Large-scale Agent-based simulations of pandemic influenza in Australia: framework, historical trends, interventions

Presented by
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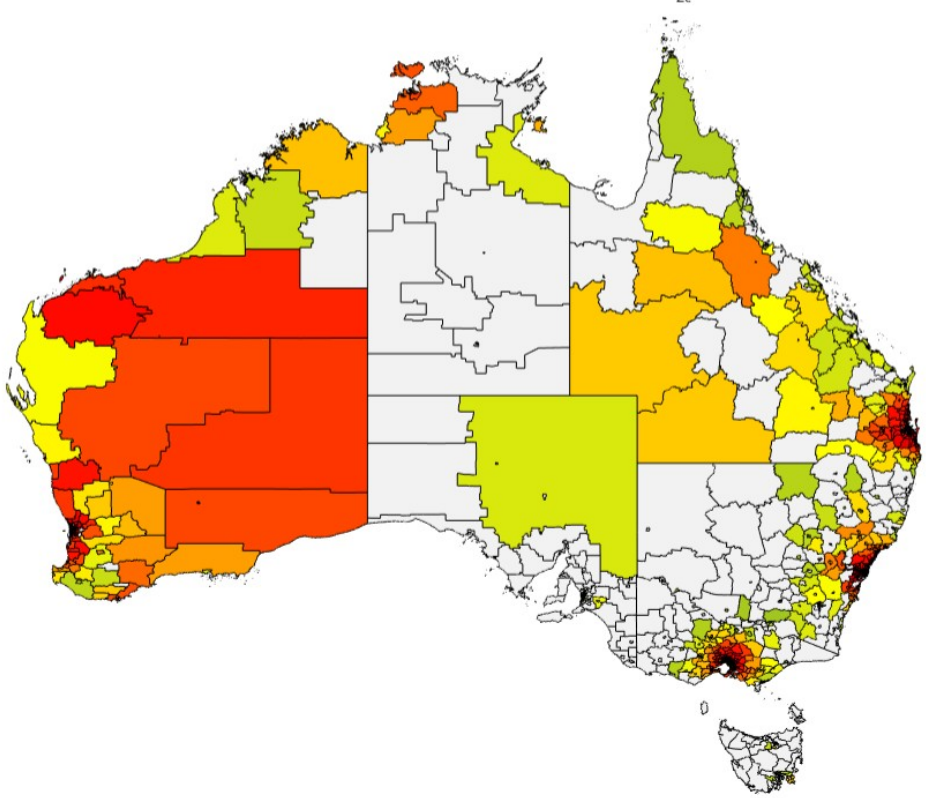
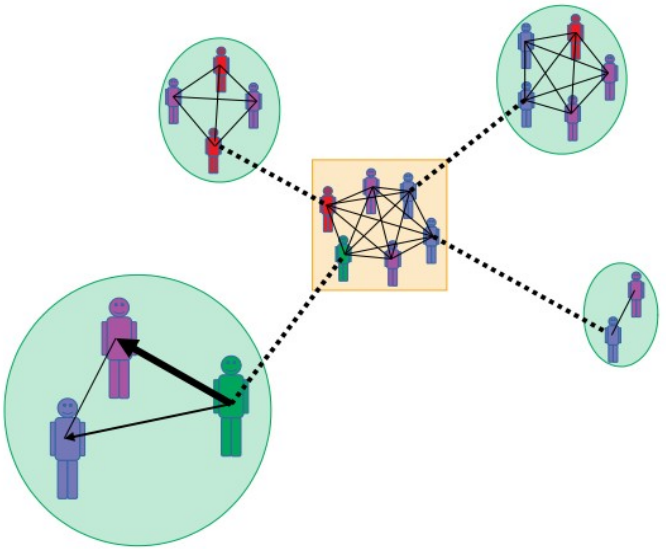
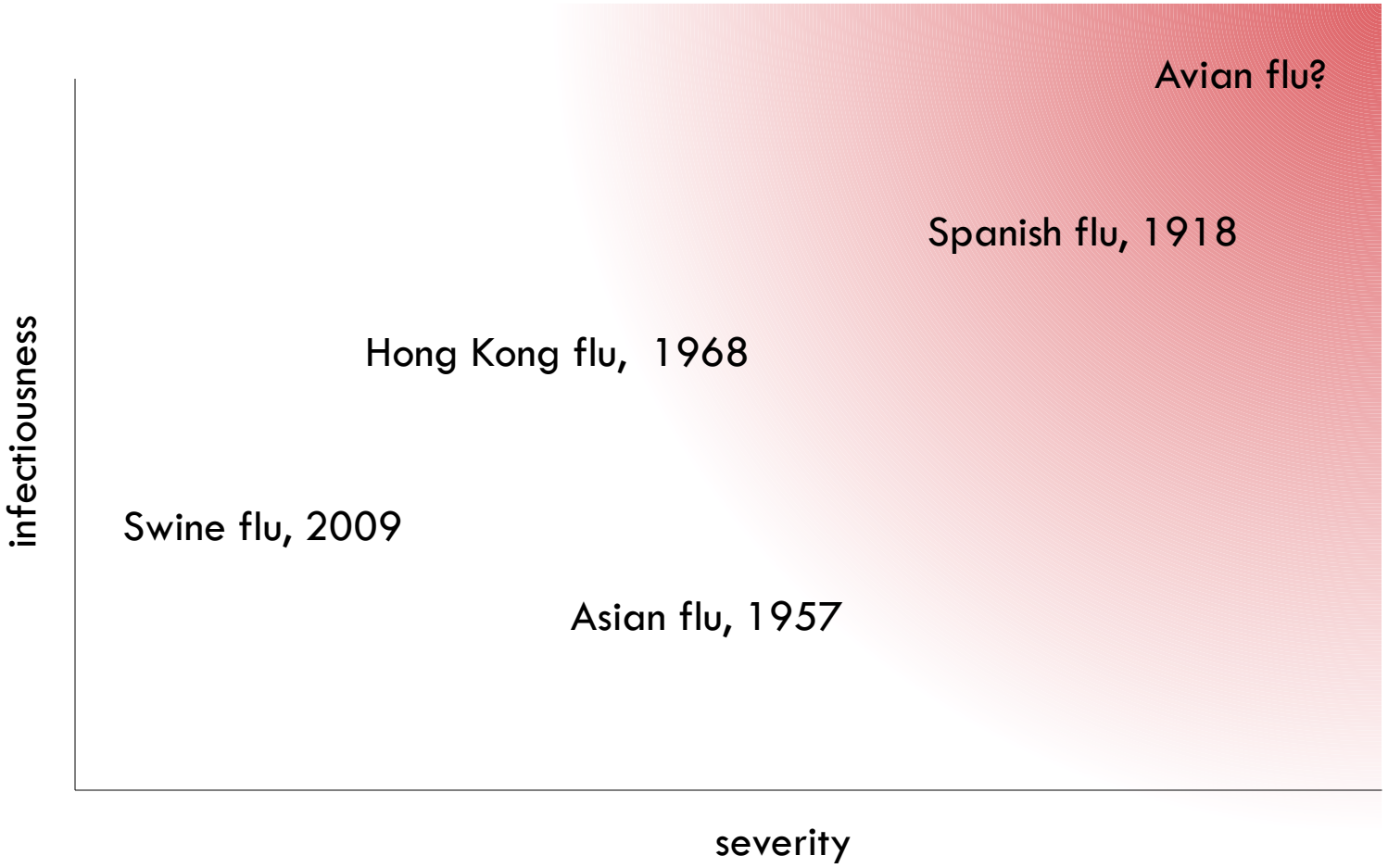




