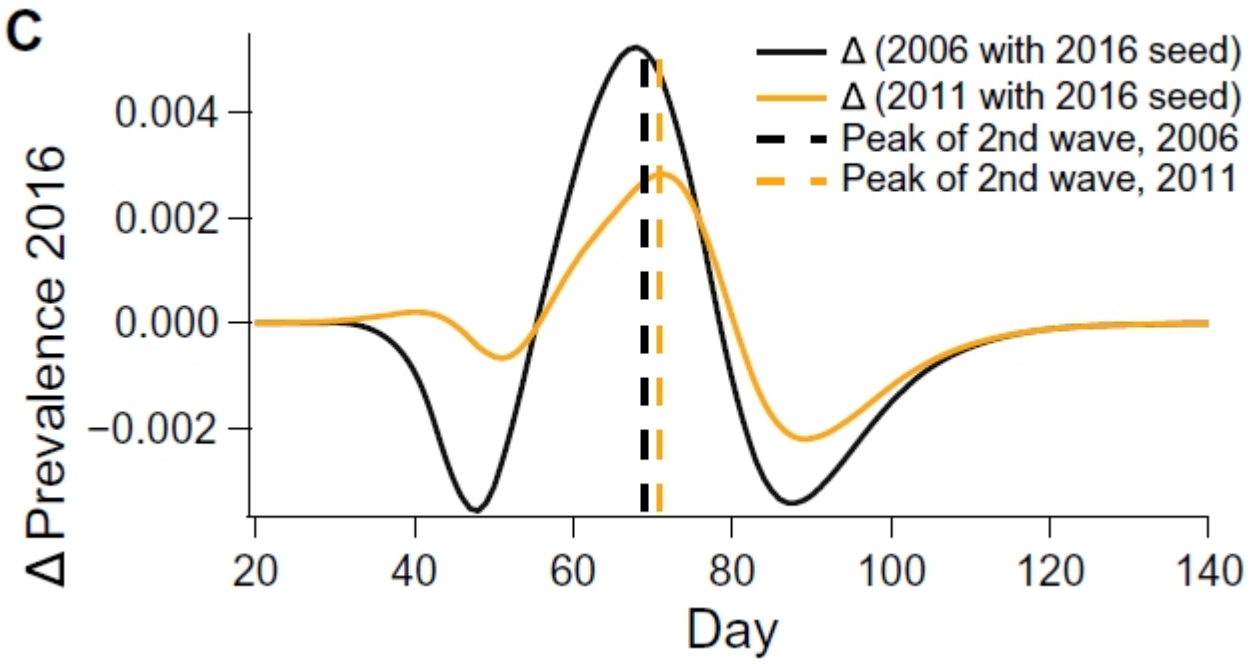


Bimodality: 2016





Key factors: higher urbanisation or more air traffic?



- seeding conditions have a larger impact on the first wave than on the second
- seeding does not account for the decrease in the intensity of the second pandemic wave from year to year, a trend that we ascribe to increased urbanisation

Summary

- ACEMod (Australian Census-based Epidemic Model): calibrated and validated ABM
- "zooming in" on specific pathways and patterns of epidemics
- studying global spatiotemporal system dynamics: epidemic peaks, prevalence, waves and bimodality, synchrony, etc.
- contrasting historical periods (Australian census datasets: 2006, 2011, 2016)
- comparing prevention and intervention strategies (“what-if” scenarios)
- planning healthcare resources

References

- S. Cauchemez, A. Bhattarai, T. L. Marchbanks, R. P. Fagan, S. Ostroff, N. M. Ferguson, D. Swerdlow; Pennsylvania H1N1 Working Group, Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic influenza, *Proceedings of the National Academy of Sciences of the U.S.A.*, 108, 2825–2830, 2011.
- S. L. Chang, M. Piraveenan, M. Prokopenko, The effects of imitation dynamics on vaccination behaviours in SIR-network model, *International Journal of Environmental Research and Public Health*, 16, 2477, 2019.
- O. M. Cliff, N. Harding, M. Piraveenan, E. Erten, M. Gambhir, M. Prokopenko, Investigating spatiotemporal dynamics and synchrony of infuenza epidemics in Australia: An agent-based modelling approach, *Simulation Modelling Practice and Theory*, 87, 412-431, 2018.
- K. M. Fair, C. Zachreson, M. Prokopenko, Creating a surrogate commuter network from Australian Bureau of Statistics census data, *Scientific data*, 6, 150, 2019.
- T. C. Germann, K. Kadau, I. M. Longini Jr., C. A. Macken, Mitigation strategies for pandemic influenza in the United States, *Proceedings of the National Academy of Sciences of the U.S.A.*, 103, 5935–5940, 2006.
- K. Kadau, T. C. Germann, P. Lomdahl, Large-Scale Molecular-Dynamics Simulation of 19 Billion Particles, *International Journal of Modern Physics C*, 27(15): 193-201, 2004.
- C. Viboud, O. N. Bjørnstad, D. L. Smith, L. Simonsen, M. A. Miller, B.T. Grenfell, Synchrony, waves, and spatial hierarchies in the spread of influenza, *Science*, 312(5772): 447–451, 2006.
- C. Zachreson, K. M. Fair, O. M. Cliff, N. Harding, M. Piraveenan, M. Prokopenko, Urbanization affects peak timing, prevalence, and bimodality of influenza pandemics in Australia: Results of a census-calibrated model, *Science Advances*, 4(12), eaau5294, 2018.