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wellcome

Optimal Control Theory applied to COVID-19 social distancing interventions

Marc Choisy, DMo workshop, 18th August 2021

Acknowledgements





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Quentin Richard (ages)
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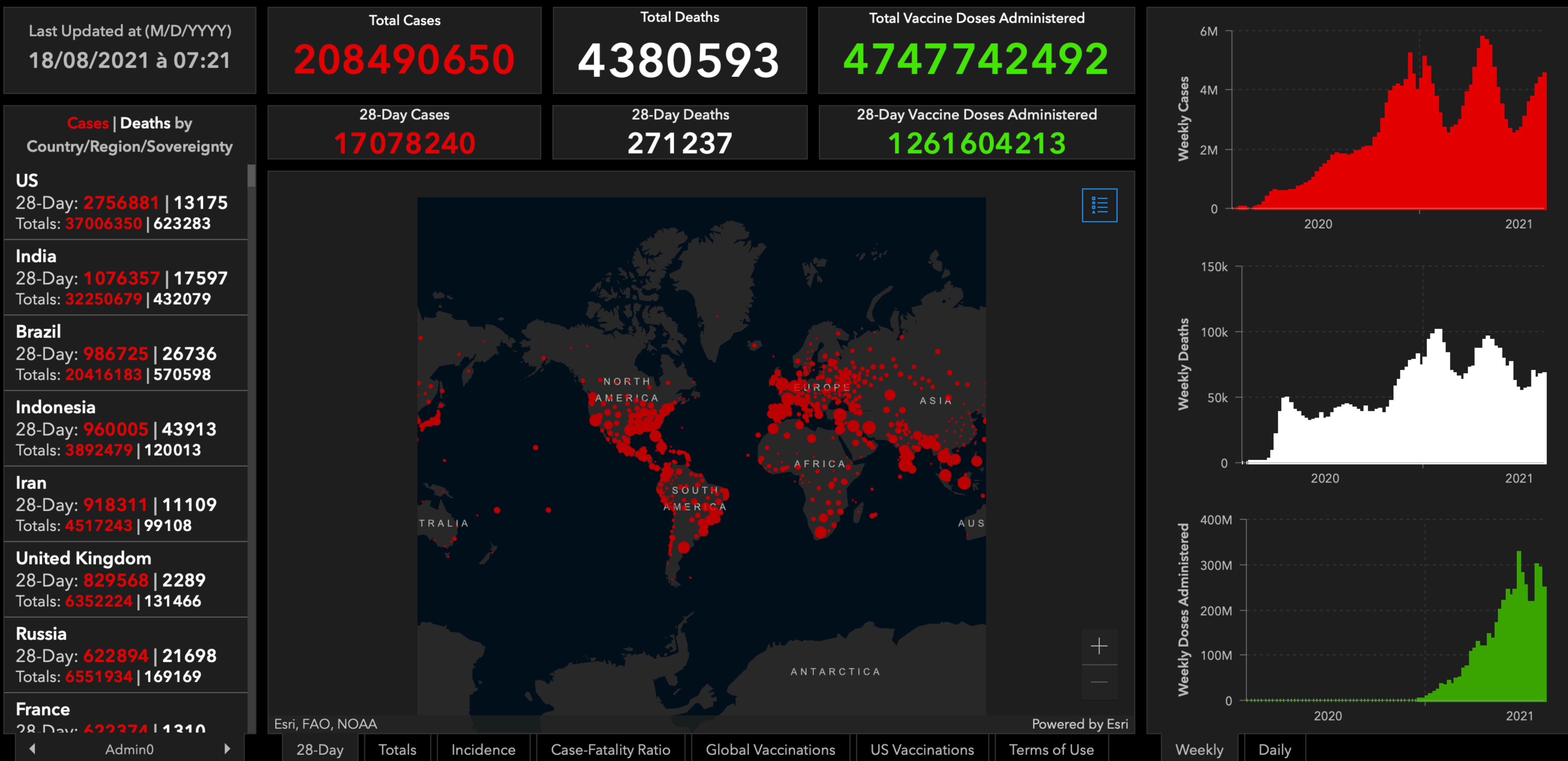
Nguyen Cong Khanh (NIHE, Hanoi)
Pham Quang Thai (NIHE, Hanoi)


COVID-19

John Hopkins University



SARS-CoV-2: new virus

this is actually a good news
from a modelling point of view!

- very little knowledge
- world population largely susceptible
- no treatment and almost a year without vaccine

What we learned:

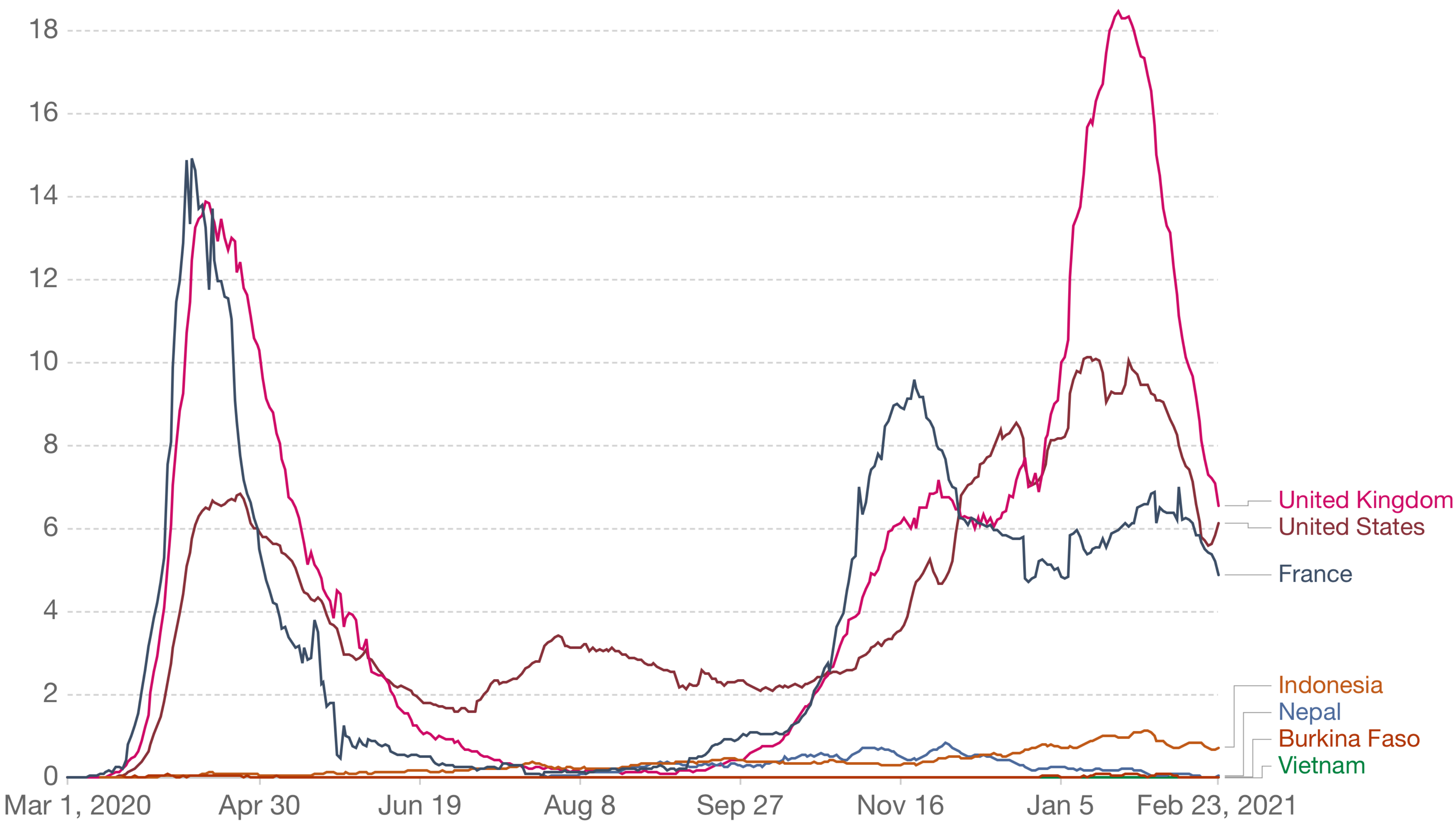
- large spectrum of severity
- asymptomatic transmission
- variability of infectiousness