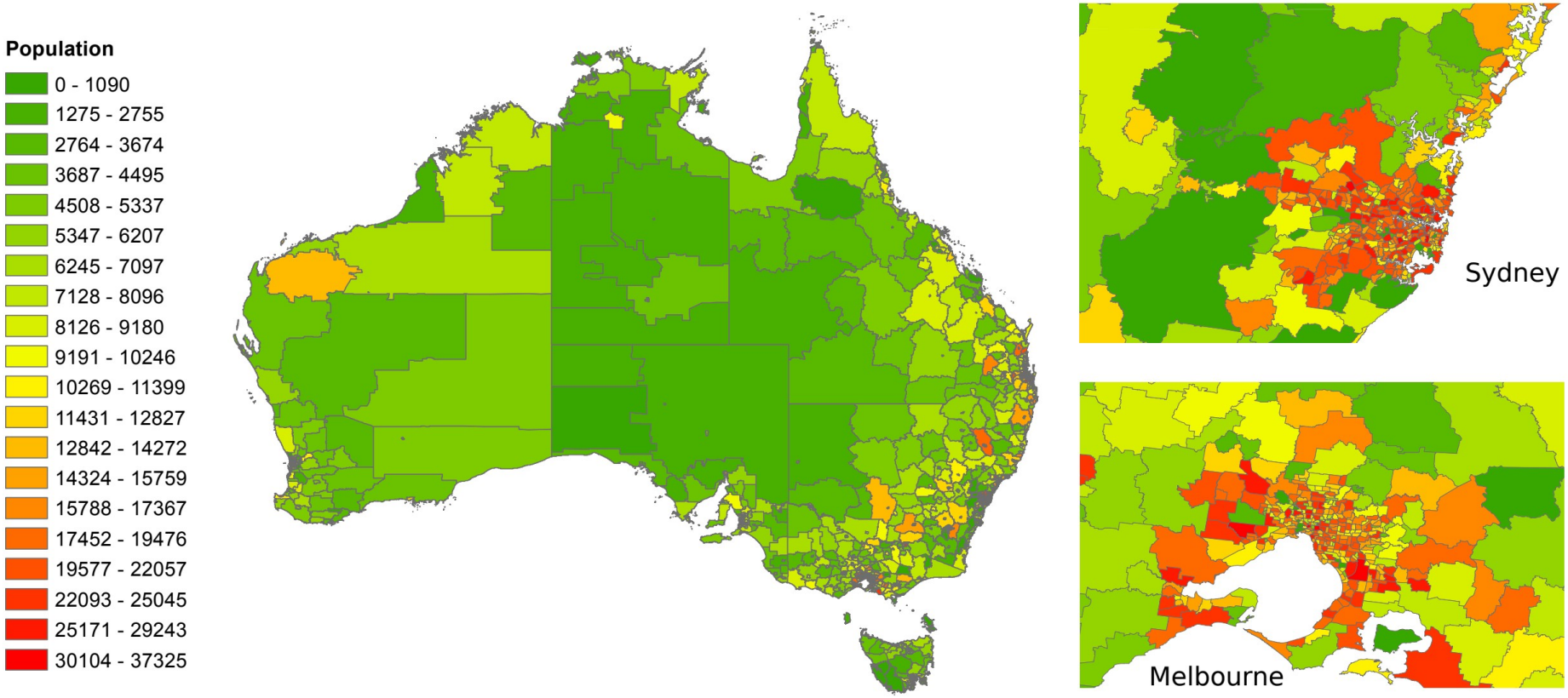
What is the problem?

pandemic influenza - a killer virus of the future (“not if... but *when*”)



What is the context?

Australia - a highly urbanised nation with vast, sparsely populated rural areas



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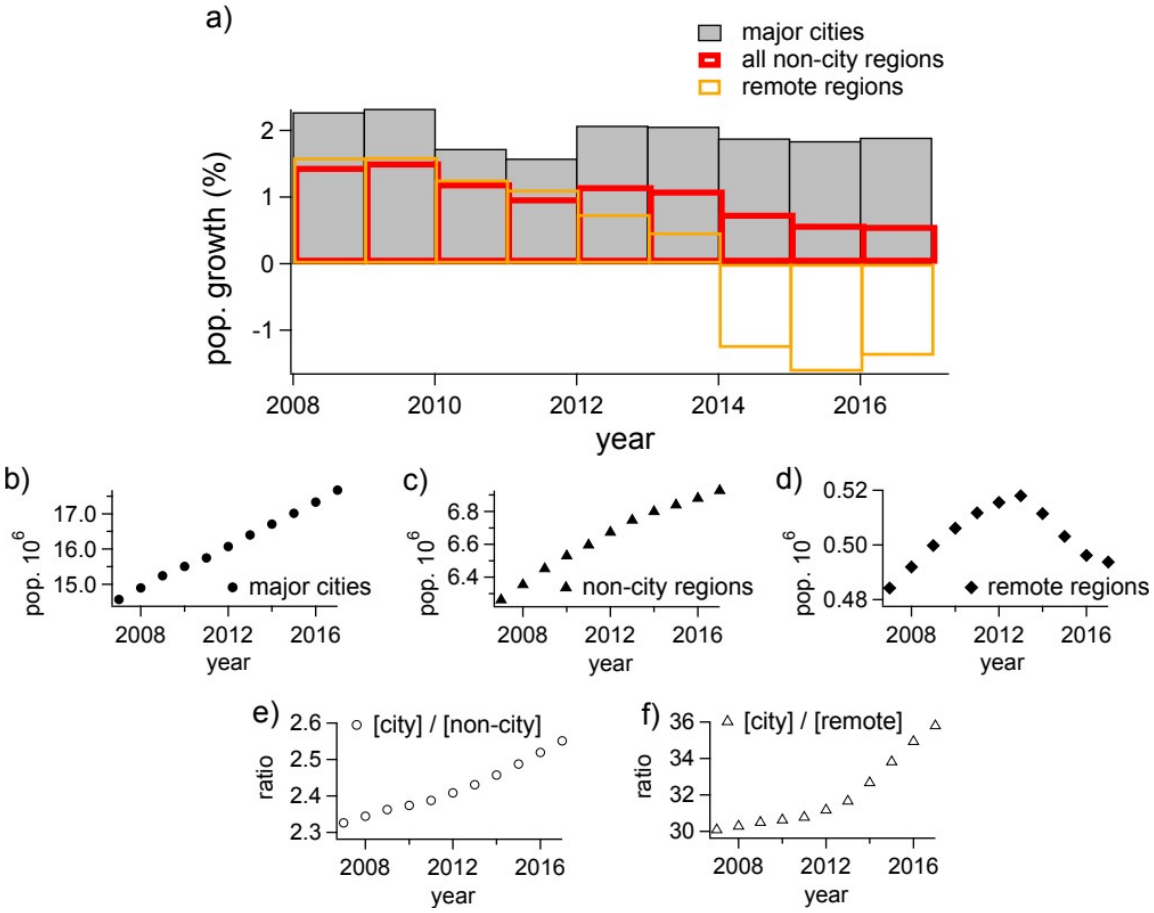

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Introduction

Key messages

Why use ABMs to simulate epidemics?

- ABM modelling framework

Role of population structure

- Comparison with networked metapopulation model

- Results: Historical trends - the effects of urbanisation

Unintended consequences of reactive interventions

- Results: intervention strategies – reactive targeted prophylaxis

Australian Census-based Epidemic Model (ACEMod)

Individual-based simulation platform for pandemic influenza in Australia

Surrogate population sampled from the Australian Census

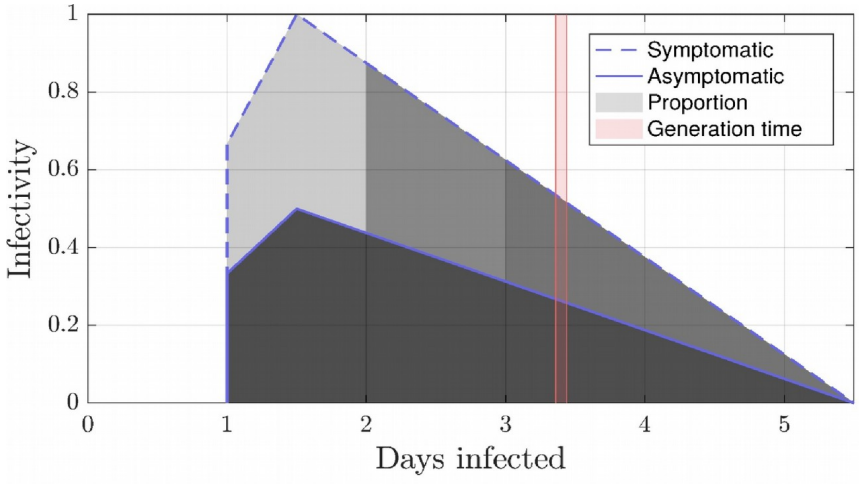
- Recurrent travel patterns – Commuting data, estimated school attendance
- Complex interaction topology – households, schools, work groups, etc.
- Heterogeneous age and sex – context-dependent transmission factors

International influenza pandemic scenario

- Stochastic "seeding" conditions (international airports)
- Stochastic transmission dynamics, asymptomatic cases etc.

