Modelling tipping points and amplification effects of the COVID-19 pandemic response

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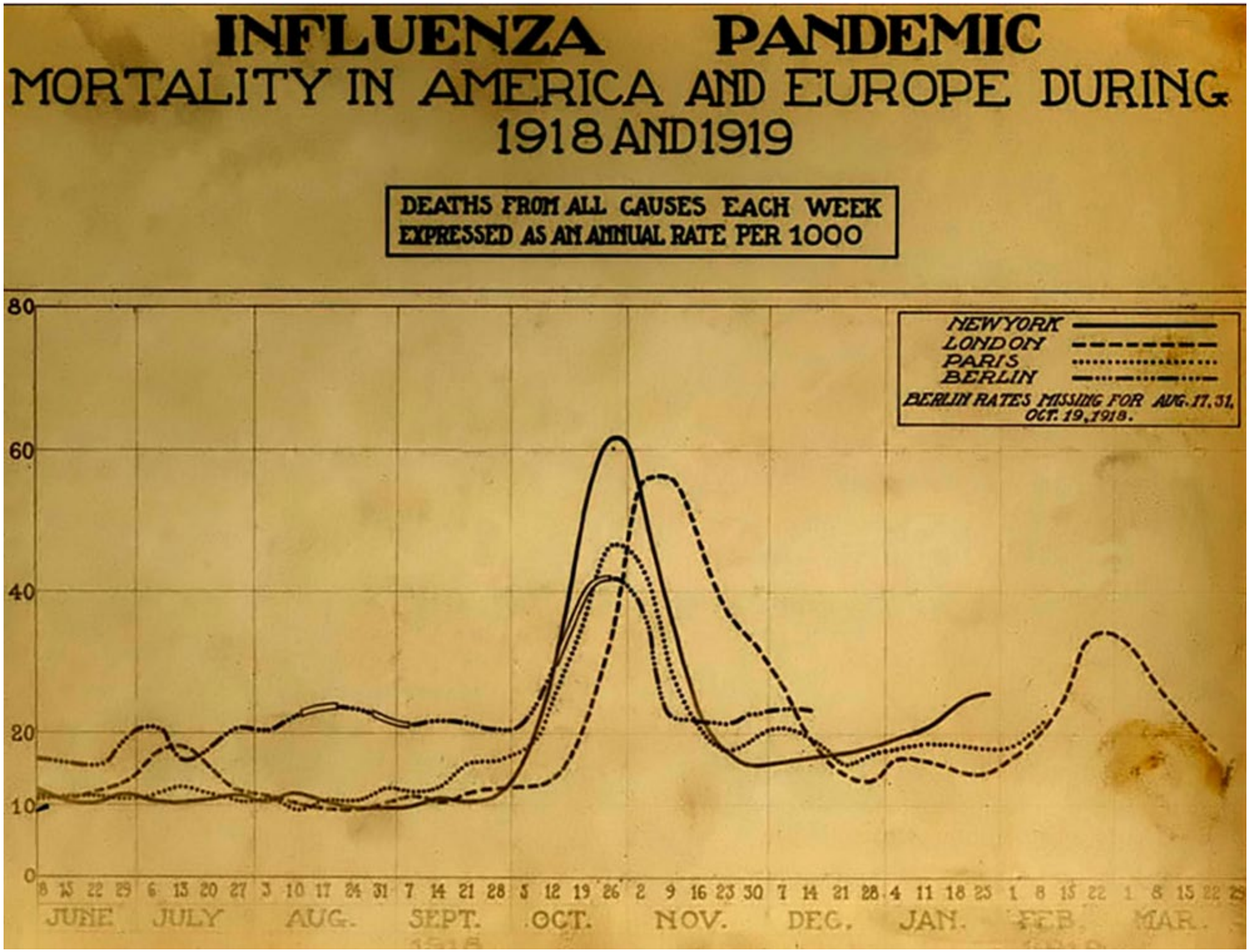
ARC DP220101688:
High-resolution multiscale computational modelling
of pandemics: COVID-19 and beyond

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"

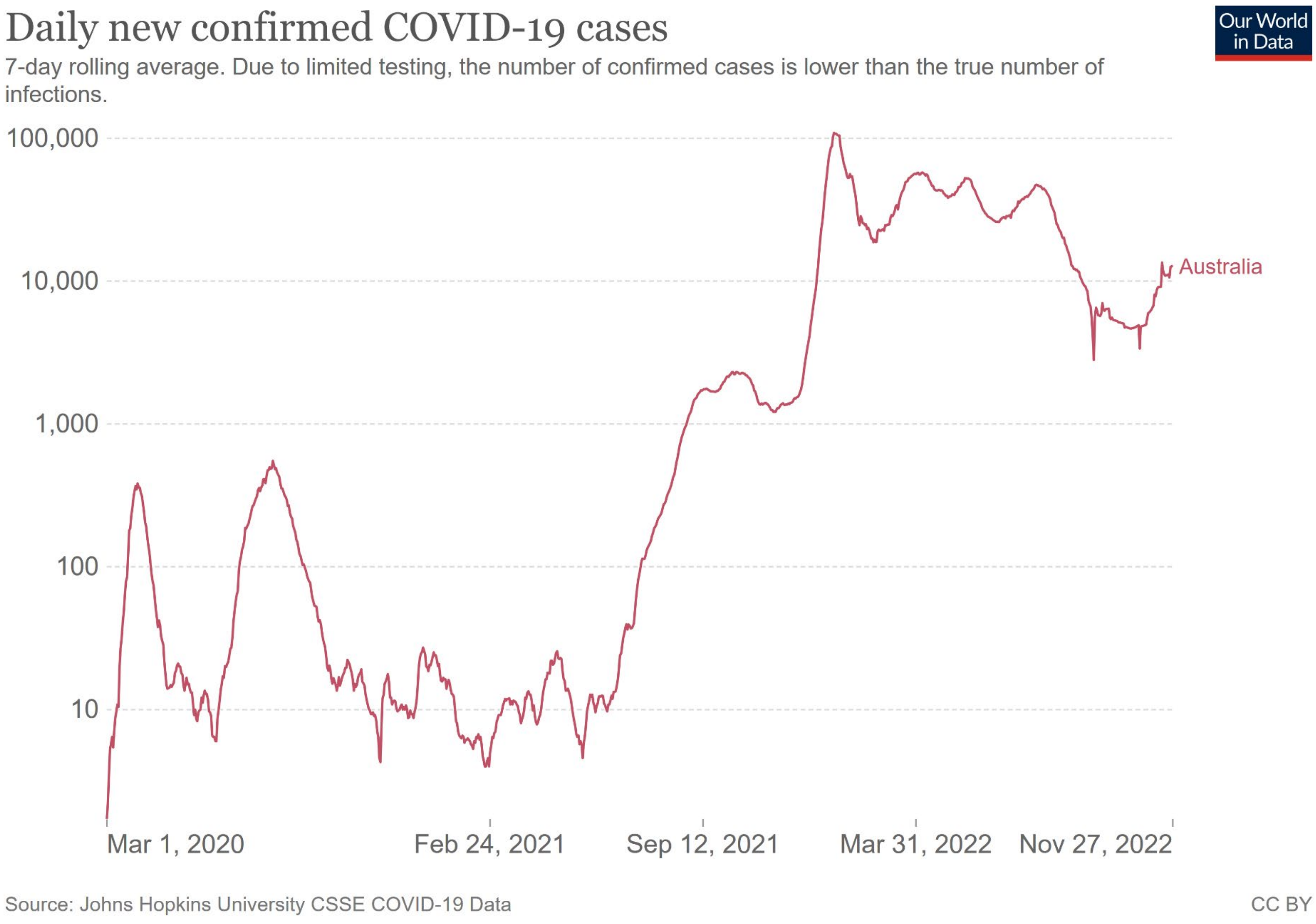
Bill Gates
Chair of Bill & Melinda Gates Foundation
2018

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

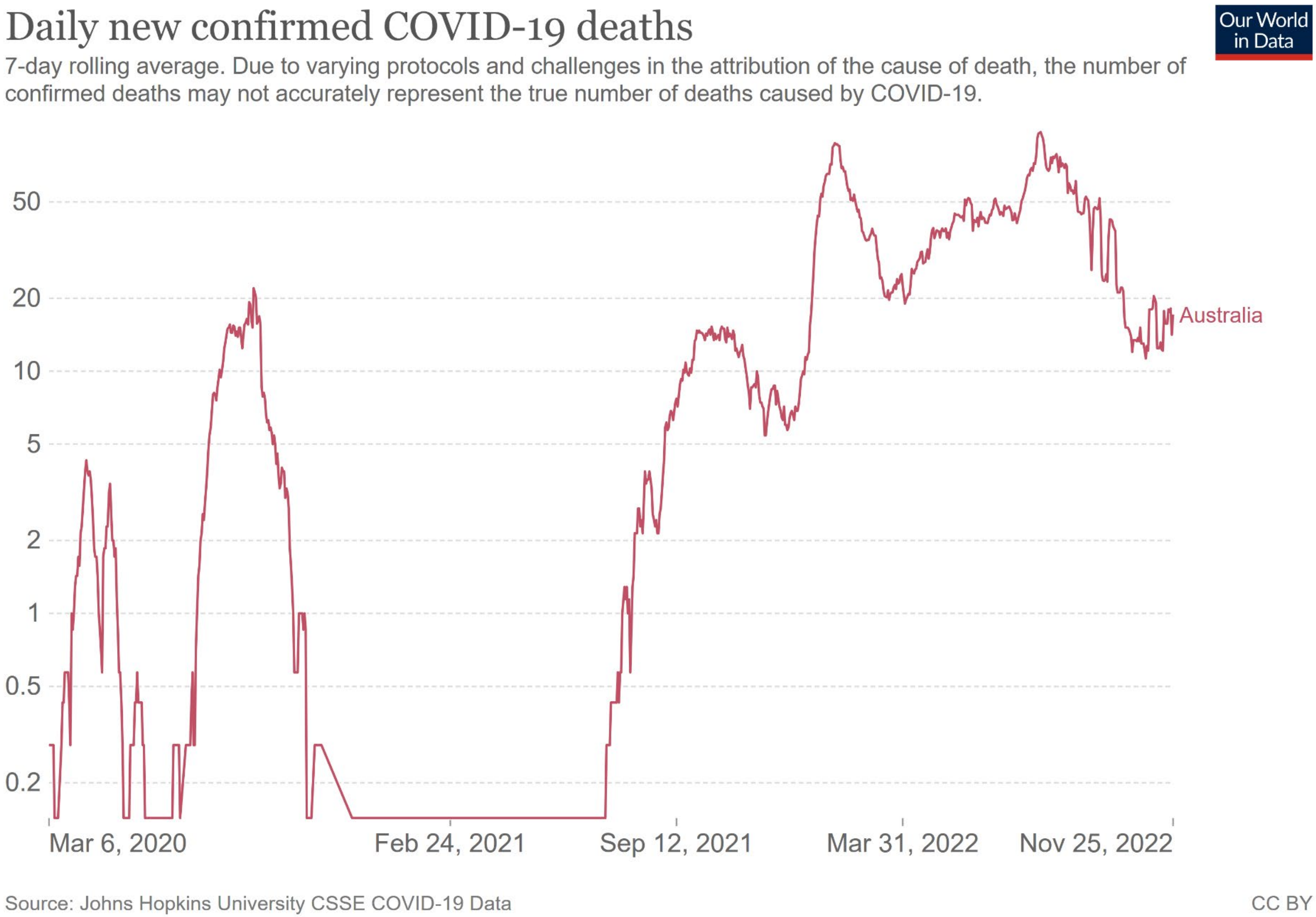
Sources of complexity

- complexity of human behaviour
- socio-economic complexity
- bio-complexity

The COVID-19: four pandemic stages in Australia (incidence, as of November 25, 2022)