“epidemiological hell”

Today:

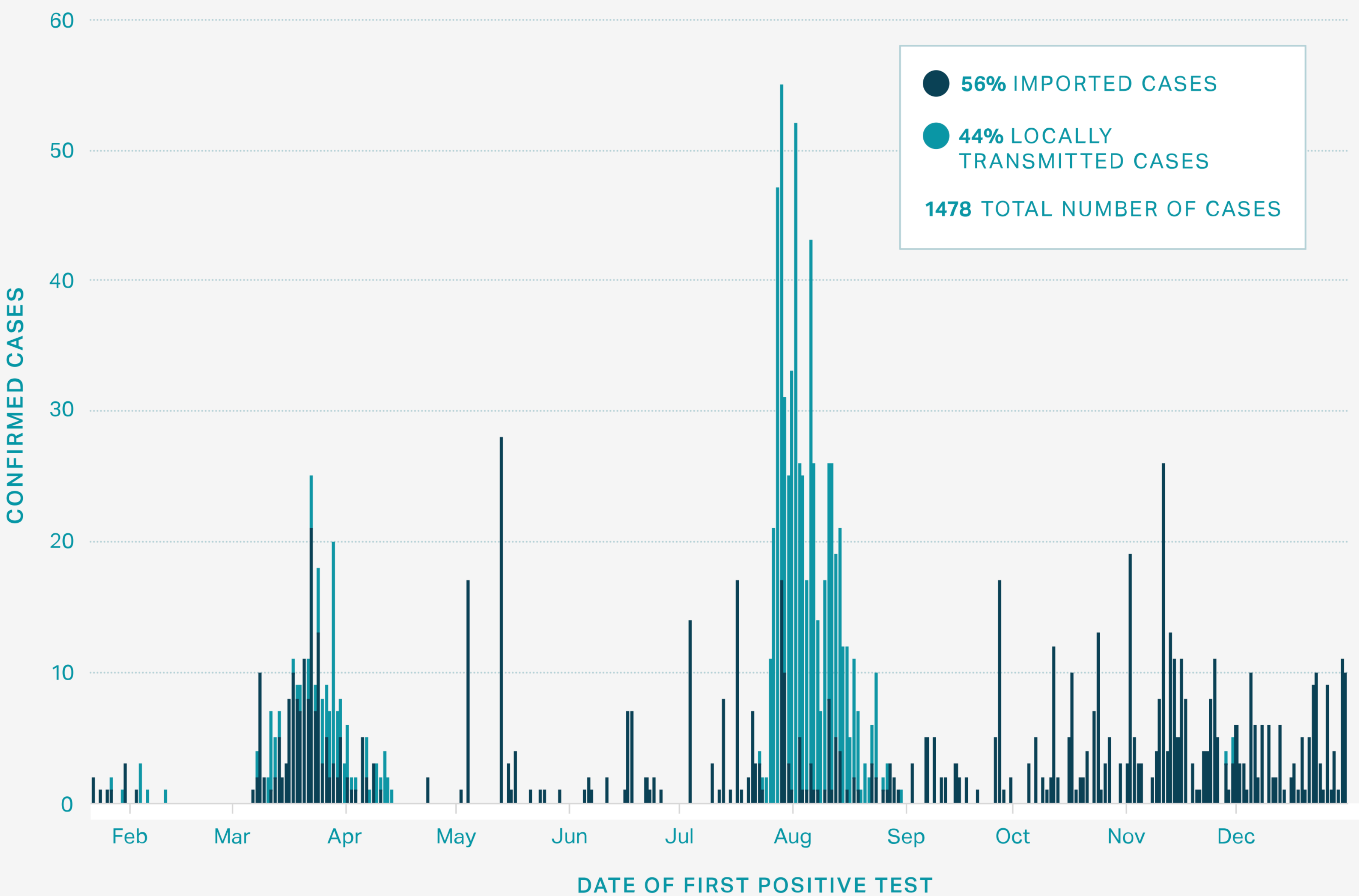
- vaccines newly available
- variants of concern newly available too!!!