The components of ACEMod

Internal processes and states: natural history of influenza



Susceptible → Infected exposed, not contagious, not symptomatic → Infected contagious, 70% symptomatic 30% asymptomatic → Recovered

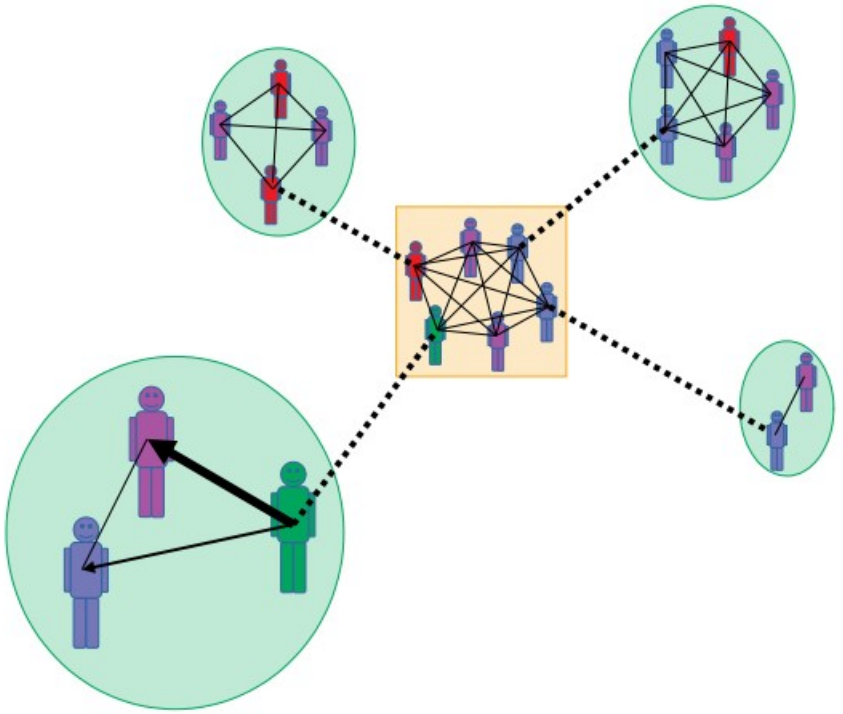
Transmission and infection

"Transmission probability" (force of infection):

$$p^g_{j\to i}(n) = \kappa\ f(n - n_j \mid j, i)\ q^g_{j\to i}$$

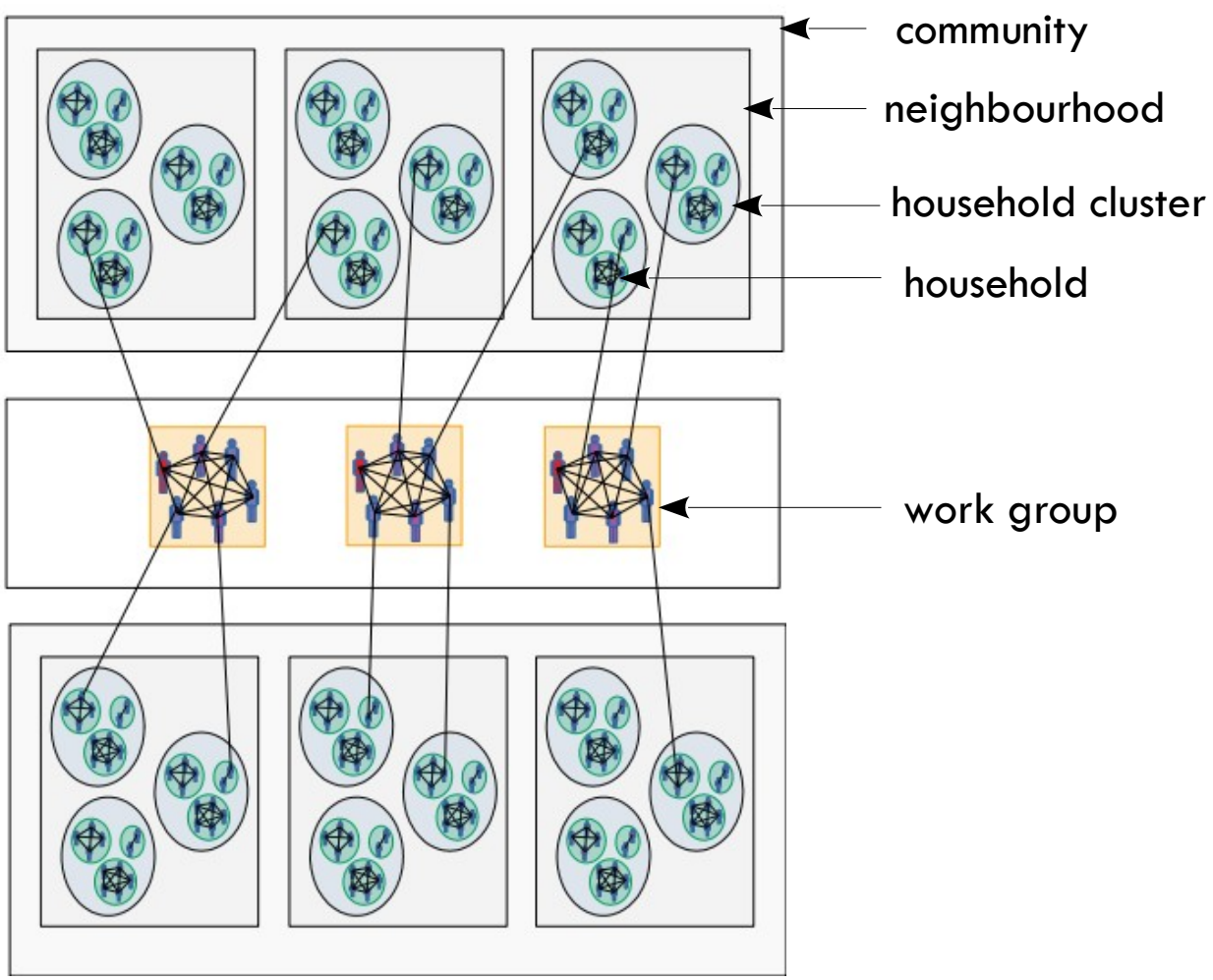
Infection probability:

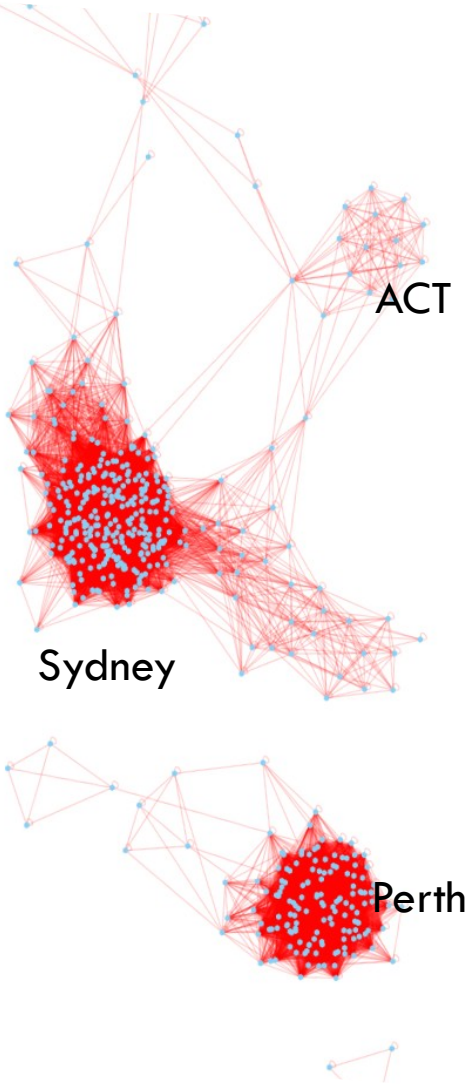
$$p_i(n) = 1 - \prod_{g\in\mathcal{G}_i(n)} \left[\prod_{j\in\mathcal{A}_g\setminus i} \left(1 - p^g_{j\to i}(n)\right) \right]$$



Pairwise transmission factors depend on **mixing group** (g), **age groups** of both individuals, **infection state** of both individuals (f), and **infectiousness** of the virus κ

Components of ACEmod: interaction structure





Components of ACEmod: Initial conditions

Pandemic begins abroad and comes to Australian cities via international air travel

Airport location	Daily international arrivals (2016)
Sydney NSW	19,991
Melbourne VIC	12,802
Brisbane QLD	7299
Perth WA	5906
Gold Coast QLD	1435
Adelaide SA	1170
Townsville QLD	824
Darwin NT	355
Australian Capital Territory	39

Why ABMs?

What are the modelling objectives?

- High fidelity dynamics
- population heterogeneity
- complex reactive interventions

Given these objectives, what other possible frameworks are available?

Metapopulation models offer a (possibly less complex) alternative.

- deterministic dynamics
- continuum equations
- historically well-established

Let's compare them

Comparison with Metapopulation model

Standard metapopulation models use continuous dynamics to compute disease transmission between regions or distinct demographic groups (or both)

A metapopulation model constructed from an ACEMod population, with SIR dynamics:

$$\frac{dS}{dt} = -\beta SI \quad ; \quad \frac{dI}{dt} = \beta SI - \gamma I \quad ; \quad \frac{dR}{dt} = \gamma I \qquad \boxed{R_0 = \frac{\beta}{\gamma}}$$

"well-mixed" assumption

Aggregate Travel network (bipartite) ⟶ Metapopulation mixing network

$$\phi_{ij} = \mathrm{OD}(\mathrm{SA2UR}_i \to \mathrm{SA2POW}_j)$$

$$\Psi_{ij} = \sum_{k=1}^{N} \phi_{ik}\phi_{jk}\frac{1}{N_k^p} \qquad N_j^p = \sum_{i=1}^{N} \phi_{ij}$$

Transmission and recovery dynamics: Next-Generation matrix

$$K_{ij}(t) = \beta \mathbf{\Psi}_{ij} S_i(t) - \gamma \mathbb{I}_{ij} \,,$$

$$\boldsymbol{I}(t + \Delta t) = \boldsymbol{I}(t) \left[K(t)\Delta t + \mathbb{I} \right]$$

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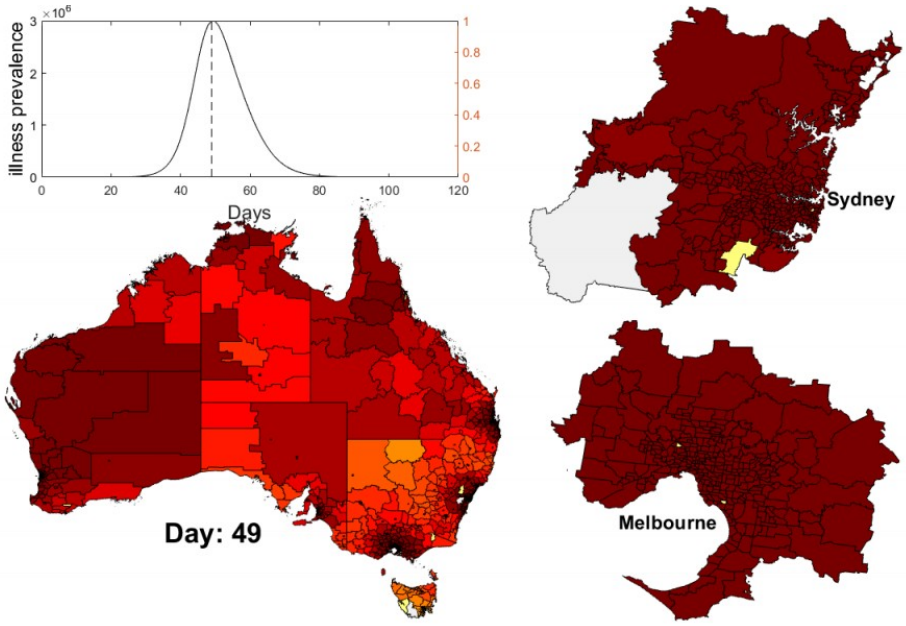
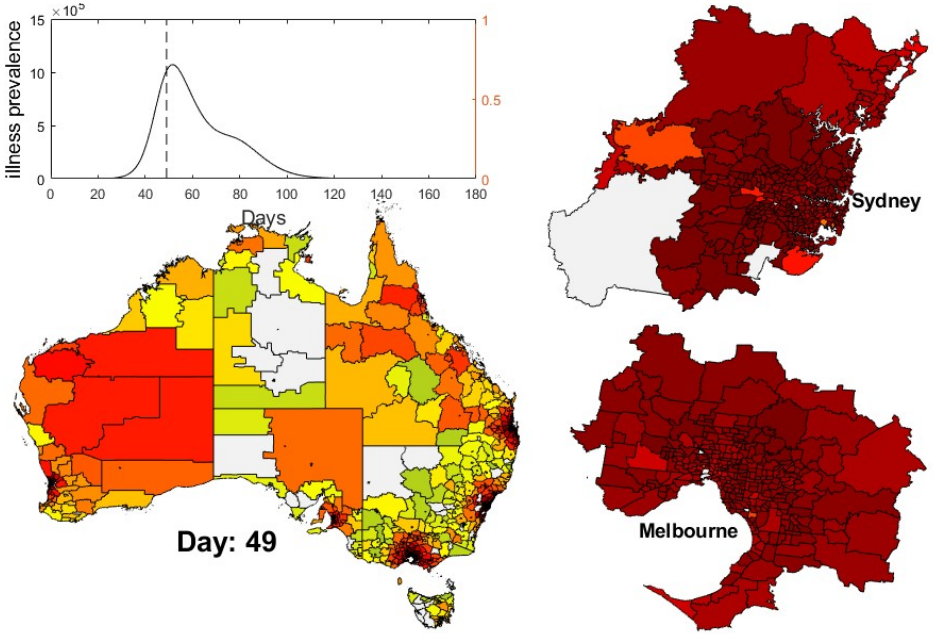
Comparison with Metapopulation model