The COVID-19: four pandemic stages in Australia (deaths, as of November 25, 2022)



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Pandemic modelling using Agent-based Models

- Large-scale high-resolution agent-based models
  - *demographics*: from census based data to agents
  - *mobility*: travel patterns including long-distance
  - *infection*: epidemiology

- AMTraC-19: **A**gent-based **M**odel of **Tra**nsmission and **C**ontrol of the COVID-**19** pandemic in Australia (~ 24M agents)

- Model calibration and validation during COVID-19 pandemic
  - 1st stage, ancestral (March – June 2020)
  - 2nd stage, ancestral (July – September 2020)
  - 3rd stage, Delta (June – November 2021)
  - 4th stage, Omicron (December 2021 – November 2022)

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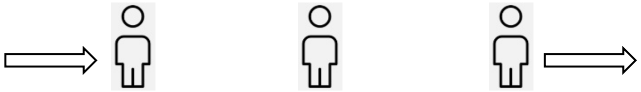
Features of AMTraC-19

- ~24M stochastically generated agents (Census, ABS & ACARA data)
- household size and composition vary across different local areas
- commuting patterns between residence and work / study
- flexible infection seeding scenarios
- transmission within mixing contexts
- different symptomatic ratios for children and adults
- vaccination rollout with two vaccines

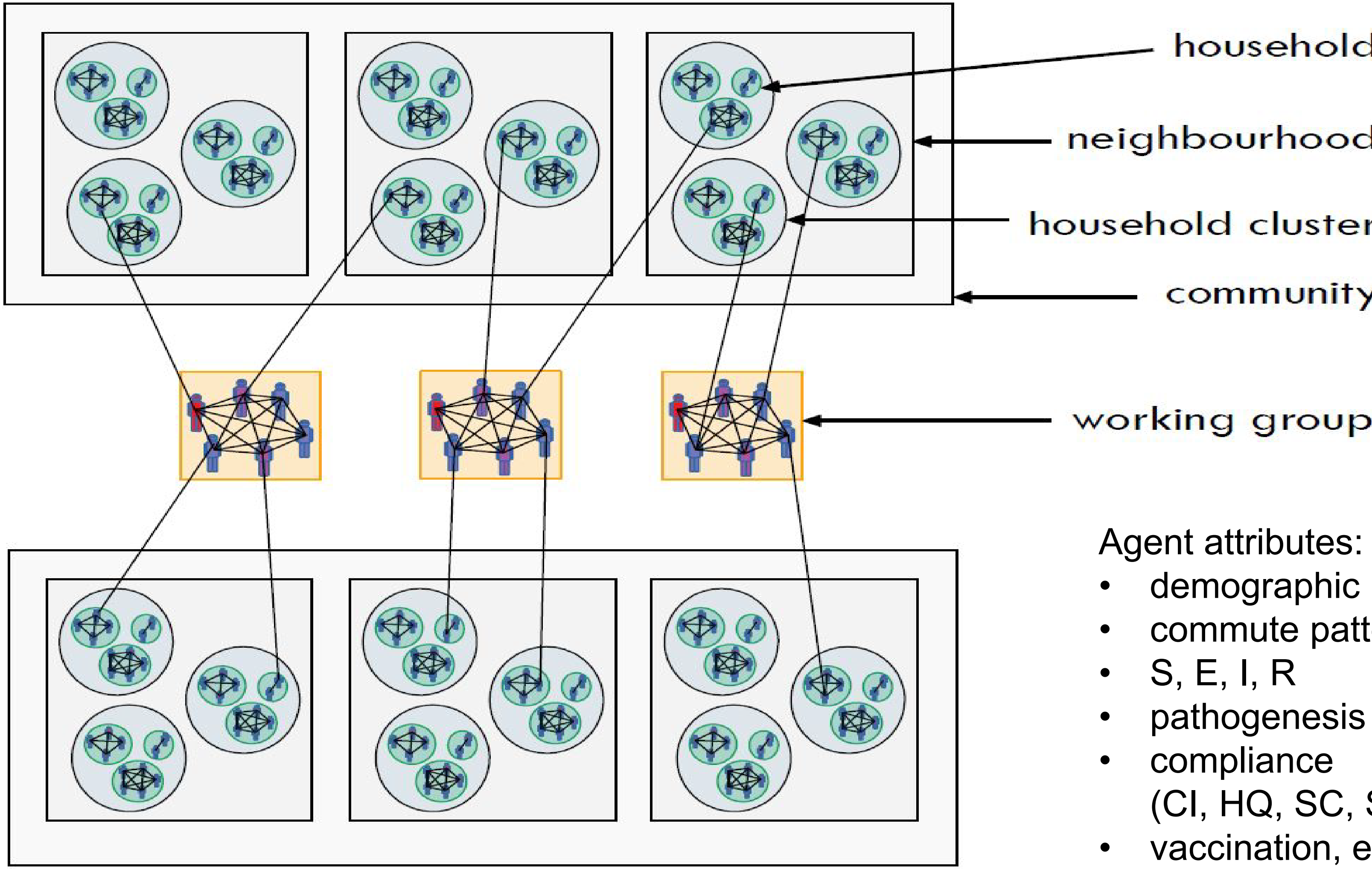


- vaccine efficacy split across components (infection, symptoms, transmission)
- varying social distancing (“stay-at-home” restrictions)

S. L. Chang, N. Harding, C. Zachreson, O. M. Cliff, M. Prokopenko, Modelling transmission and control of the COVID-19 pandemic in Australia, *Nature Communications*, 11, 5710, 2020.

C. Zachreson, S. L. Chang, O. M. Cliff, M. Prokopenko, How will mass-vaccination change COVID-19 lockdown requirements in Australia? *The Lancet Regional Health – Western Pacific*, 14: 100224, 2021.

"Same storm, different boats": Agent-based Modelling



Agent attributes:

- demographic
- commute pattern
- S, E, I, R
- pathogenesis
- compliance (CI, HQ, SC, SD)
- vaccination, etc.

C. Zachreson, K. M. Fair, N. Harding, M. Prokopenko, Interfering with influenza: nonlinear coupling of reactive and static mitigation strategies, *Journal of Royal Society Interface*, 17(165): 20190728, 2020.

Population partitions: residential areas and destination zones

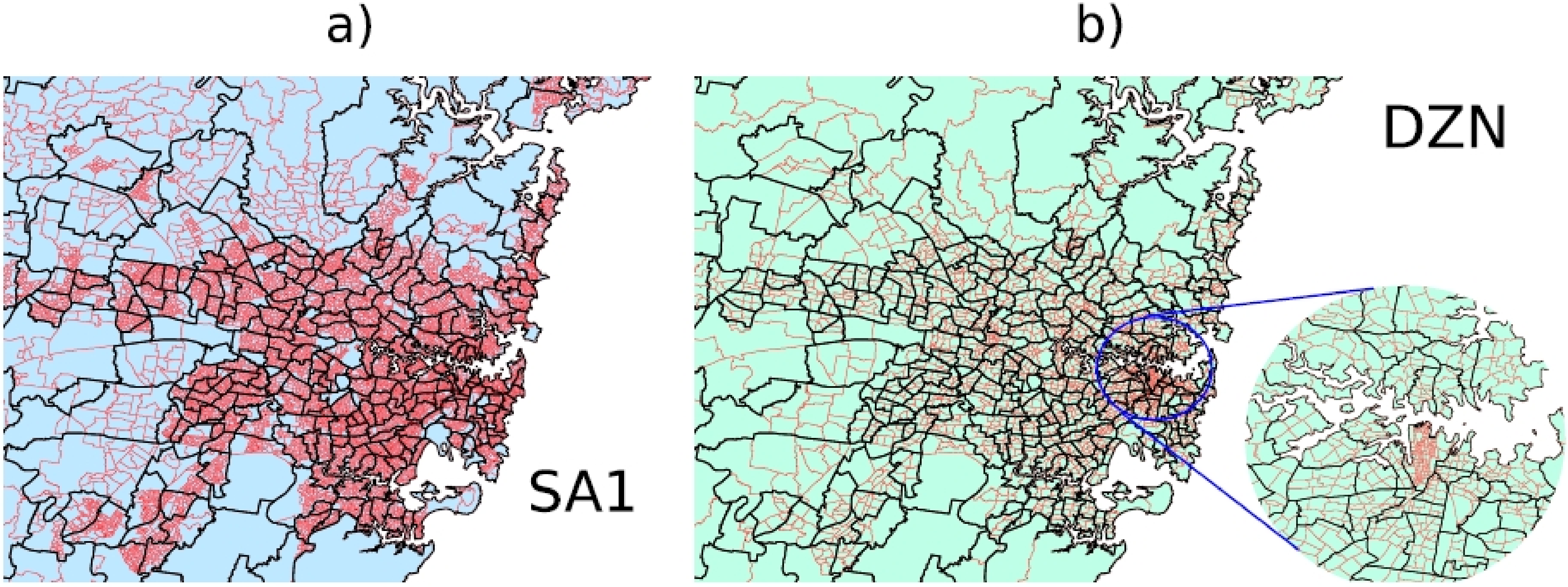
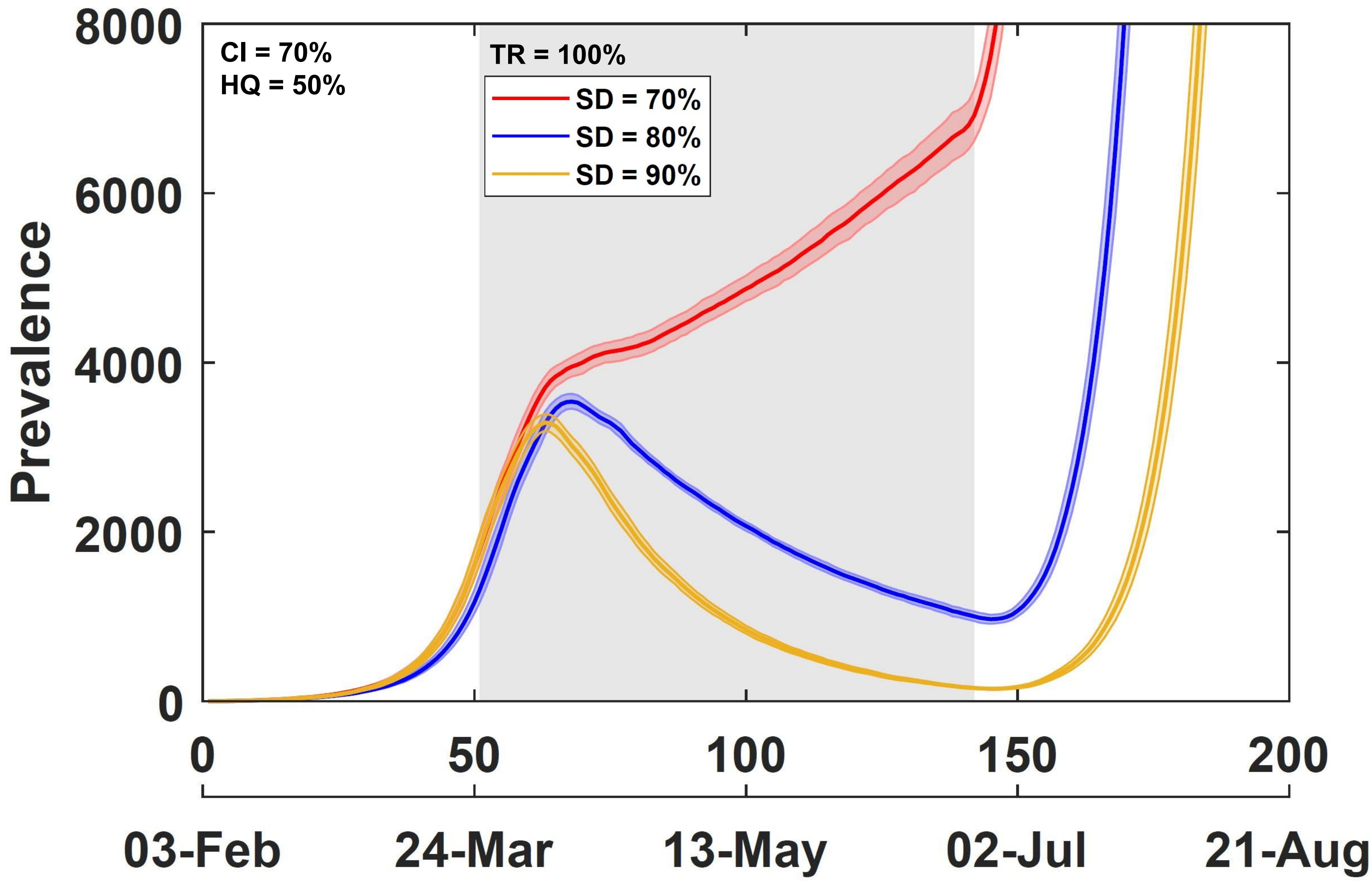