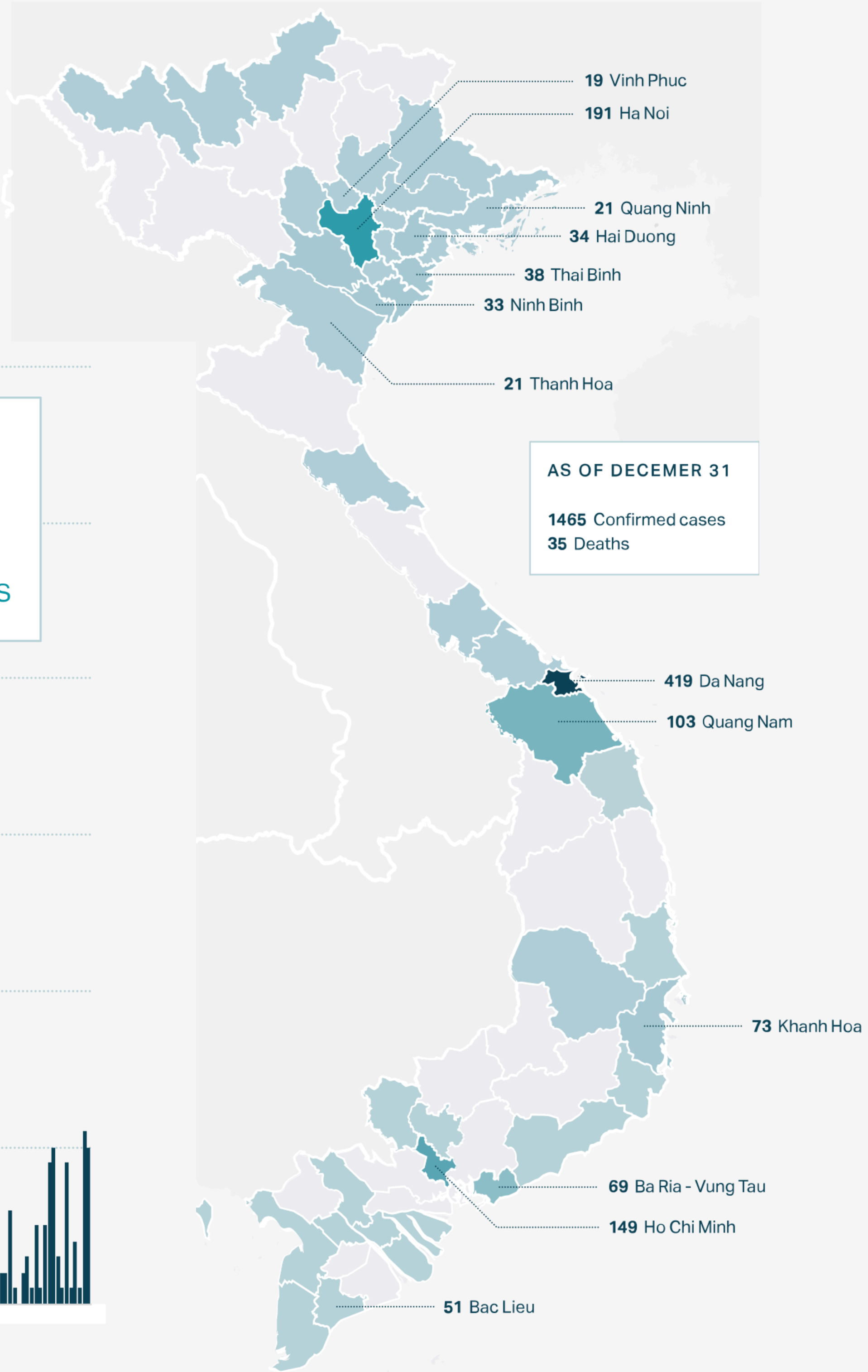
Daily mortality / million



Situation in Vietnam in 2020

2,412 confirmed cases
569 currently hospitalized
35 deaths





https://www.exemplars.health/emerging-topics/epidemic-preparedness-and-response/covid-19

Credit: Le Van Tan

COVID-19 control in Vietnam

Early preparedness, contact tracing, isolation and testing, coupled with timely border closure, physical distancing and community adherence, have been key measures in controlling COVID-19 in Vietnam.

Vietnam is a lower-middle income country of 97 million people. Per capita, its GDP in 2018 was US$2,566, and around US$150 per person per year was spent on healthcare. The country shares a 1,300-km border with China, where SARS-CoV-2 first emerged. Yet, by the end of 2020, Vietnam had experienced only two peaks of community transmission (March–April and July–August) and reported a total of 1,465 PCR-confirmed cases of SARS-CoV-2 infection and 35 deaths. Here, I reflect on how Vietnam has succeeded in controlling the virus.

The experience Vietnam gained from previous epidemics, such as SARS-CoV-1 in 2003 and bird flu (H5N1) in 2004, was critical in informing its rapid response to COVID-19. On 16 January, well in advance of the first case of SARS-CoV-2 in the country, the Vietnamese Government issued the first diagnostic and management guidelines for COVID-19. The guidelines provided instructions on contact tracing and 14-day isolation of direct contacts (F1) of a confirmed case. This allowed Vietnam to successfully diagnose the first two epidemiologically linked COVID-19 cases (a father and son) on 23 January. The father arrived from Wuhan, China, to visit his son in Mekong Delta, representing the first instance of human-to-human transmission of SARS-CoV-2 outside of China. Their contacts were traced, isolated and tested; one was positive for SARS-CoV-2. Thus the first community transmission chain in the country was quickly identified and contained.

Immediately following the detection of these cases, Vietnam suspended all flights from Wuhan. At that time, the WHO advised against travel restrictions. Shortly after this, in February, the country also closed its border and banned international flights to and from China, extending this to the rest of the world in March.

Schools were closed early, initially for the Lunar New Year from late January to early February, but closures were extended to early May, when the first wave was successfully controlled. In parallel, physical distancing, wearing a face mask in public and in-country travel restrictions were applied with increasing stringency, with strong public support and adherence. Suspected transmission hotspots (for example, a city or a community) were locked down to stop community transmission. On 31 March, when community transmission was escalating and the total reported cases in Vietnam exceeded 200, the prime minister enacted a nationwide lockdown for 15 days, which was extended to 30 April for high-risk cities. Accordingly, non-essential businesses and public transport were shut down, and only essential travel between cities and provinces was allowed. Gatherings of >2 people in public places were prohibited. People were asked to not leave their houses unless it was for essential activities (for example, seeking medical care or buying food).

Nasal and throat swab testing by PCR was applied to all F1s (regardless of symptoms) and travelers entering Vietnam. Confirmed cases, their F1s (regardless of the PCR results) and travelers were all subjected to a minimum quarantine of 14 days at one of the government-run isolation centers, deployed across the country since March. Meanwhile, home isolation for a maximum of 14 days was mandatory for those in contact with an F1. By the end of 2020, 730,000 individuals had been quarantined at one of the isolation centers across Vietnam, and 1.7 million people had been tested for SARS-CoV-2. Mass testing coupled with a creative sample-pooling strategy, whereby nasal and throat swabs from 2–7 individuals were placed in one tube at collection, was key to the success of suppressing the second wave in central Vietnam between July and August (Thanh, T. T. et al. Preprint at *medRxiv* https://doi.org/10.1101/2020.09.11.20192484, 2020).