Metapopulation



$R_0 = 2$ ($\beta = 0.7, \gamma = 0.35$)
Attack rate: 13 M
Peak Prevalence: 2 M

ABM (ACEMod), n = 30 instances



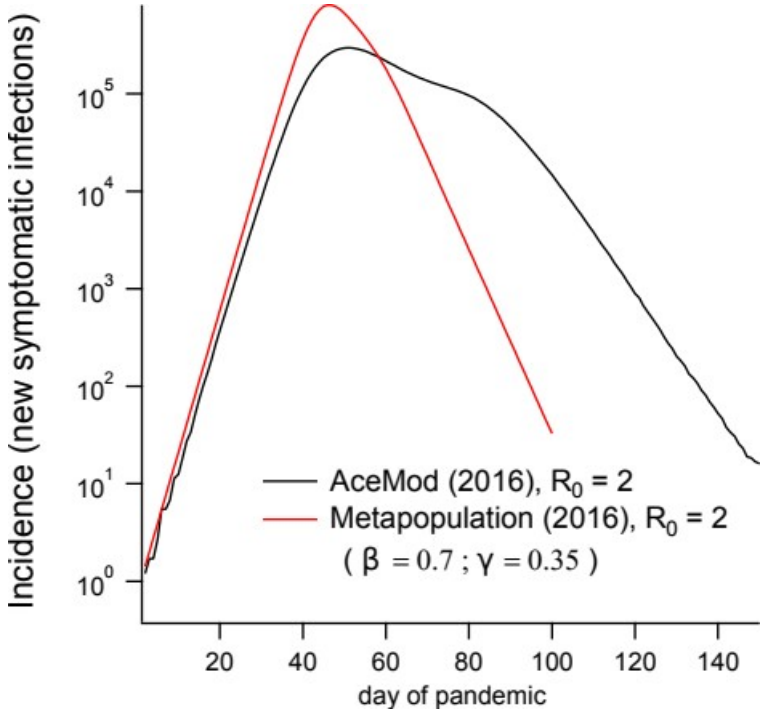
$R_0 = 2$
Attack rate: 9 M
Peak Prevalence: 1 M

Comparison with Metapopulation model

- Initial growth rates are (almost) identical

- ABM saturates more quickly
  (susceptible population becomes depleted)

- ABM produces significant bi-modality



Speculation: This is because of recurrent mobility patterns that produce social clustering in the contact network (not accounted for by the metapopulation model).

Other possibly important factors: dependence between interaction range and number of contacts (i.e., school students have many contacts at short geographical range, while adults may have fewer contacts over longer distances)

Results - Overview

Susceptibility comparison across census years (2006, 2011, 2016)

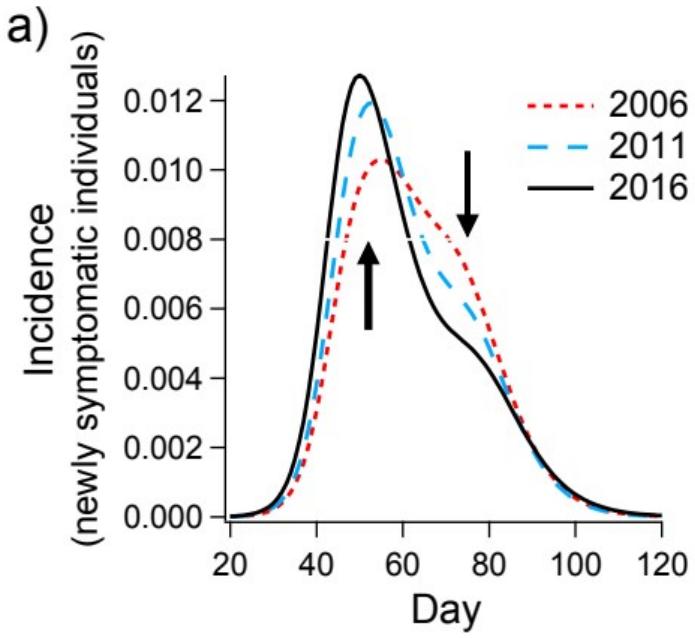
- Increasing peak prevalence
- earlier epidemic peak
- changes in bi-modal structure
- international air traffic and urbanisation are the culprits

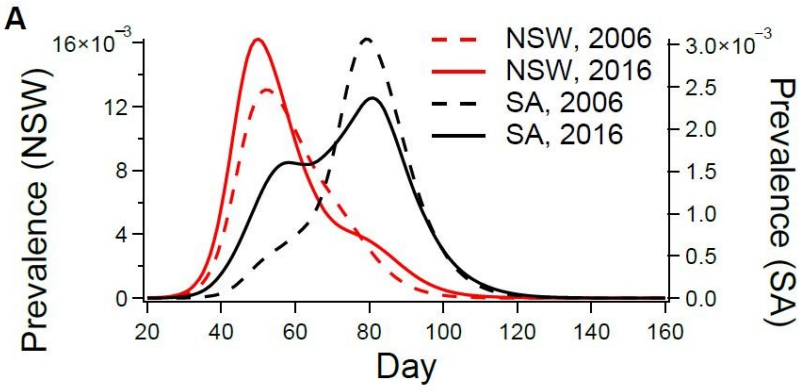
Interventions: Reactive targeted antiviral prophylaxis

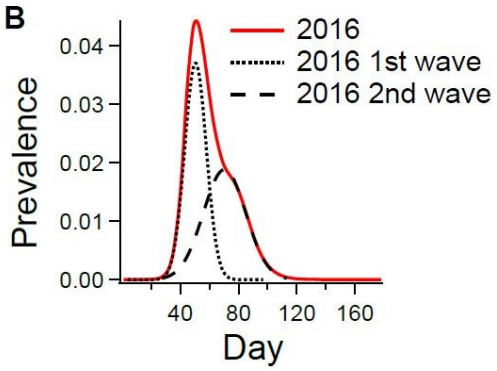
- complex, individual-level intervention strategies
- coupling between reactive prophylaxis and pre-pandemic vaccination

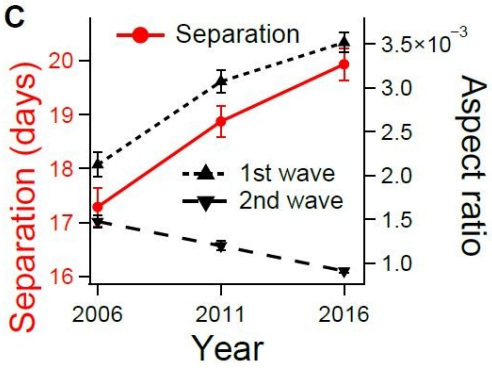
Results 1: same virus, different years

Compare epidemic dynamics using census data from 2006, 2011, 2016









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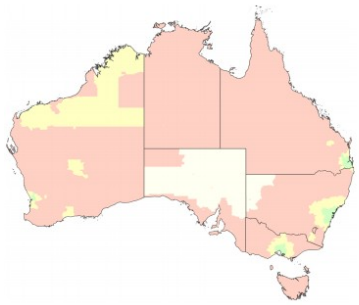
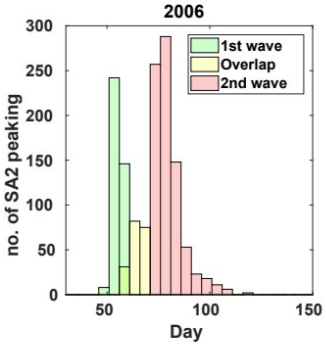
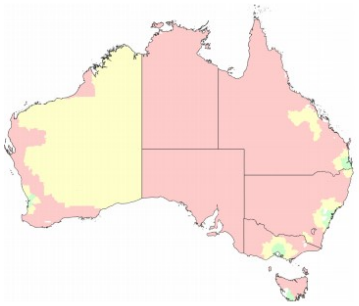
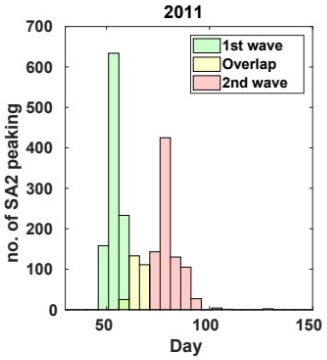
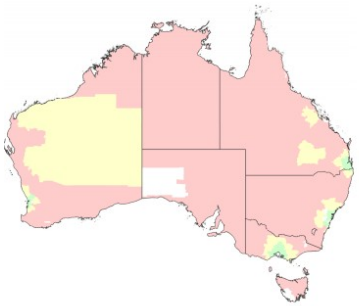
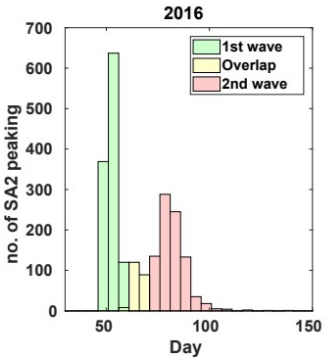