Fig. 1 Maps of the Greater Sydney region illustrating the distribution of population partitions. (**a**) A map of the Greater Sydney region showing SA2 (black) and SA1 (red) population partitions. (**b**) A map of the same area showing SA2 (black) and DZN (red) partitions. The inset in (**b**) zooms in on the Sydney central business district to illustrate the much denser packing of DZN partitions in that area.

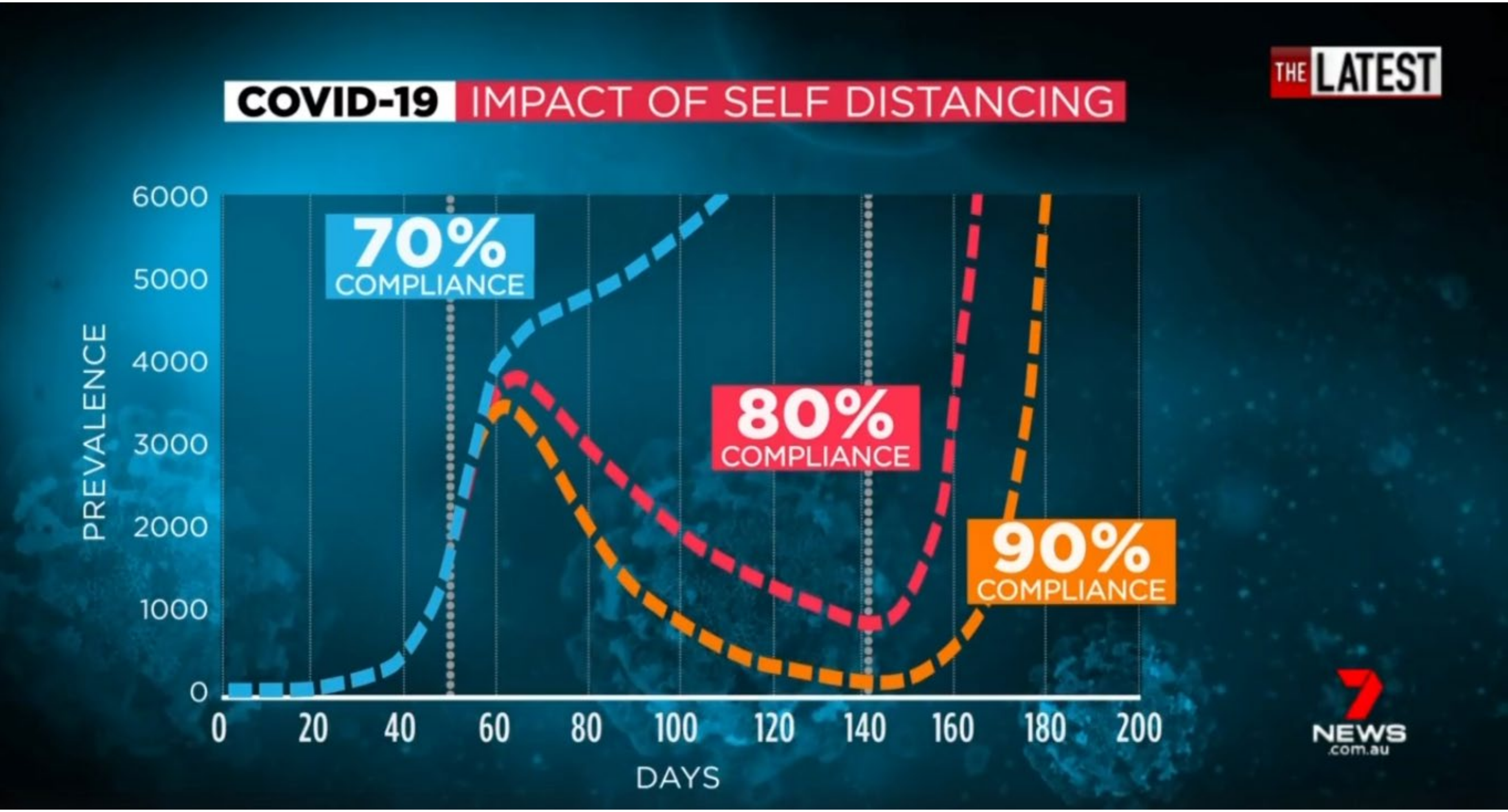
K. M. Fair, C. Zachreson, M. Prokopenko, Creating a surrogate commuter network from Australian Bureau of Statistics census data, *Scientific Data*, 6, 150, 2019.

2020 model: a tipping point in social distancing

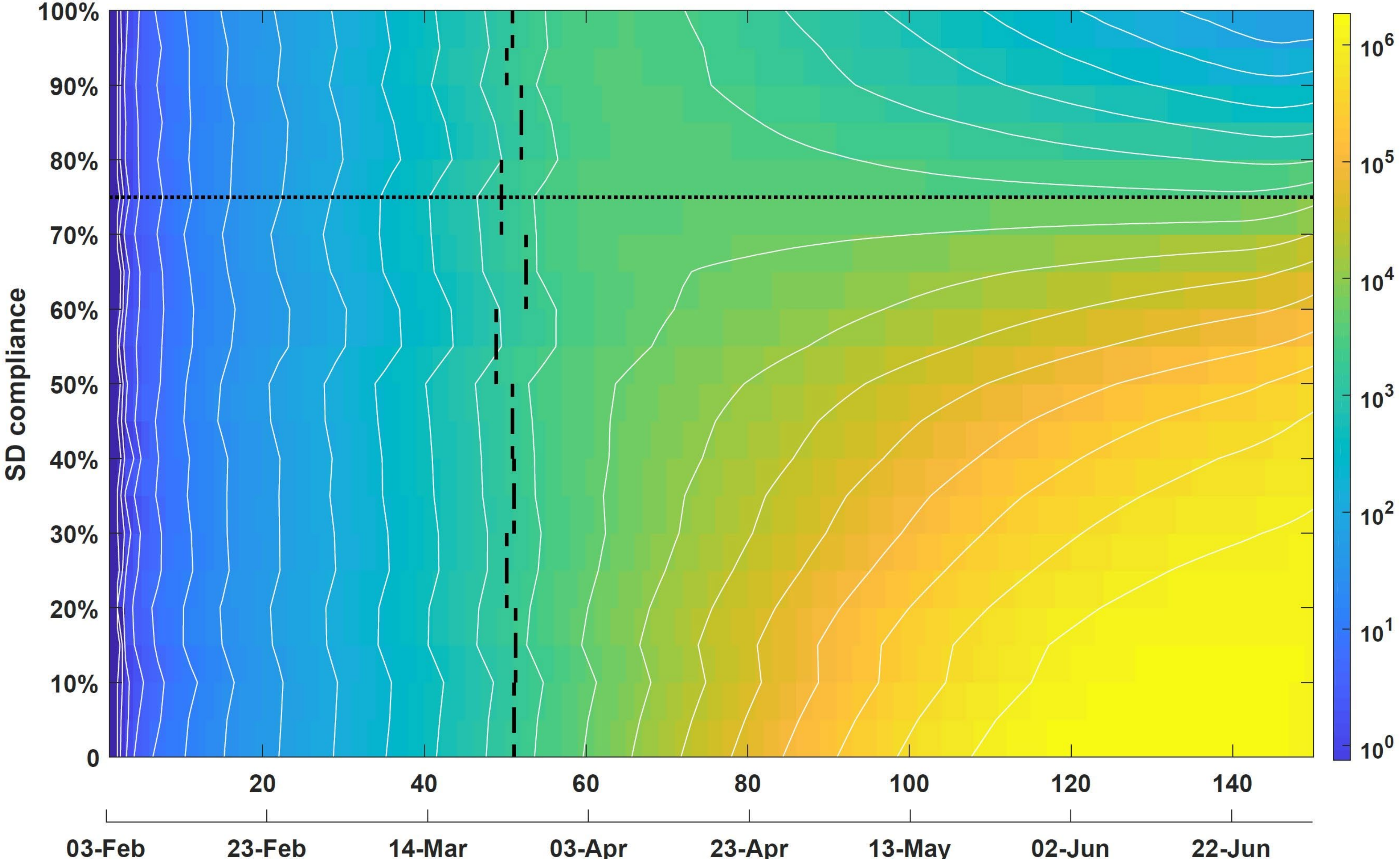


S. L. Chang, N. Harding, C. Zachreson, O. M. Cliff, M. Prokopenko, Modelling transmission and control of the COVID-19 pandemic in Australia, *Nature Communications,* 11, 5710, 2020.