An innovative communication strategy was developed to keep the public informed and safe. From the start of the pandemic, the government sent regular updates on COVID-19-preventive responses and the national situation via SMS texts. Mobile apps, especially those developed locally, such as Bluezone, helped users to identify whether they were in contact with a confirmed case. In February, a popular song was given new lyrics, 'Ghen Co Vy' (Jealous Coronavirus), to raise public awareness of the disease and to promote good hygiene habits to reduce the risk of acquiring COVID-19. To date, the song has attracted ~70 million views.

The government has also sought to mitigate the socioeconomic impacts of COVID-19. From August, Vietnam slowly opened its borders to allow highly skilled workers and experts to enter the country, although everyone entering undergoes a compulsory 14-day isolation period in designated hotels or government facilities, with SARS-CoV-2 PCR screening on days 1 and 14. The government has arranged >200 flights to repatriate >60,000 citizens stuck abroad and issued financial assistance packages to support businesses and employees affected by COVID-19. Vietnam's GDP growth rate was 2.91% in 2020 — one of the highest rates in the world.

Collectively, early preparedness, contact tracing, isolation and mass PCR screening, coupled with timely border closure, physical distancing and community adherence, have been the key components that have determined the success of Vietnam's control of COVID-19. Heading into the second year of the pandemic, phase 1 clinical trials of locally developed vaccine candidates are ongoing in Vietnam, and 30 million doses of the Oxford–AstraZeneca vaccine have been ordered for 2021. Until then, the Government will continue to enforce the measures that gave it such exemplary control of COVID-19 in 2020.

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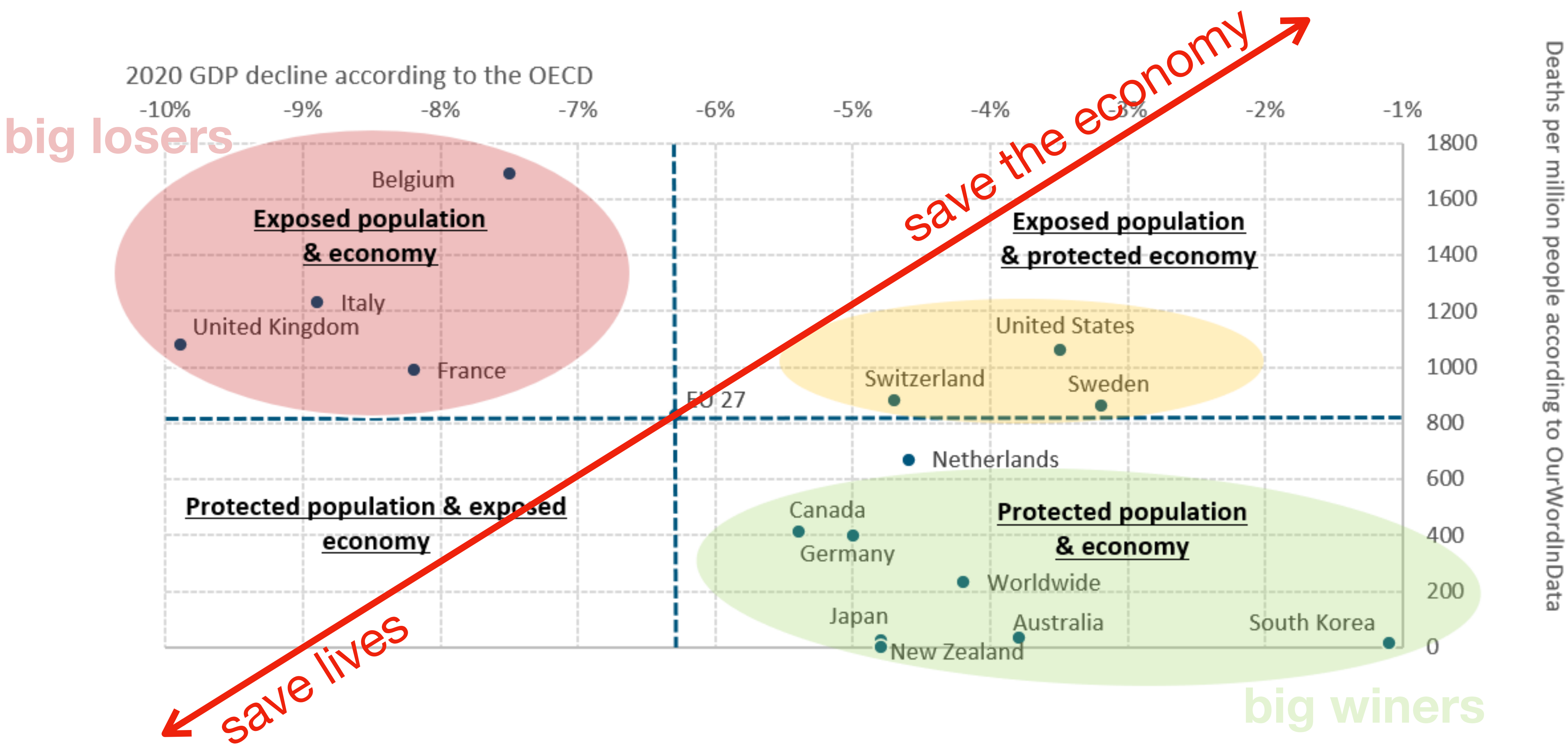
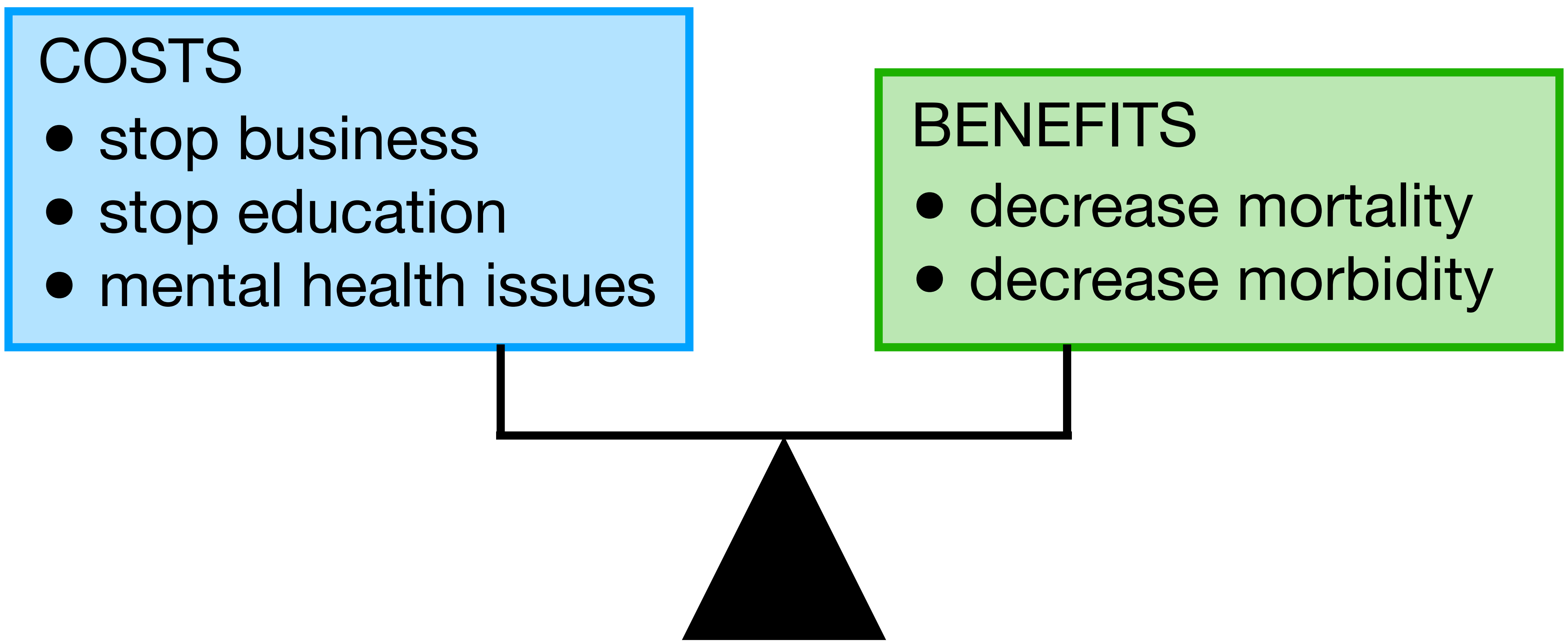
Competing interests
The author declares no competing interests.