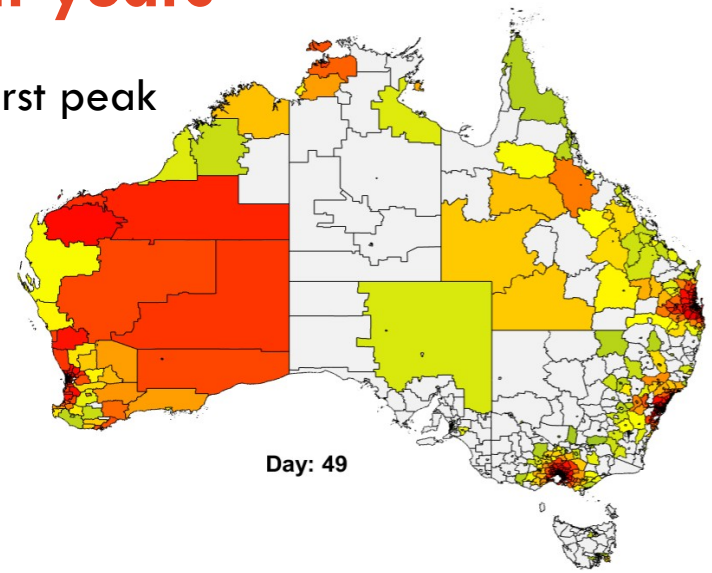




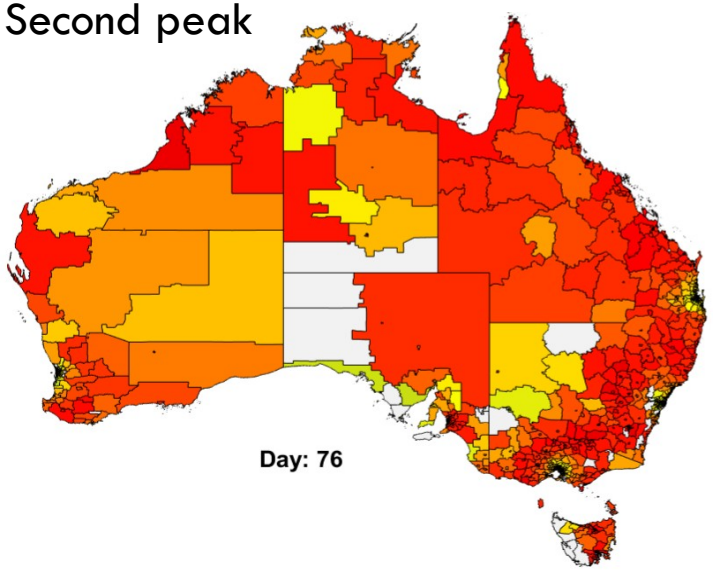




First peak



Second peak



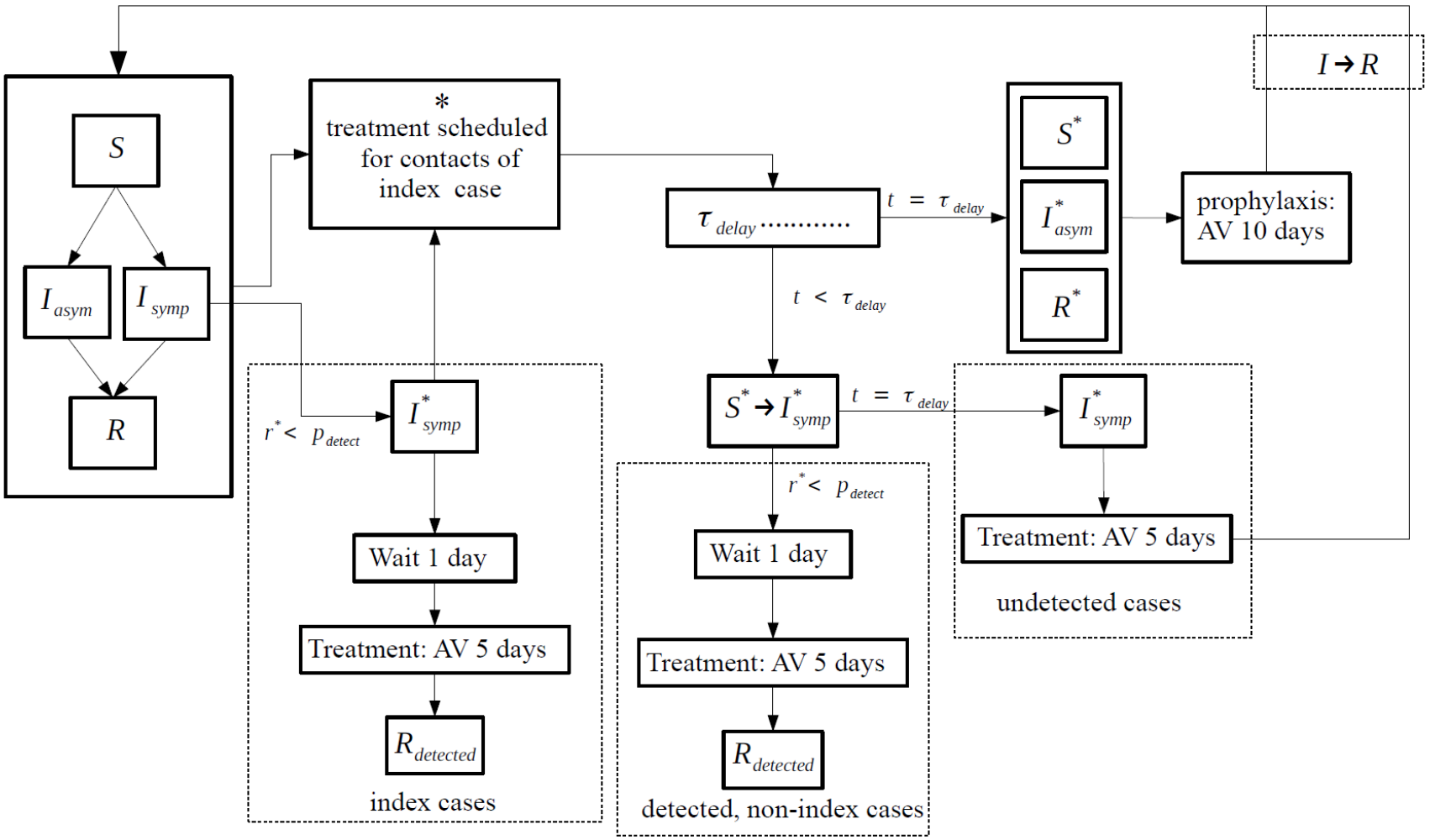
Results 2: Reactive interventions

This is where the ABM framework shines.