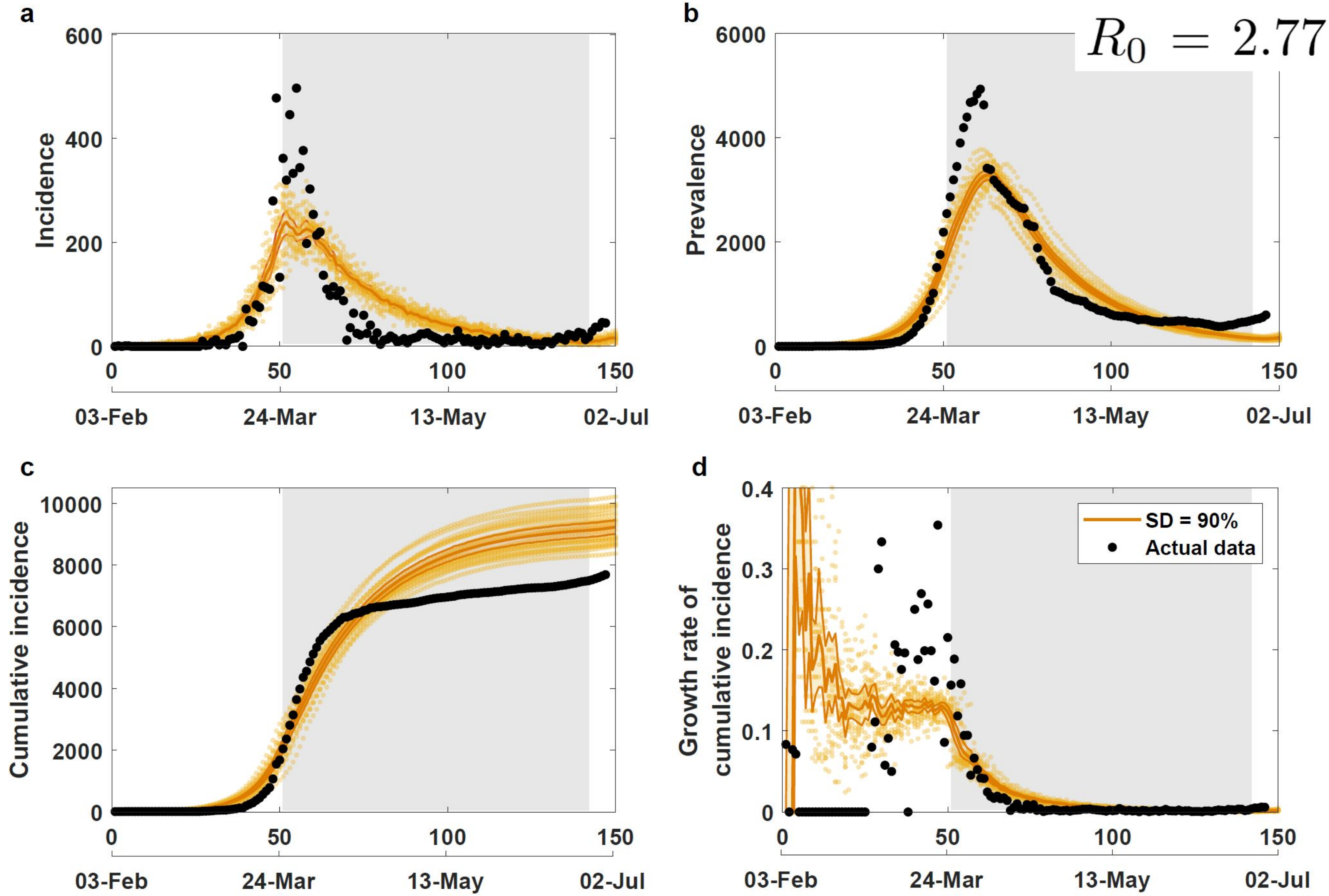
Media coverage (April 2020)



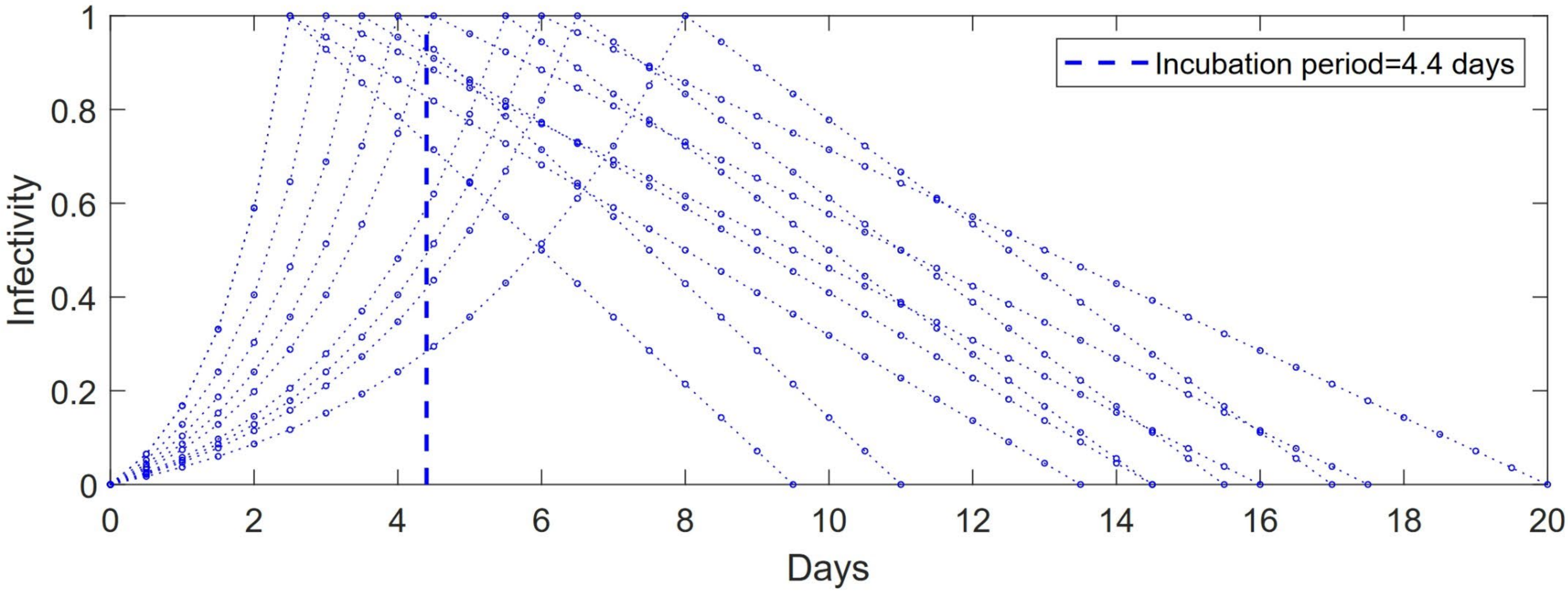
Tipping point (phase transition) in SD compliance



AMTraC-19 validation (version 6.1)



Natural history of the disease (the Delta variant model: AMTraC-19 version 7.7)



	R_0	T_{gen} (days)	T_{inc} (days)	T_{rec} (days)
Mean	6.2	6.93	4.4	10
95% CI	6.16 – 6.23	6.87 – 6.99	3.9 – 5.0	range: 7 – 14 (uniform)

S. L. Chang, O. M. Cliff, C. Zachreson, M. Prokopenko, Simulating Transmission Scenarios of the Delta Variant of SARS-CoV-2 in Australia, *Frontiers in Public Health,* 10, 10.3389/fpubh.2022.823043, 2022.

Non-pharmaceutical interventions (NPIs)

NPI	Compliance	Interaction strength		
		Household	Community	Workplace
Case isolation	0.7 – 0.8	1.0	0.1 – 0.25	0.1 – 0.25
Home quarantine	0.5 – 0.7	2.0	0.1 – 0.25	0.1 – 0.25
School (students)	1.0	1.0	0.1 – 0.5	0.0
School (parents)	0.5	1.0	0.1 – 0.5	0.0
Social distancing	0.0 – 1.0	1.0	0.1 – 0.25	0.1

S. L. Chang, O. M. Cliff, C. Zachreson, M. Prokopenko, Simulating Transmission Scenarios of the Delta Variant of SARS-CoV-2 in Australia, *Frontiers in Public Health,* 10, 10.3389/fpubh.2022.823043, 2022.

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Social Distancing (SD): "stay-at-home" restrictions

Table 2 The micro- and macro-distancing parameters: macro-compliance levels and context-dependent micro-distancing levels.

Strategy	Macro-distancing	Micro-distancing contacts		
	Compliance levels	Household	Community	Workplace/school
No intervention	100%	100%	100%	100%
Case isolation	70%	100%	25%	25%
Home quarantine	50%	200%	25%	25%
School closure (children)	100%	150%	150%	0%
School closure (parents)	25 or 50%	150%	150%	0%
Social distancing	0-100%	100%	50%	0%

$$p_i(n) = 1 - \prod_{g \in G_i(n)} \left[\prod_{j \in A_g \setminus i} \left(1 - p^g_{j \to i}(n)\right) \right]$$

$$p_i(n) = 1 - \prod_{g \in G_i(n)} \left[\prod_{j \in A_g \setminus i} \left(1 - F_g(j)\, p^g_{j \to i}(n)\right) \right]$$

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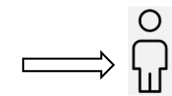
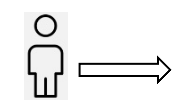
Modelling vaccination rollout (our 2021 model: AMTraC-19 version 7.6)

- Efficacy for susceptibility (VEs): impacts immunity in those susceptible to the virus (reduces the probability of becoming infected if exposed)



- Efficacy for disease (VEd): impacts the expression of illness in those who are vaccinated and subsequently become infected (reduces the probability of expressing symptoms if infected)

- Efficacy for infectiousness (VEi): impacts the potential for vaccinated individuals to transmit the virus if infected (reduces the force of infection produced by infected individuals who are vaccinated)



$$VE = VEd + VEs - VEs \times VEd \qquad VEi = \sim 0.5$$

for example:

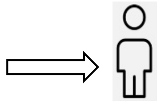
$$0.91 = 0.7 + 0.7 - 0.7 \times 0.7$$
$$0.92 = 0.8 + 0.6 - 0.8 \times 0.6$$
$$0.75 = 0.5 + 0.5 - 0.5 \times 0.5$$
$$0.65 = 0.5 + 0.3 - 0.5 \times 0.3$$

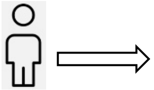
C. Zachreson, S. L. Chang, O. M. Cliff, M. Prokopenko, How will mass-vaccination change COVID-19 lockdown requirements in Australia? *The Lancet Regional Health – Western Pacific*, 14: 100224, 2021.