Optimal Control Theory

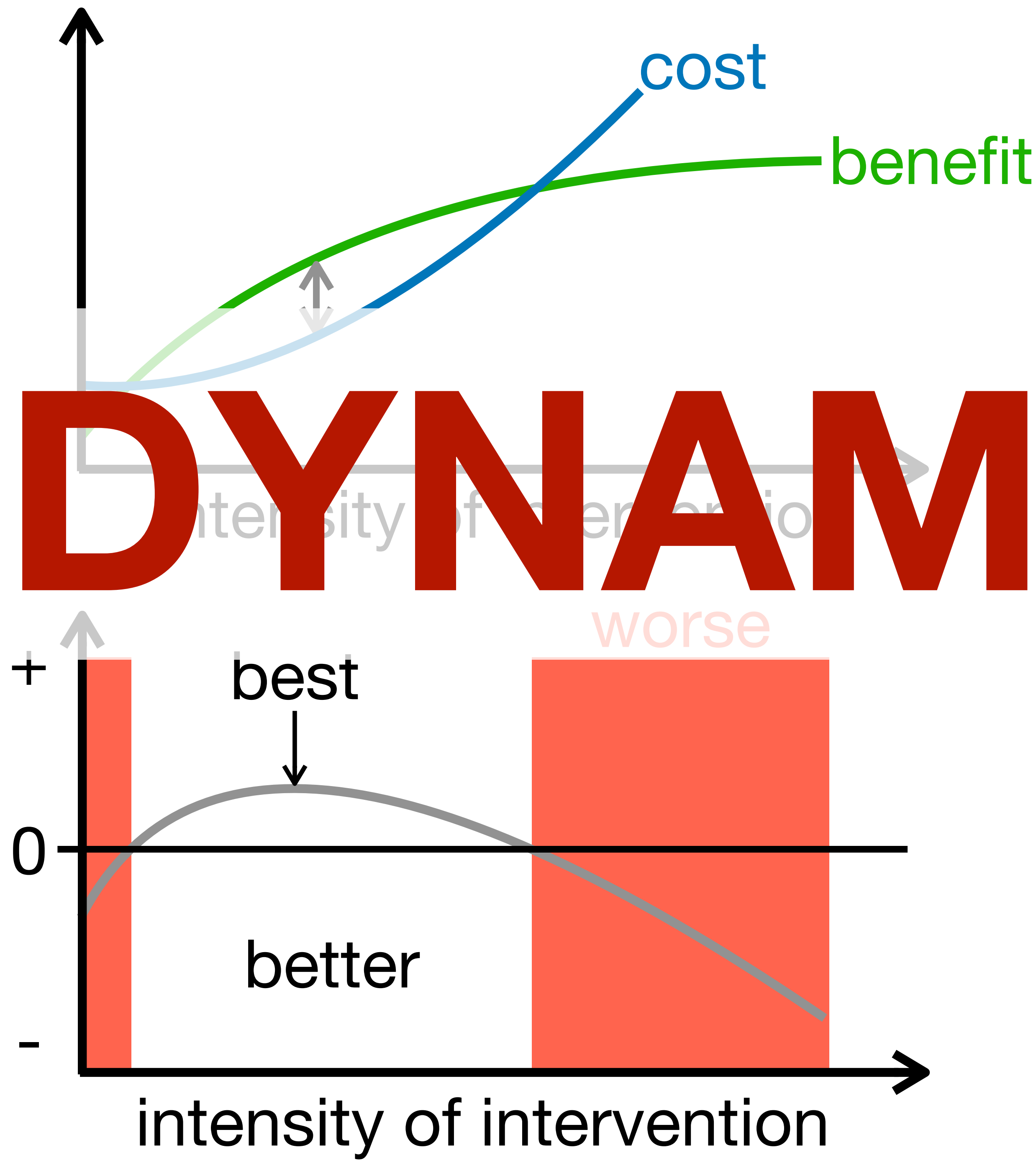
Economy vs health trade-off



Control comes with a cost

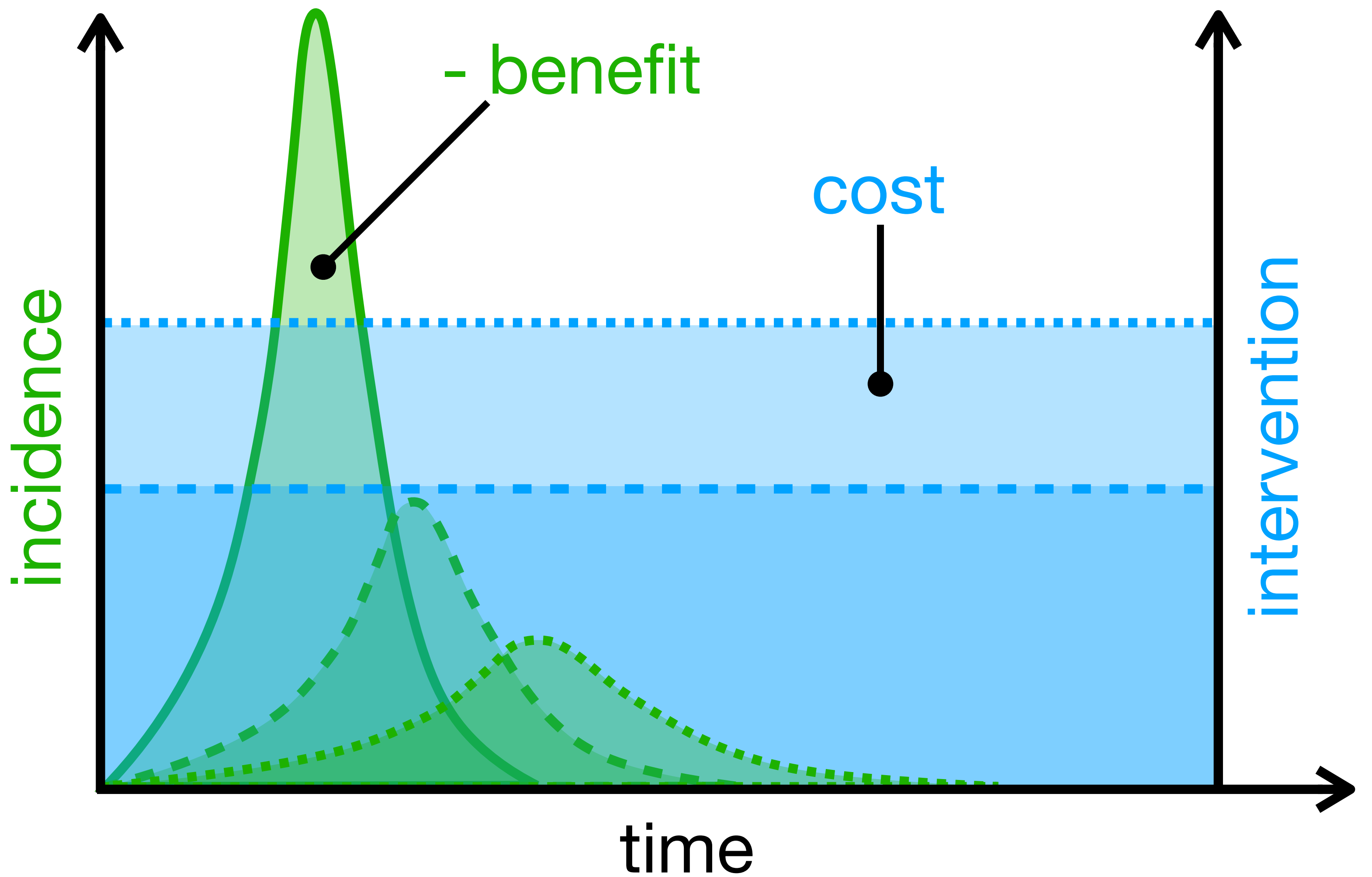


Looking for the optimal policy



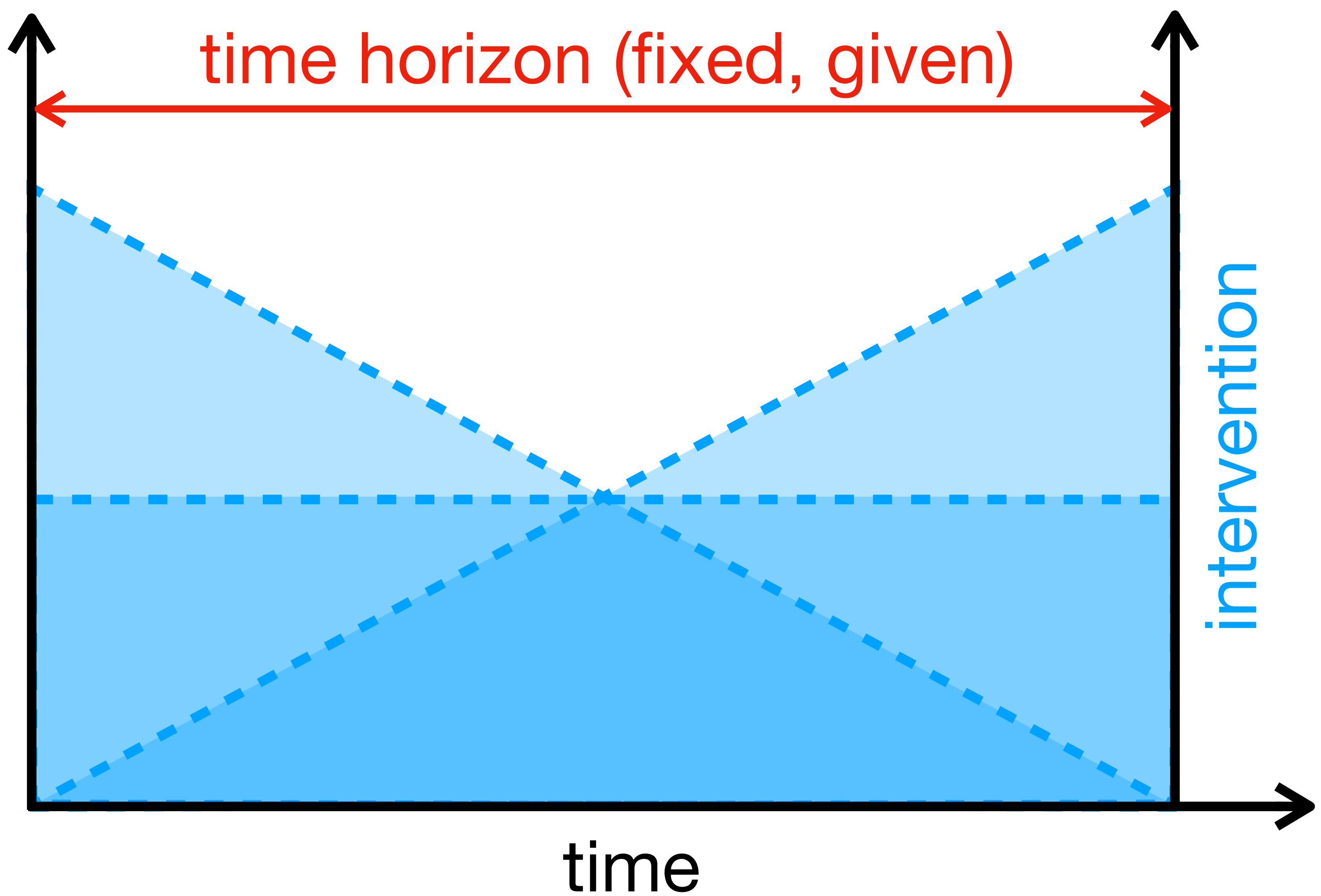
NO DYNAMICS

Constant level of intervention