- Recurrent behaviour
- Social clustering
- Spatio-temporal fluctuations
- Noisy dynamics
- Individual schedules
- Imperfect information
- Logistical details and constraints

Constraints: data availability, development time
(we can do anything, but not everything)

Results 2: Reactive interventions – Targeted Prophylaxis



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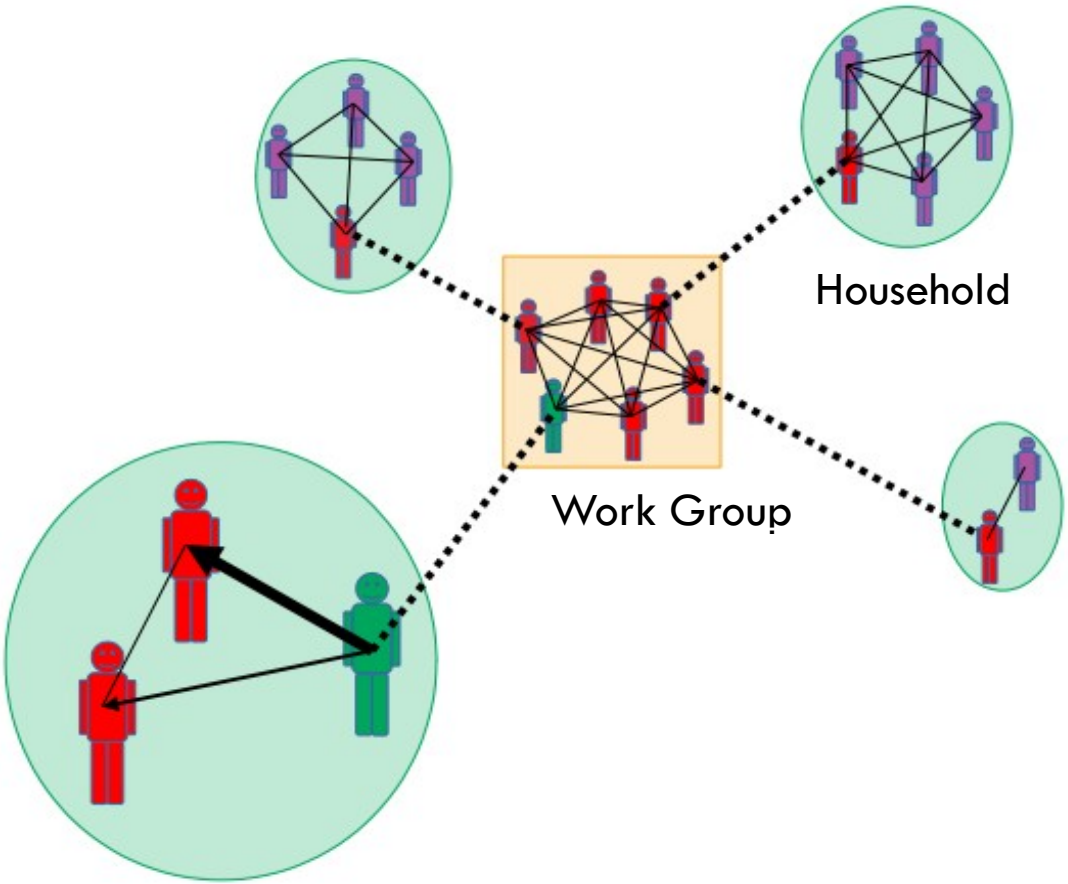
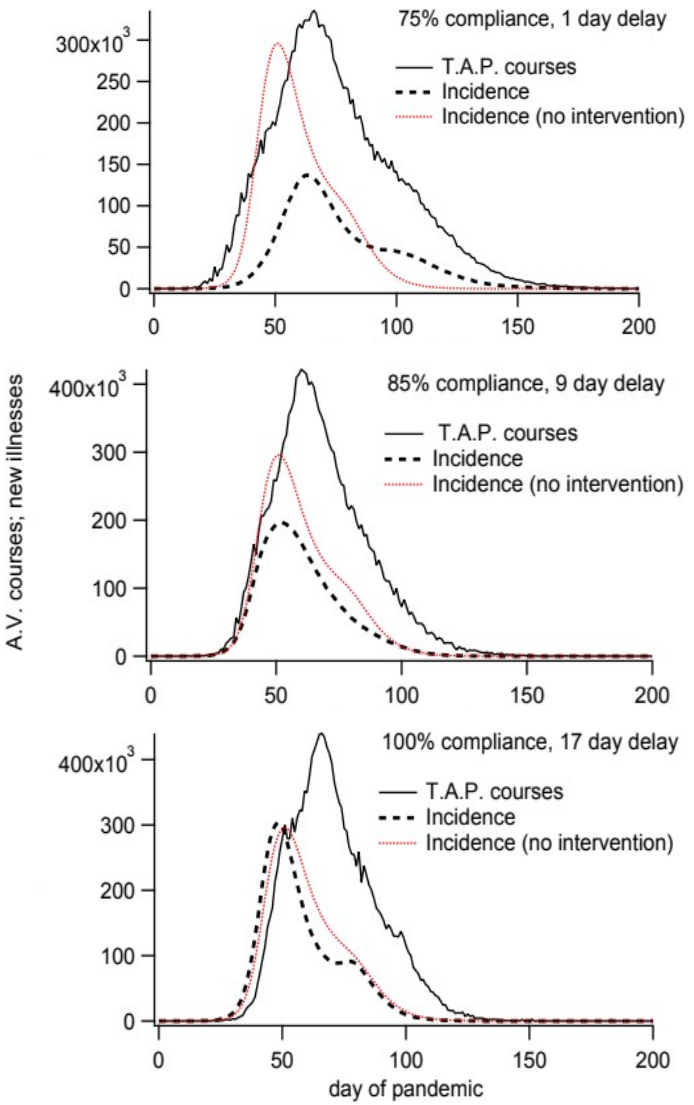
Results 2: Interventions – Contact-targeted prophylaxis





TAP targets next generation - timing is critical

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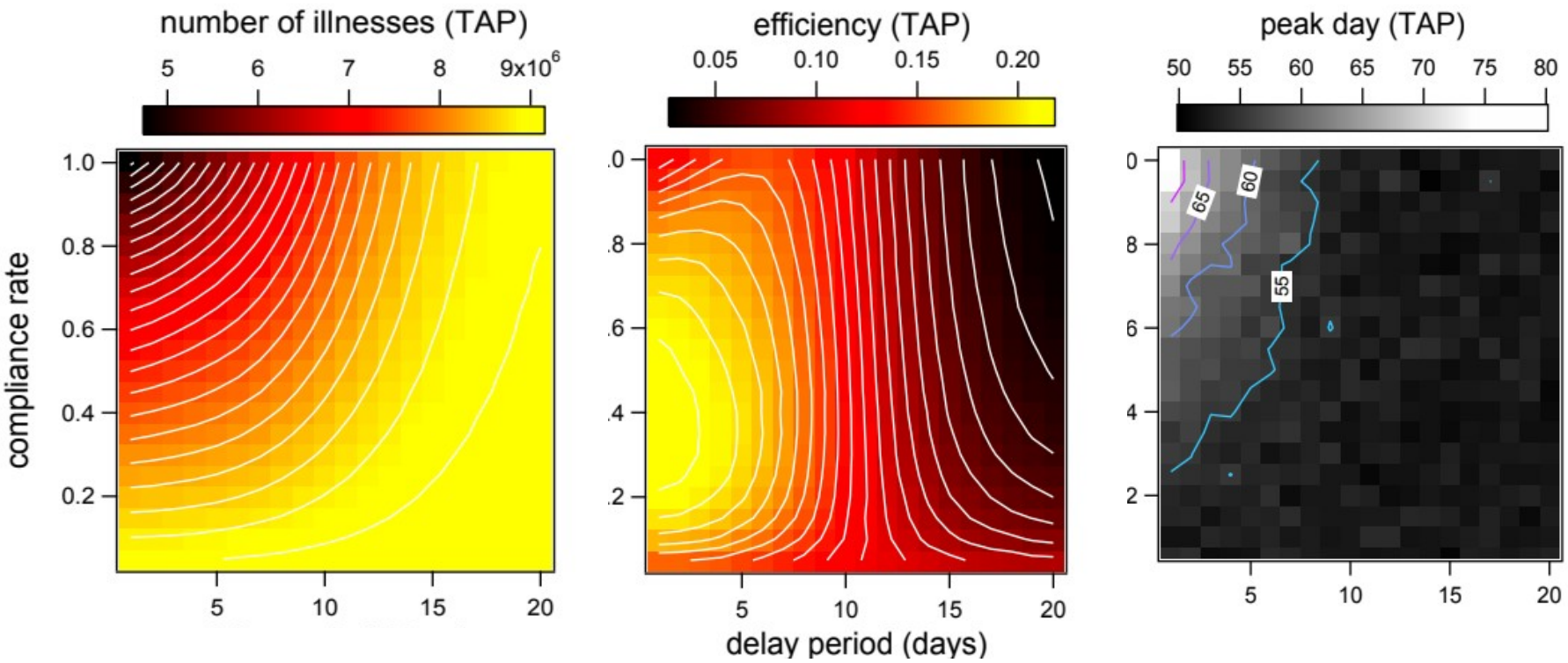
Results 2: Interventions – Contact-targeted prophylaxis