Vaccination components

$$p_i(n) = 1 - \prod_{g \in G_i(n)} \left[\prod_{j \in A_g \setminus i} \left(1 - p^g_{j \to i}(n)\right) \right]$$

$$p_i(n) = 1 - \prod_{g \in G_i(n)} \left[\prod_{j \in A_g \setminus i} \left(1 - F_g(j)\, p^g_{j \to i}(n)\right) \right]$$





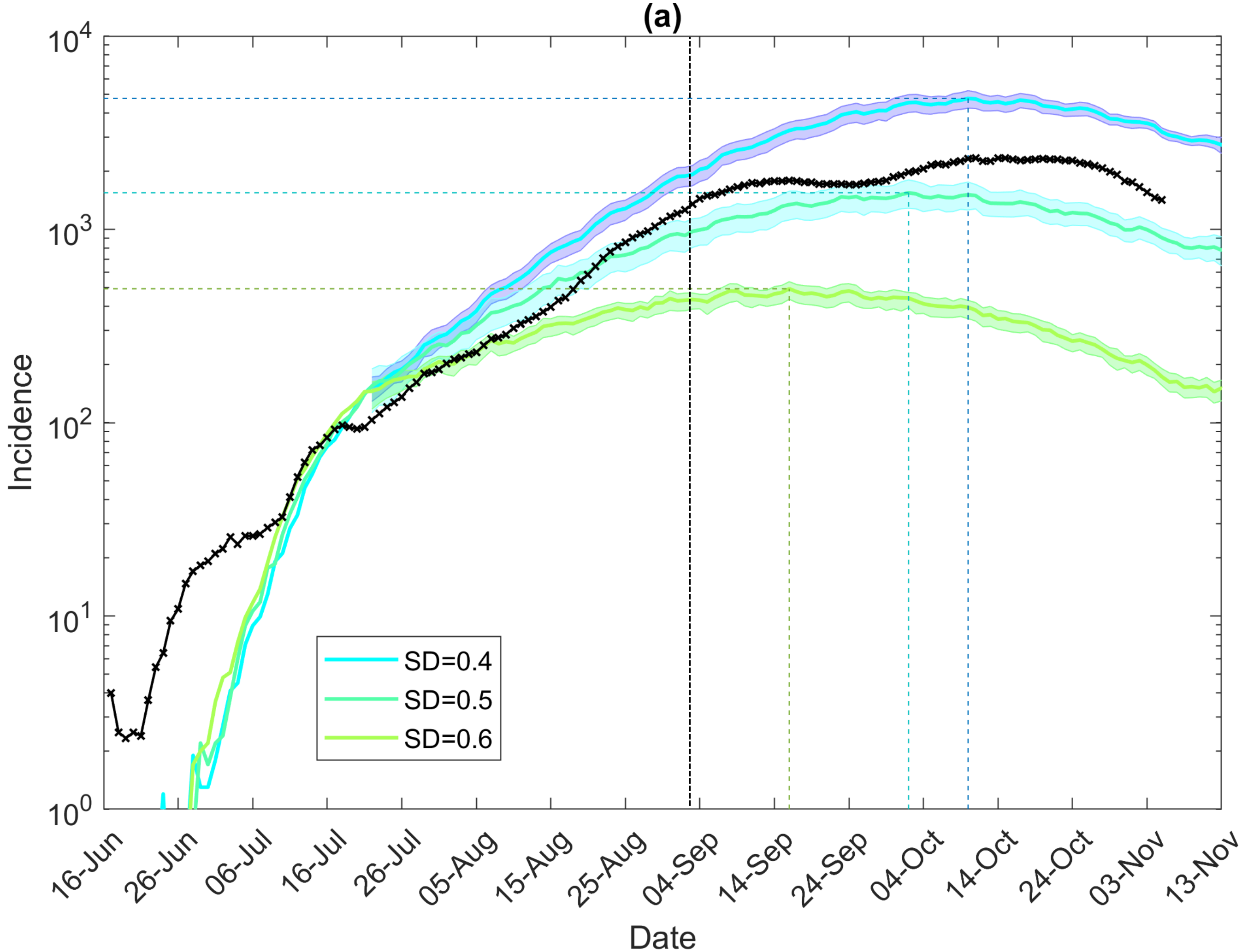
$$p_i(n) = (1 - \mathrm{VEs}_i) \left(1 - \prod_{g \in G_i(n)} \left[\prod_{j \in A_g \setminus i} \left(1 - (1 - \mathrm{VEi}_j) F_g(j)\, p^g_{j \to i}(n)\right) \right] \right)$$

$$p^d_i(n) = (1 - \mathrm{VEd}) \sigma_{a|c} p_i(n)$$

S. L. Chang, O. M. Cliff, C. Zachreson, M. Prokopenko, Simulating Transmission Scenarios of the Delta Variant of SARS-CoV-2 in Australia, *Frontiers in Public Health,* 10, 10.3389/fpubh.2022.823043, 2022.

The Delta variant: SD compliance scenarios (25 August → 5 November 2021)

$R_0 = 6.20$



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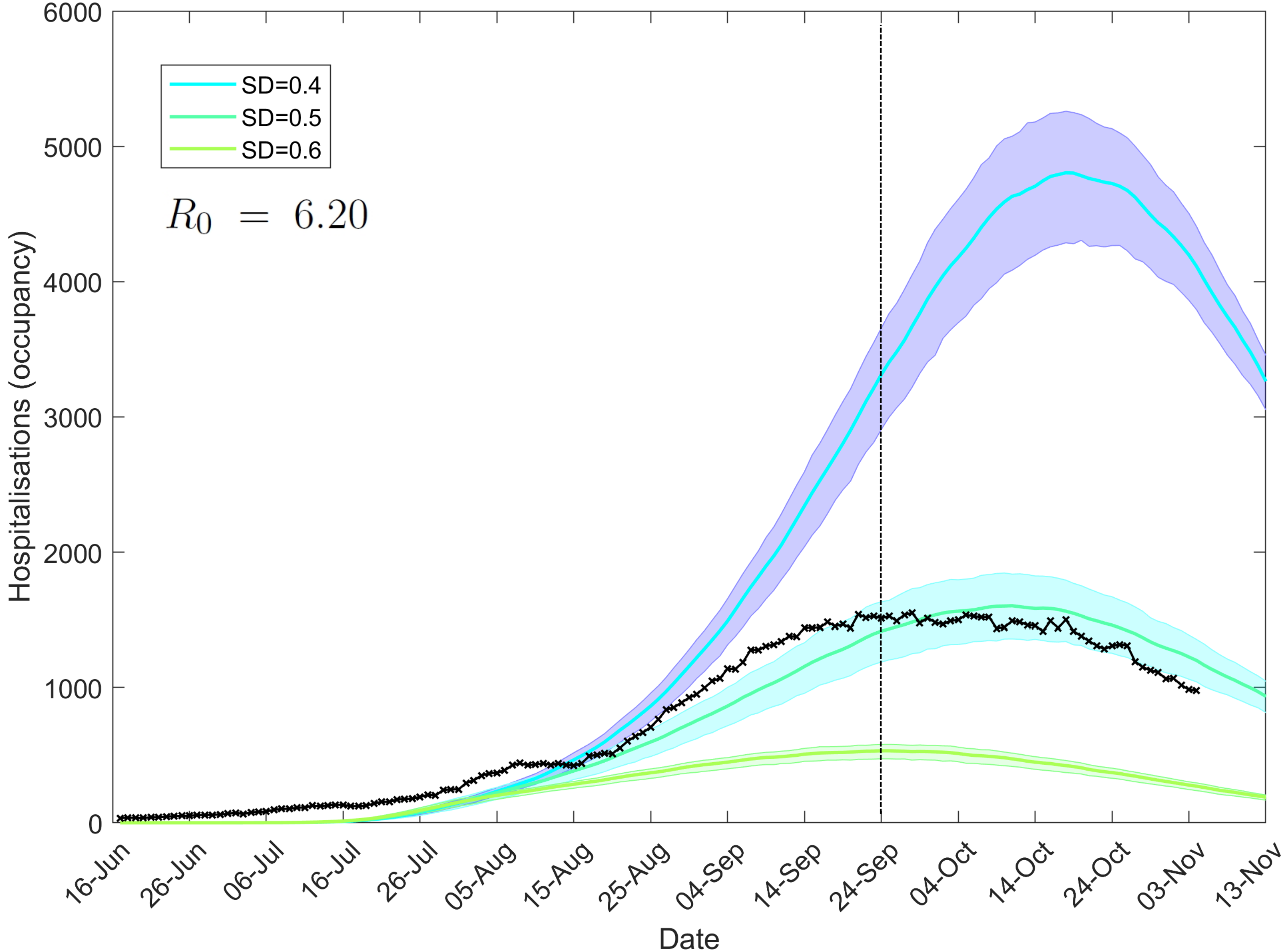
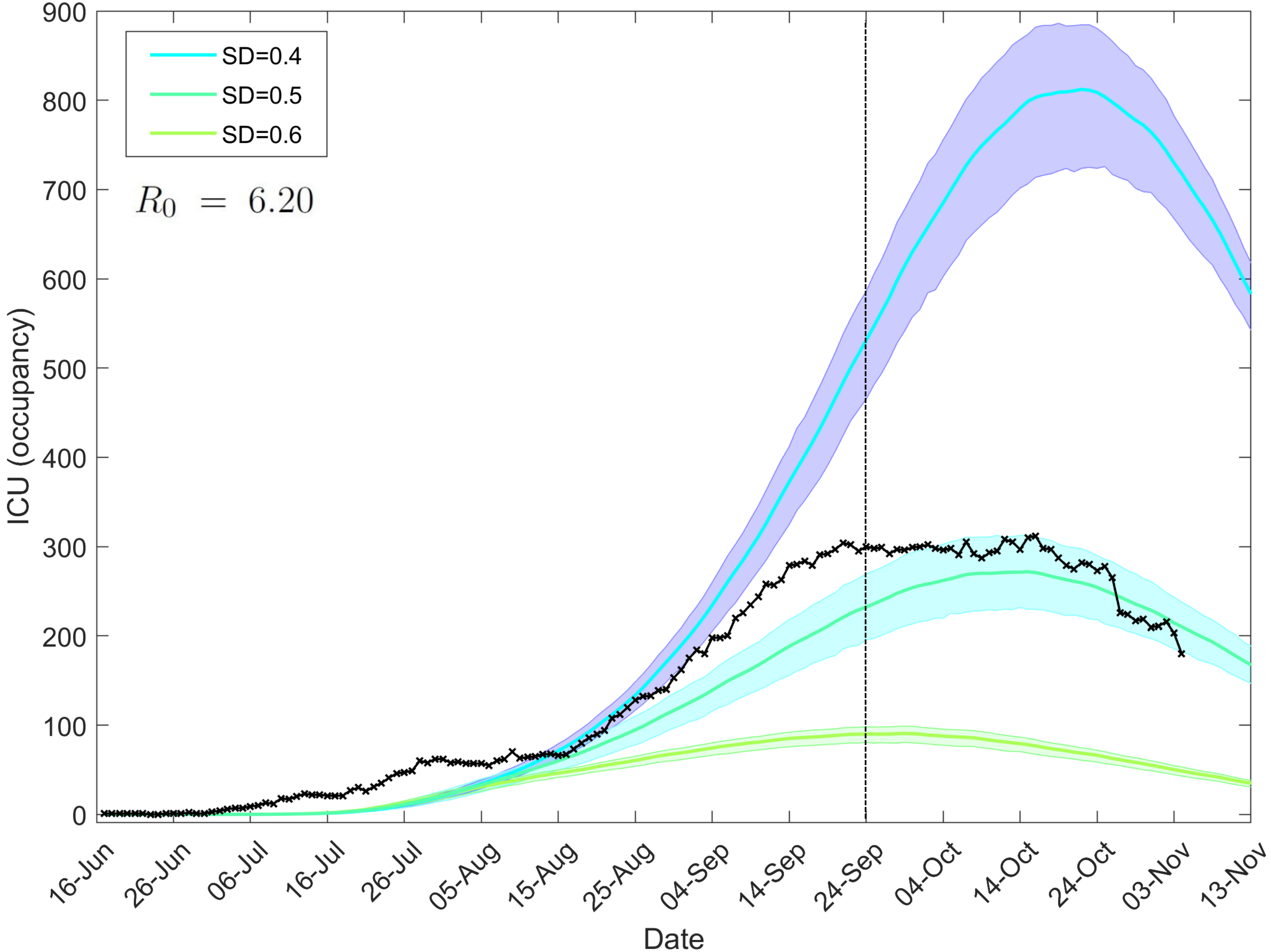
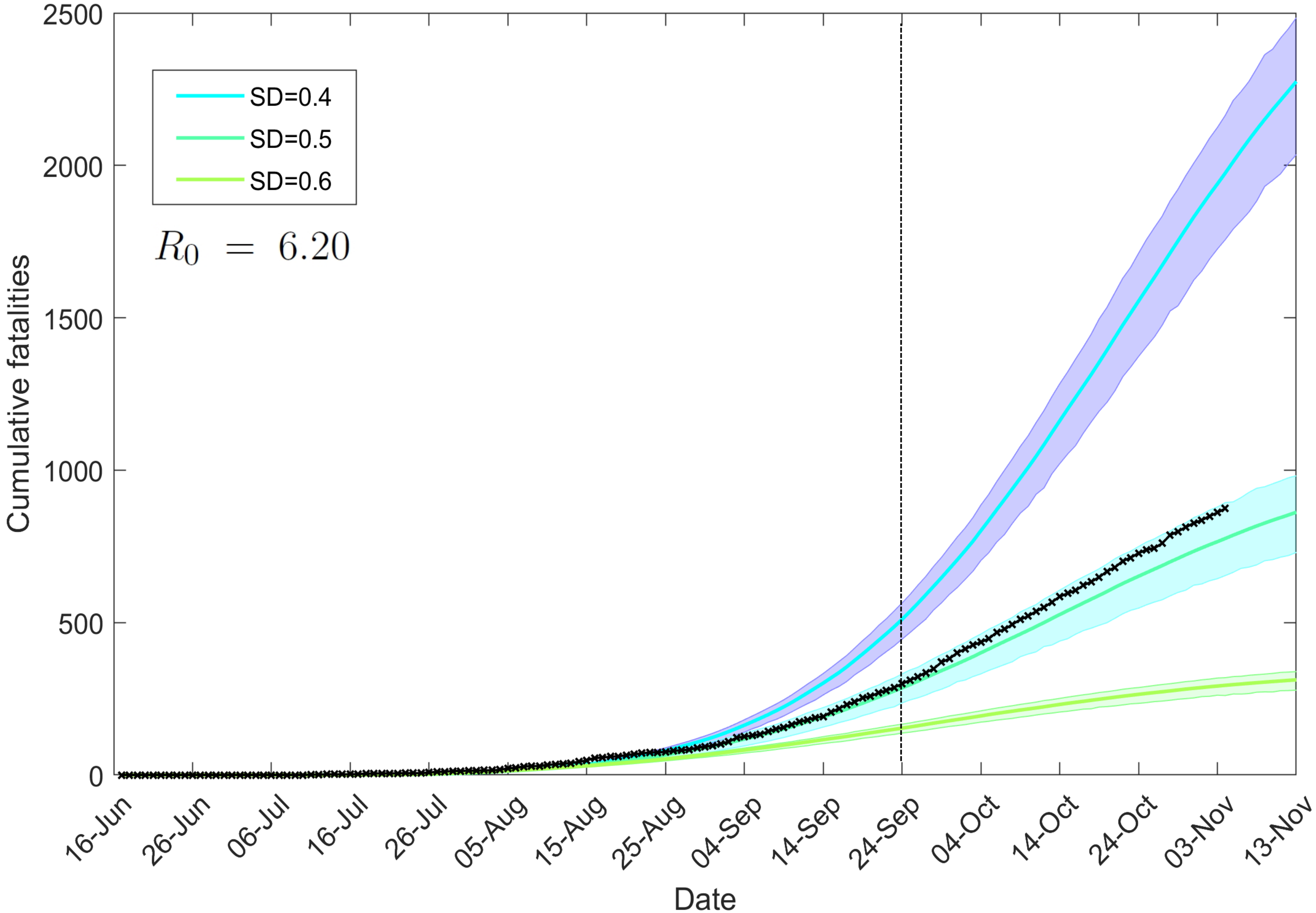
Hospitalisations (occupancy): a threefold reduction for 10% increase in SD