Varying total cost, constant level of intervention

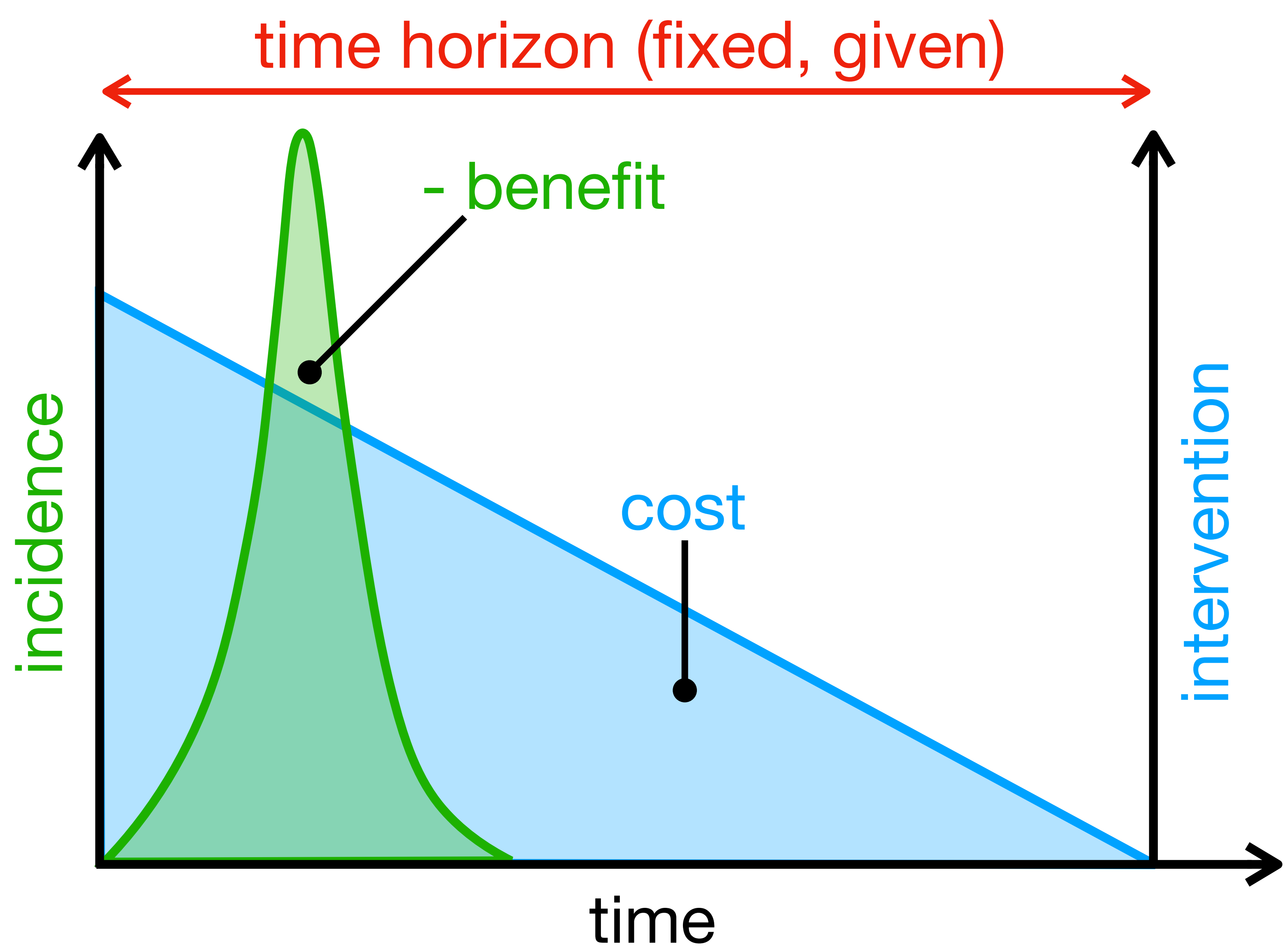
Optimal Control Theory



Varying total cost, ~~constant~~ level of intervention

varying

A model with intervention

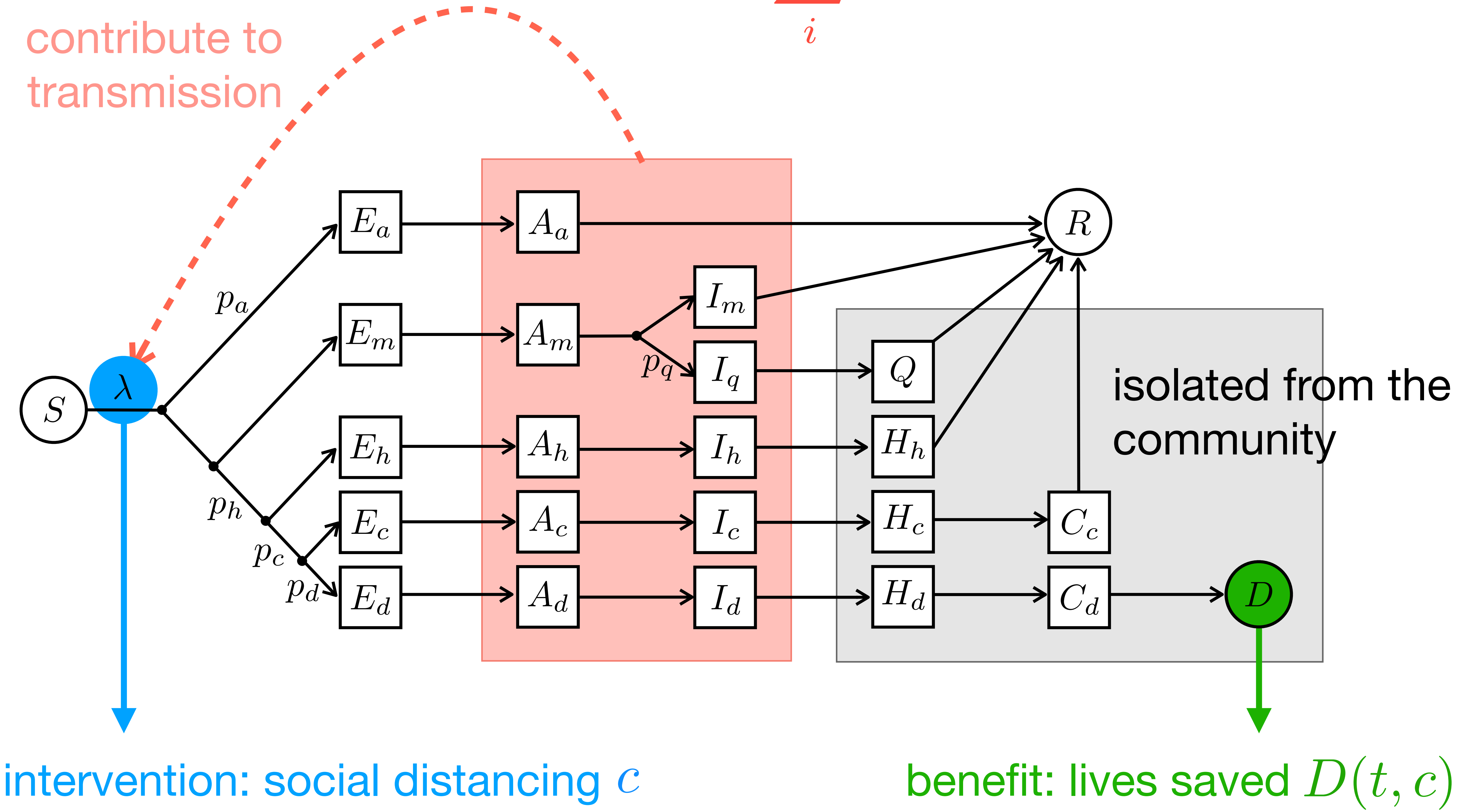


Varying total cost, ~~constant~~ level of intervention