Efficiency in this case means the number of illnesses avoided per course of antivirals

$$\eta = \frac{I_o - I_{TAP}}{c_{TAP}}$$

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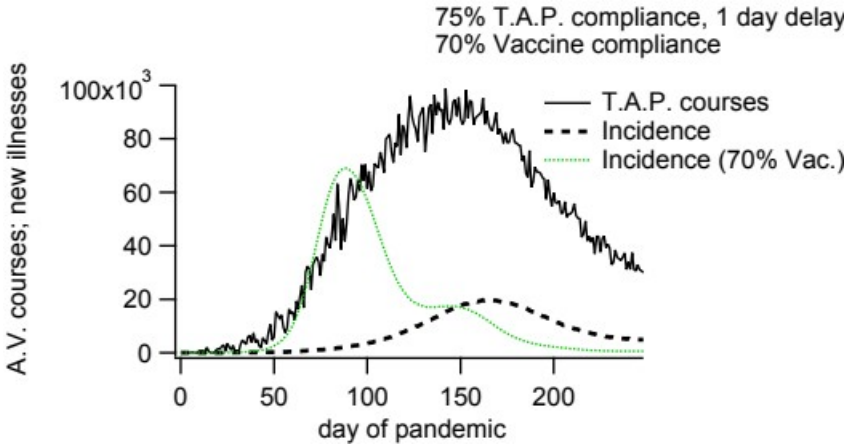
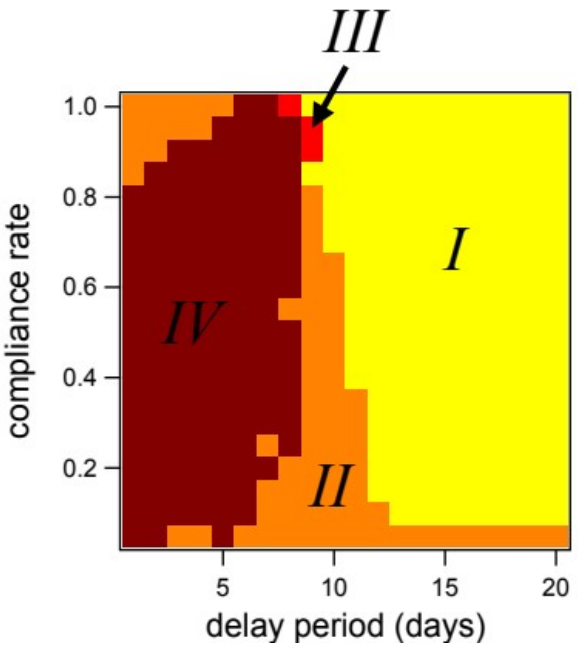
Coupling TAP with pre-pandemic vaccination





I : "whole is greater than the sum of parts" and antiviral efficiency increases

II : whole is *less than* the sum of parts, but antiviral efficiency still increases

III : whole is greater than the sum of parts, but antiviral efficiency decreases

IV : whole is less than sum of parts, and antiviral efficiency decreases

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Conclusion

- Key messages:
  - ABM framework allows explicit simulation of social structure, the effects of which cannot be captured using continuum models (at least not easily).
  - These microscale effects can have major consequences for the large-scale spread of an epidemic (i.e., bimodality).
  - ABMs can simulate complex intervention strategies, explicitly accounting for contact-tracing and key parameters such as local logistical delays.
  - Our results indicate that the effectiveness of prophylaxis programs will depend critically on targeting criteria, compliance, and response time.
  - Prophylaxis can negatively influence its own cost-effectiveness by slowing the epidemic, requiring a more protracted response.

Acknowledgements

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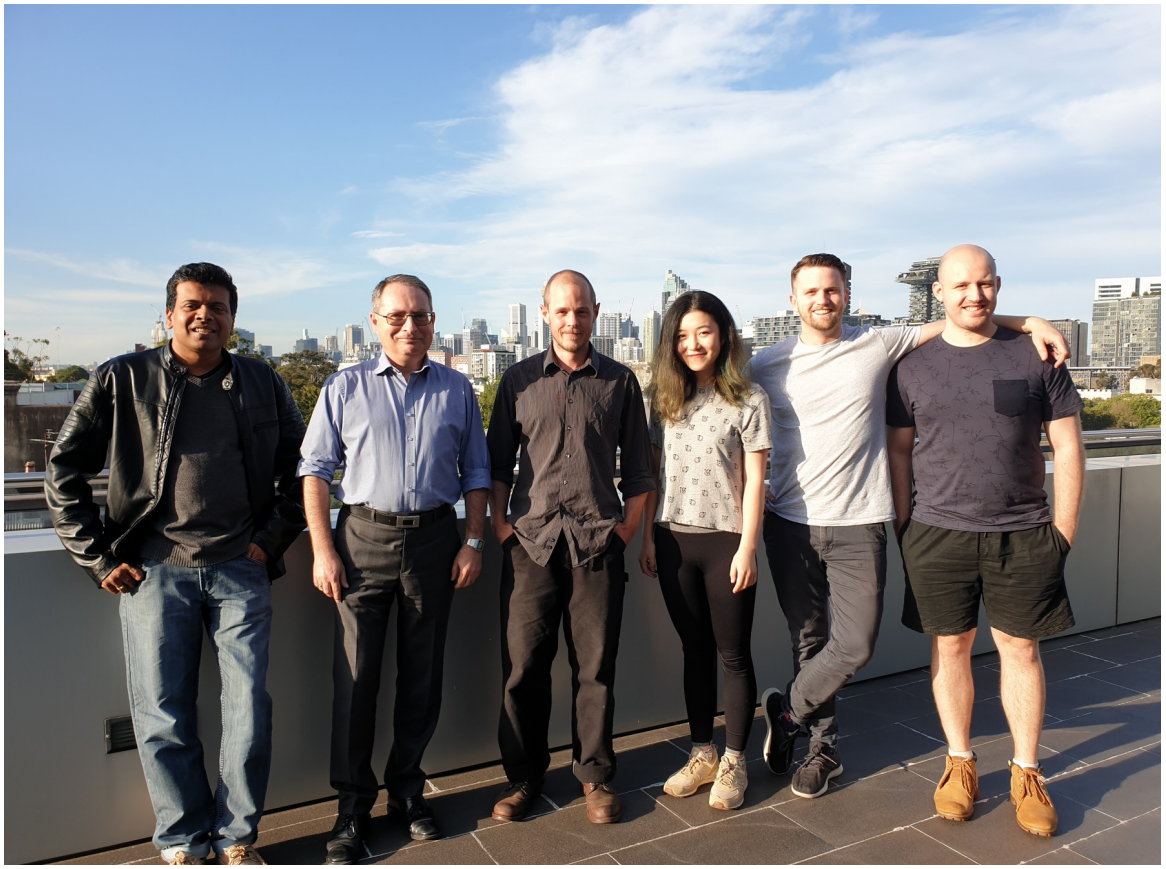
Collaborators: Mahendra Piraveenan, Mikhail Prokopenko, Sheryl Chang, Oliver Cliff, Nathan Harding, and Kristopher Fair (not pictured)



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Contact probabilities

Table C.3: 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

$$q^g_{j\to i} = \rho\ c^g_{j\to i}$$

Transmission probabilities

Table C.4: Daily transmission probabilities $q^g_{j\to i}$ for different contact groups g

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