ICU (occupancy):
a threefold reduction for 10% increase in SD



Mortality (cumulative deaths): a two-fold reduction for 10% increase in SD



Balance health and socioeconomic consequences: challenges

- how to objectively model and quantify the health and economic costs in comparative terms?
- how to remove the bias created by subjective perspectives of policy- and decision-makers?
- how to account for the diversity of demographics and human behaviour?

Q. D. Nguyen, M Prokopenko, Optimising cost-effectiveness of pandemic response under partial intervention measures, *Scientific Reports*, 12: 19482, 2022.

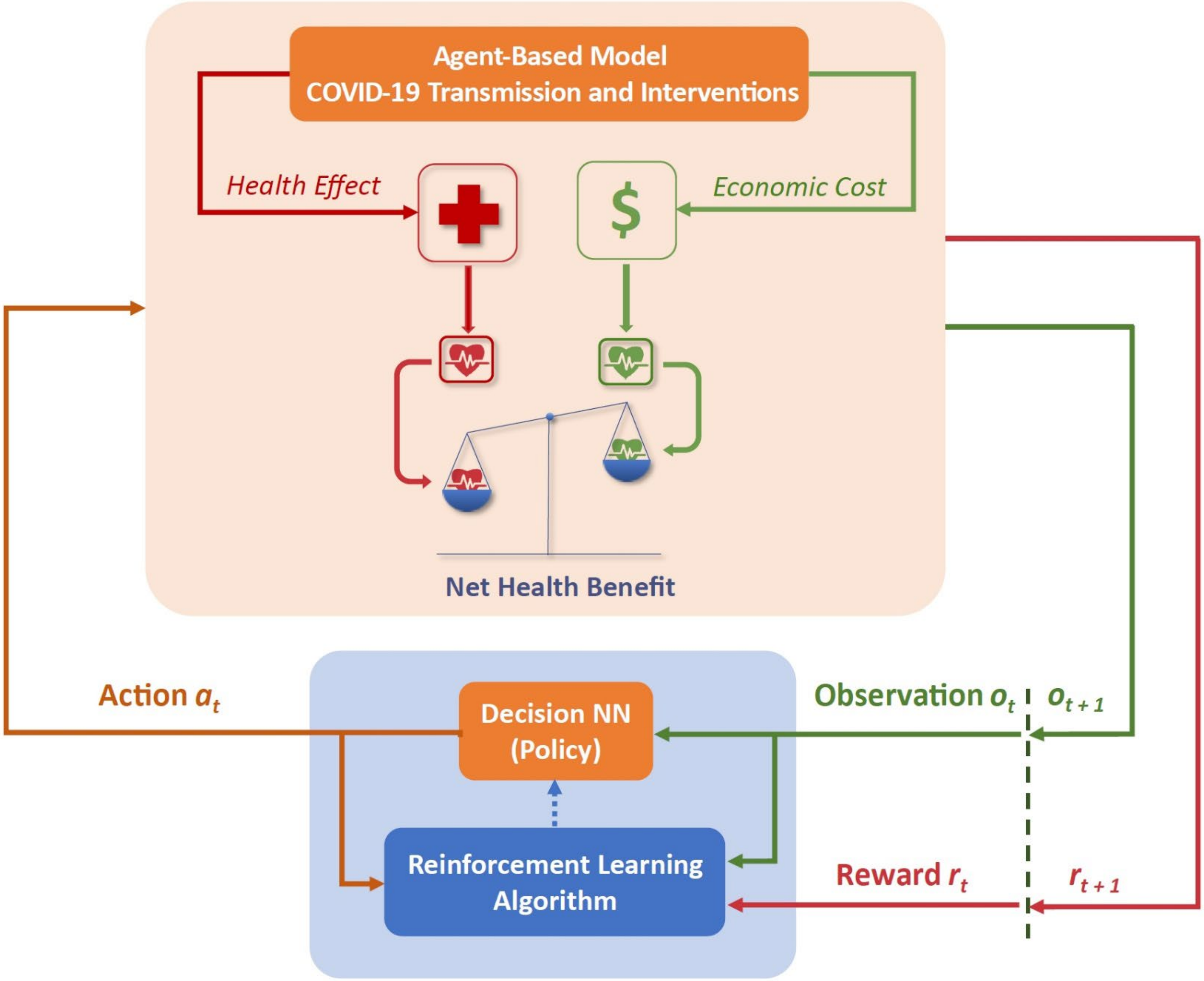
Balance health and socioeconomic consequences: approach

- how to objectively model and quantify the health and economic costs in comparative terms?
  - the Net Health Benefit (NHB)

- how to remove the bias created by subjective perspectives of policy- and decision-makers?
  - a reinforcement learning (RL) algorithm dynamically optimising feasible interventions

- how to account for the diversity of demographics and human behaviour?
  - an agent-based model (ABM) based on comprehensive demographic (census) data

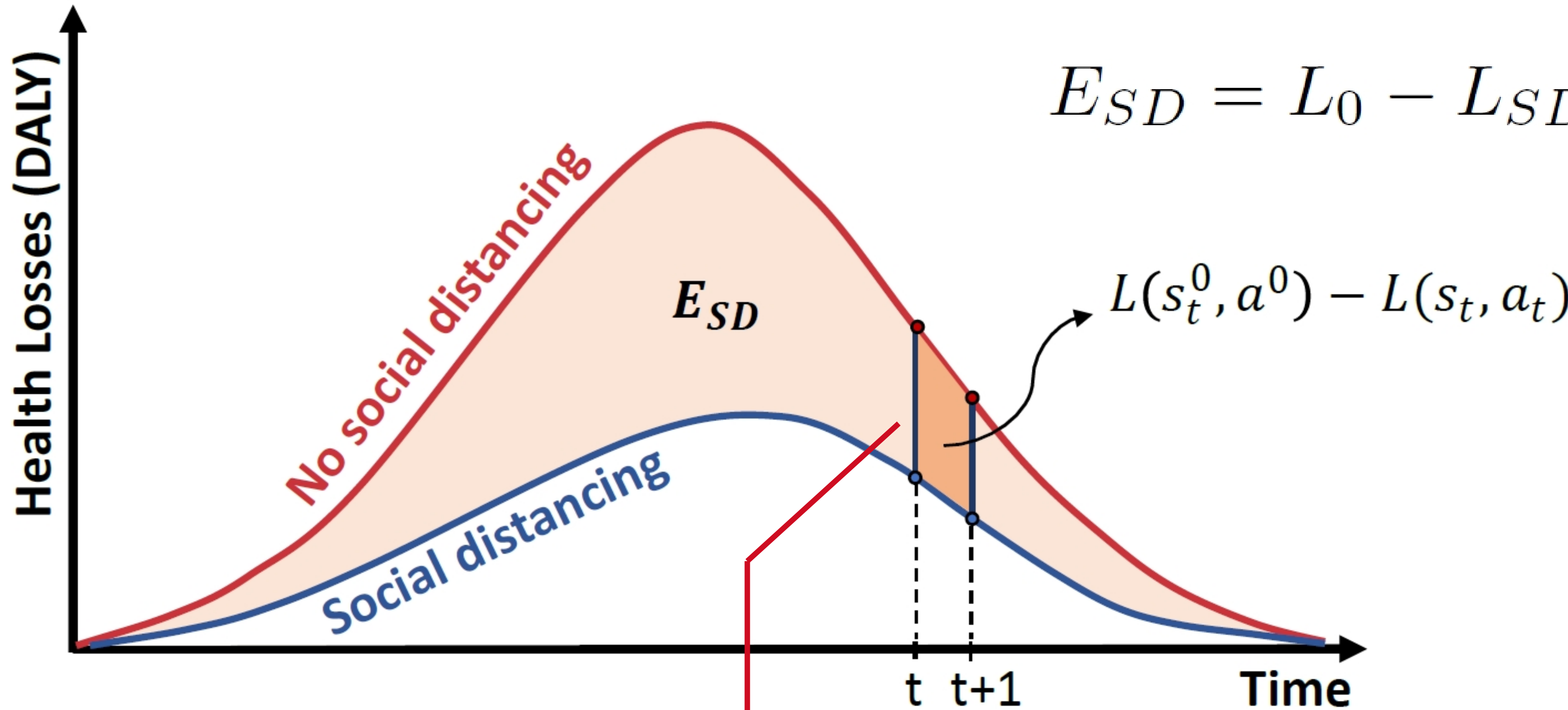
Optimisation: RL with ABM in the loop



Disability-Adjusted Life Years (DALY) and Health effects

$$\text{DALY} = \text{YLL} + \text{YLD}$$

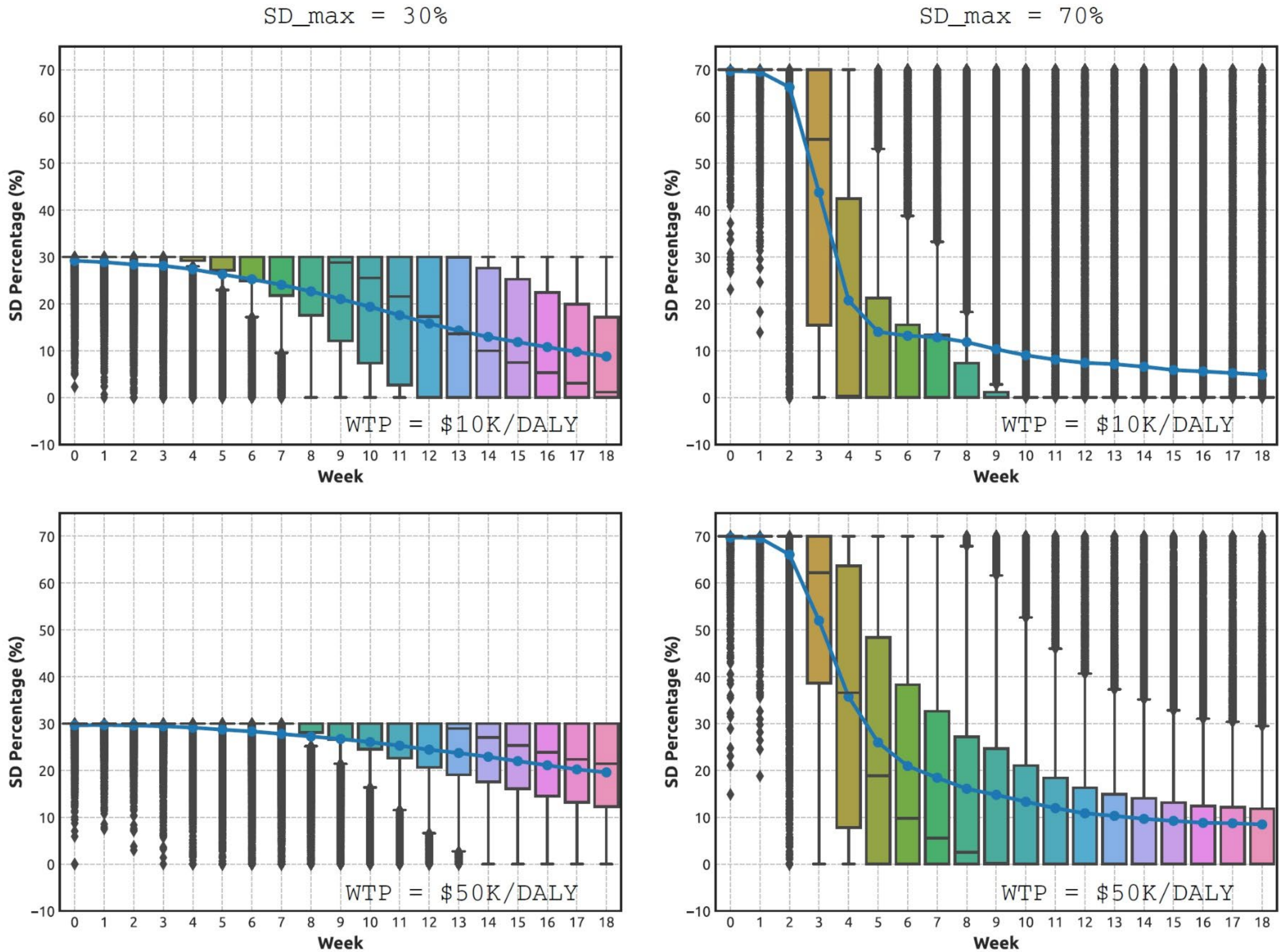
$$E_{SD} = L_0 - L_{SD}$$



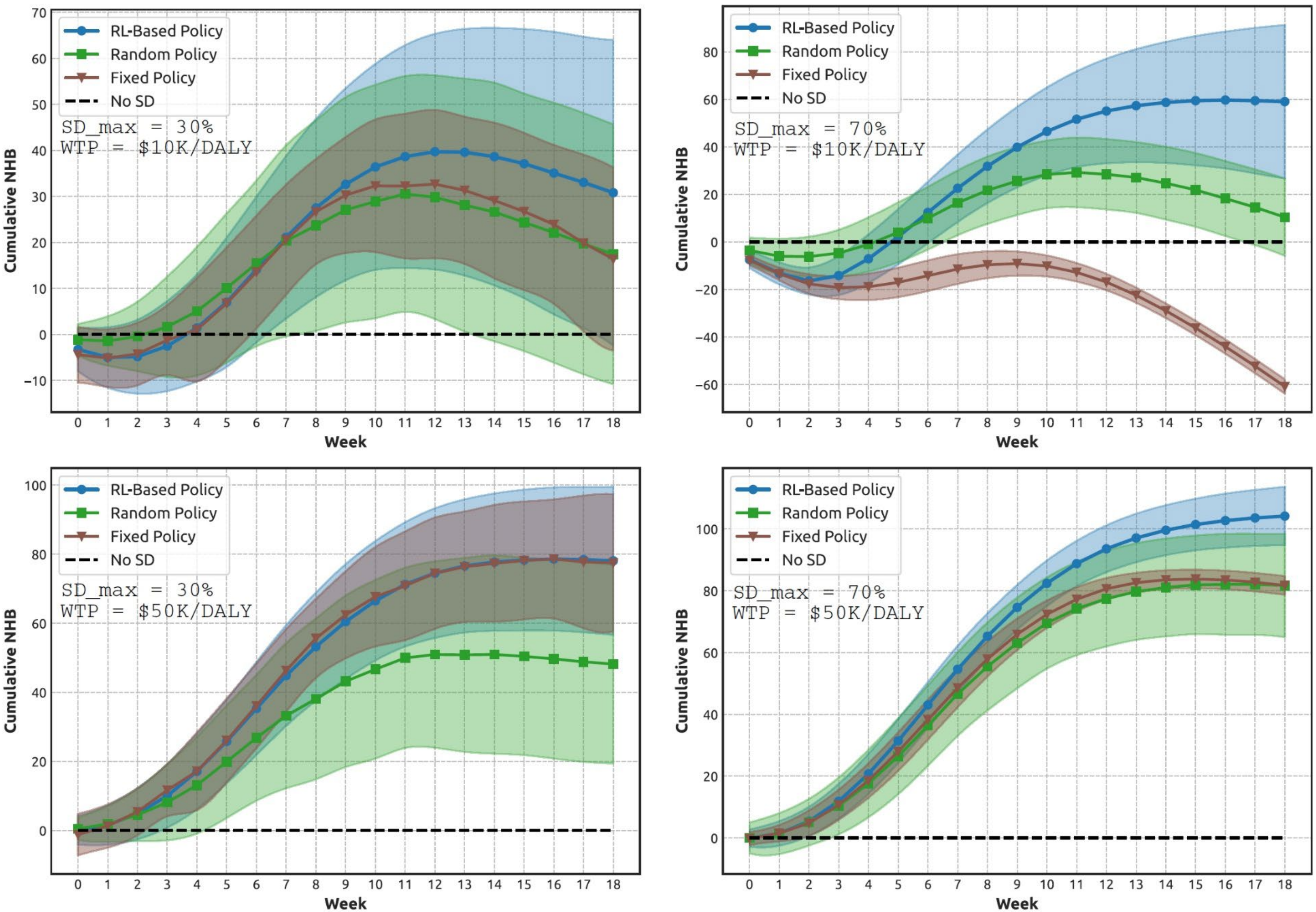
$$\text{NHB} = \mu_{E_{SD}} - \frac{\mu_{C_{SD}}}{\lambda}$$

Willingness to pay (WTP)

Adaptive SD strategies



Comparison: adaptive vs fixed | random | zero-SD



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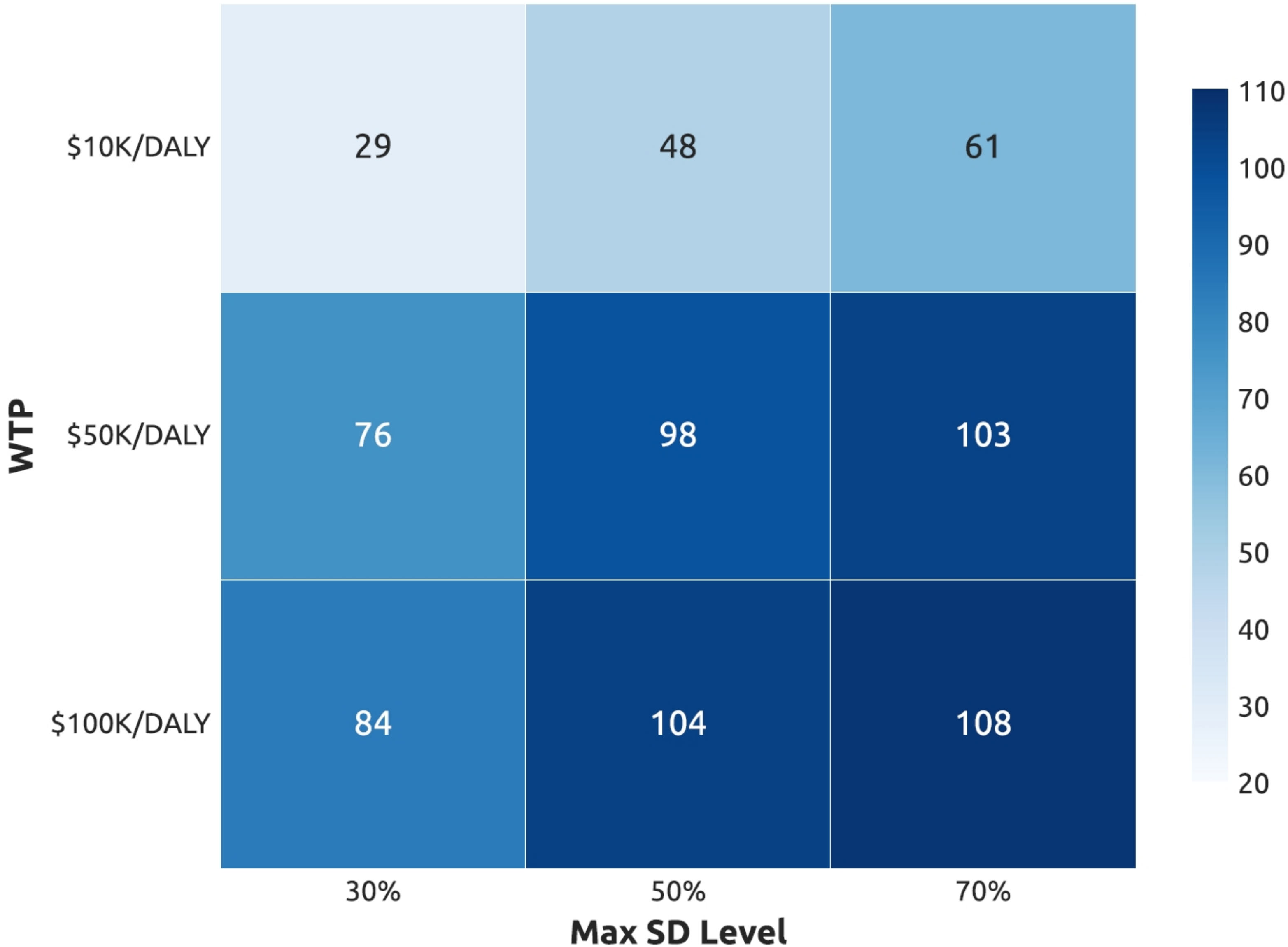
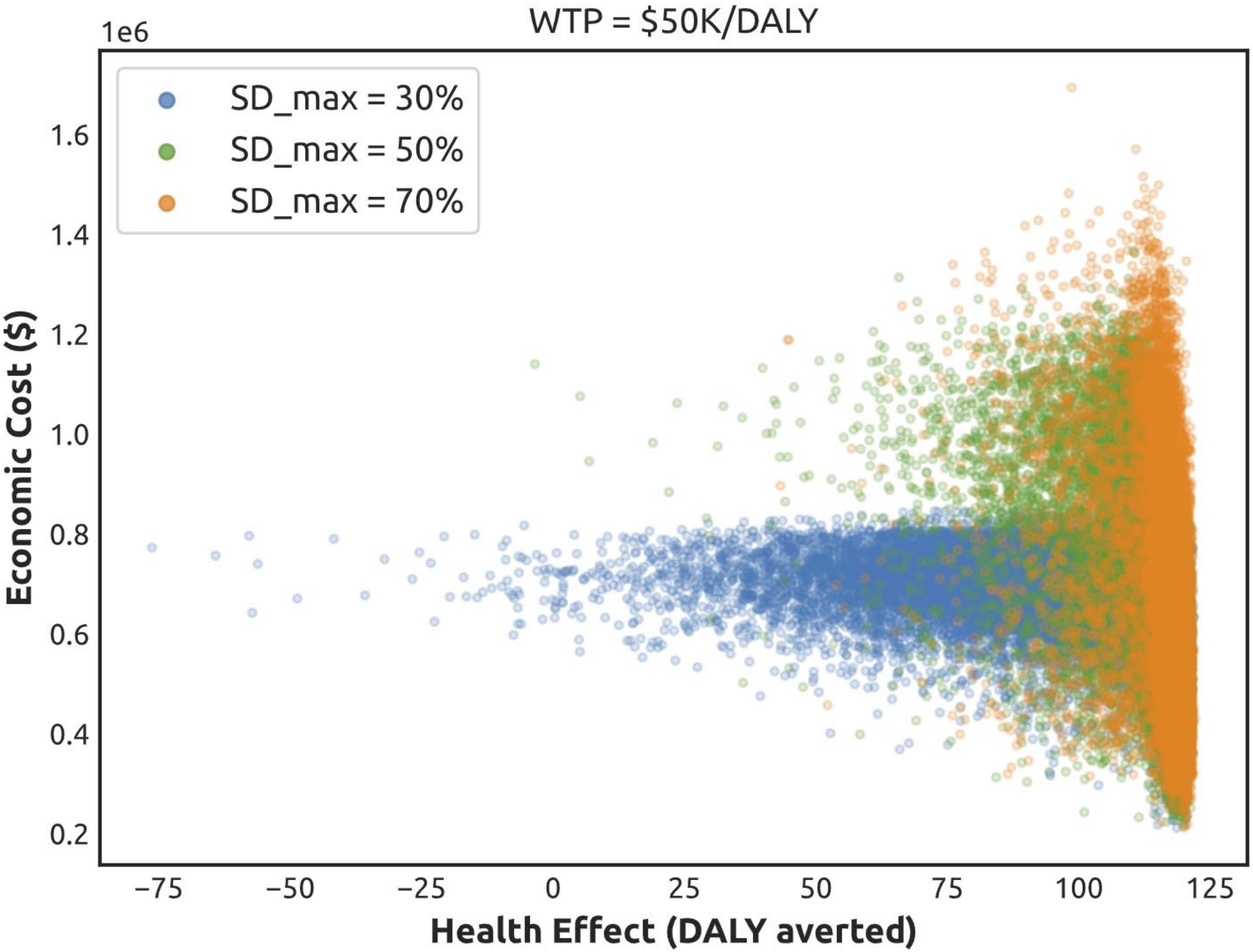
Cumulative NHB generated by adaptive SD strategies



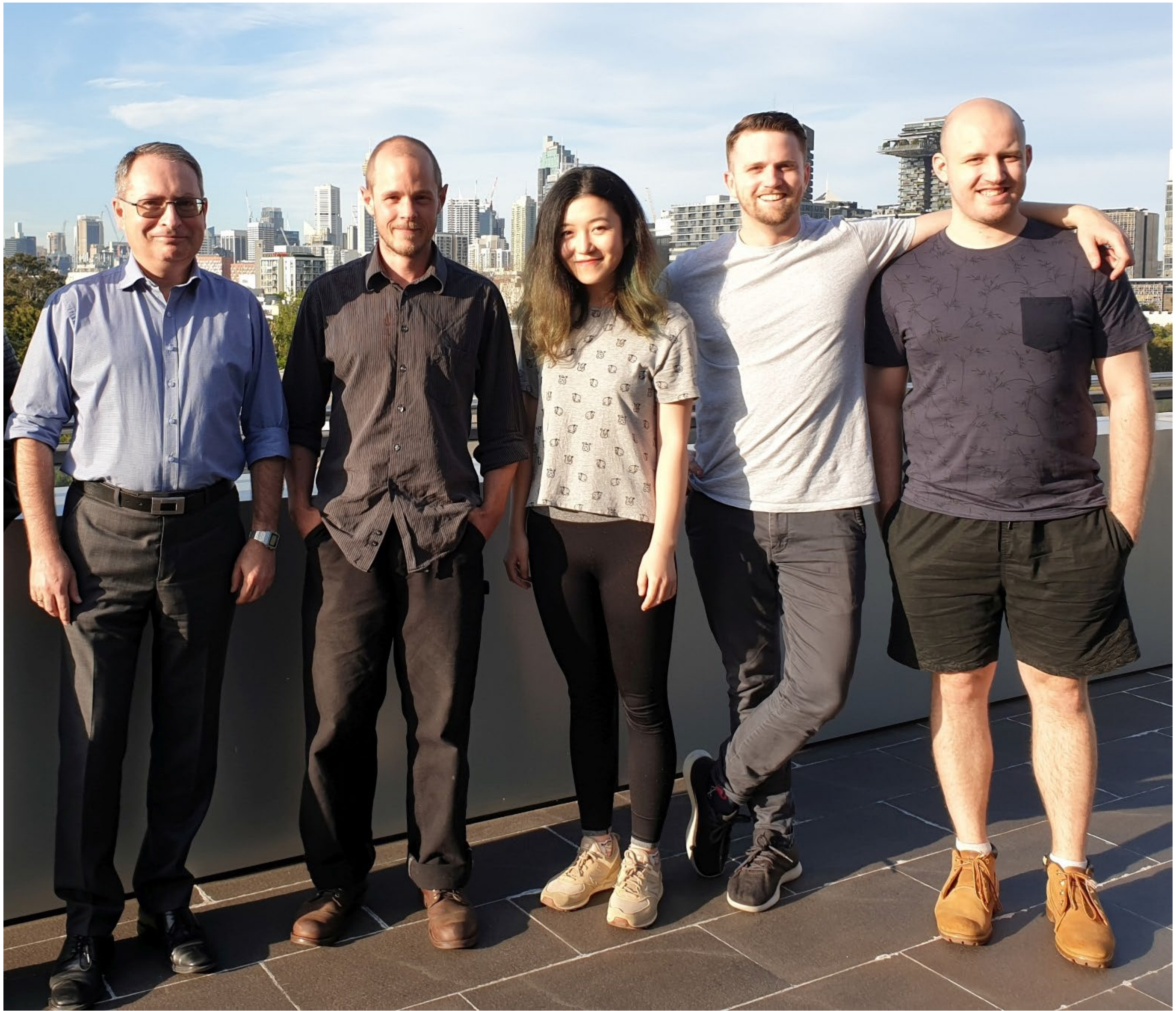
Phase diagram of the NHB dynamics: health effects vs economic costs



Challenges and feedback loops

- complexity of human behaviour:
  - tipping points in social distancing (SD) compliance / adoption
  - highly-transmissible variants strongly amplify small changes in SD adoption
  - vaccine uptake and SD levels are uneven across demographics
- socio-economic complexity:
  - subjective perspectives of policy- and decision-makers
  - capacity limits of testing, tracing, isolation, quarantine measures
  - balance of health and economic costs
- bio-complexity:
  - emergence and evolution of sub-lineages
  - vaccination efficacy diminishes over time
- recurrent waves

AMTraC-19 team



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- K. M. Fair, C. Zachreson, M. Prokopenko, Creating a surrogate commuter network from Australian Bureau of Statistics census data, *Scientific Data*, 6, 150, 2019.

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AMTraC-19 open source

https://zenodo.org/record/5778218

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December 14, 2021 Software Open Access

AMTraC-19 (v7.7d) Source Code: Agent-based Model of Transmission and Control of the COVID-19 pandemic in Australia

Chang, Sheryl L.; Harding, Nathan; Zachreson, Cameron; Cliff, Oliver M.; Prokopenko, Mikhail

The software implements an agent-based model for a fine-grained computational simulation of the COVID-19 pandemic in Australia. This model is calibrated to reproduce several features of COVID-19 transmission, including its age-dependent epidemiological characteristics. The individual-based epidemiological model accounts for mobility (worker and student commuting) patterns and human interactions derived from the Australian census and other national data sources. The high-precision simulation comprises approximately 24 million stochastically generated software agents and traces various scenarios of the COVID-19 pandemic in Australia. The software has been used to evaluate various intervention strategies, including (1) non-pharmaceutical interventions, such as restrictions on international air travel, case isolation, home quarantine, school closures, and stay-at-home restrictions with varying levels of compliance (i.e., "social distancing"), and (2) pharmaceutical interventions, such as pre-pandemic vaccination phase and progressive vaccination rollout.

The paper describing the model and the scenarios investigated with AMTRaC-19 (v7_7d):

S. L. Chang, C. Zachreson, O. M. Cliff, M. Prokopenko, Simulating transmission scenarios of the Delta variant of SARS-CoV-2 in Australia, *Frontiers in Public Health*, 10, 10.3389/fpubh.2022.823043, 2022.

Please cite it, as well as other publications referenced below, when using the software.

The dataset generated during this study is also available on Zenodo:

S. L. Chang, O. M. Cliff, C. Zachreson & M. Prokopenko. (2021). AMTraC-19 (v7.7d) Dataset: Simulating transmission scenarios of the Delta variant of SARS-CoV-2 in Australia (Version v1) [Data set]. Zenodo. https://doi.org/10.5281/zenodo.5726241

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