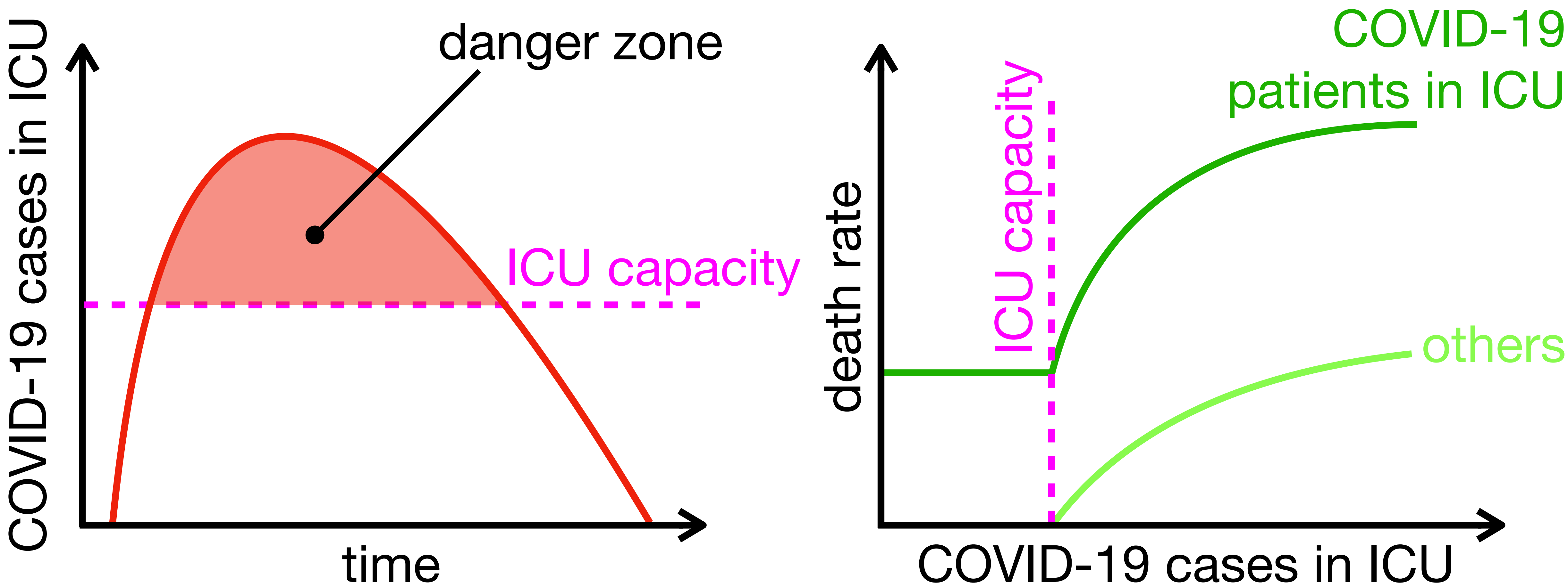
varying

A COVID-19 model

$$\lambda(t, c) = (1 - c) \sum_i (\beta_i^a A_i(t) + \beta_i^s I_i(t))$$



ICU maximal capacity



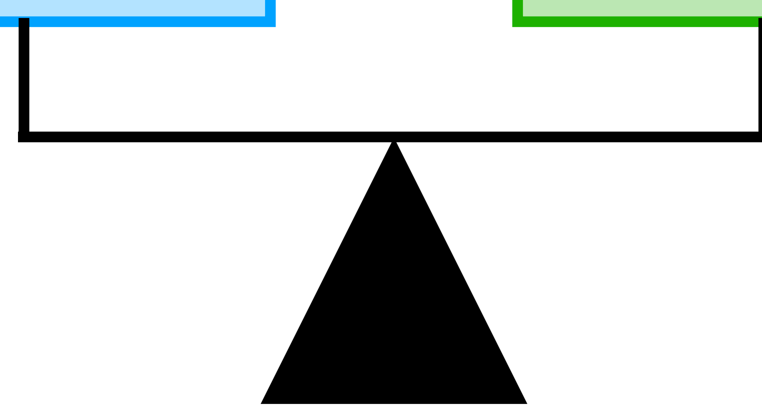
Objective function to minimize

COSTS

- stop business
- stop education
- mental health issues

BENEFITS

- decrease mortality
- decrease morbidity



time horizon

deaths of others

$$M(c) = B\int_0^T c^2(t)\,dt + \int_0^T \left(D(c,t) + D'(c,t)\right)dt$$

cost of control

social distancing

deaths of COVID-19
patients in the ICU

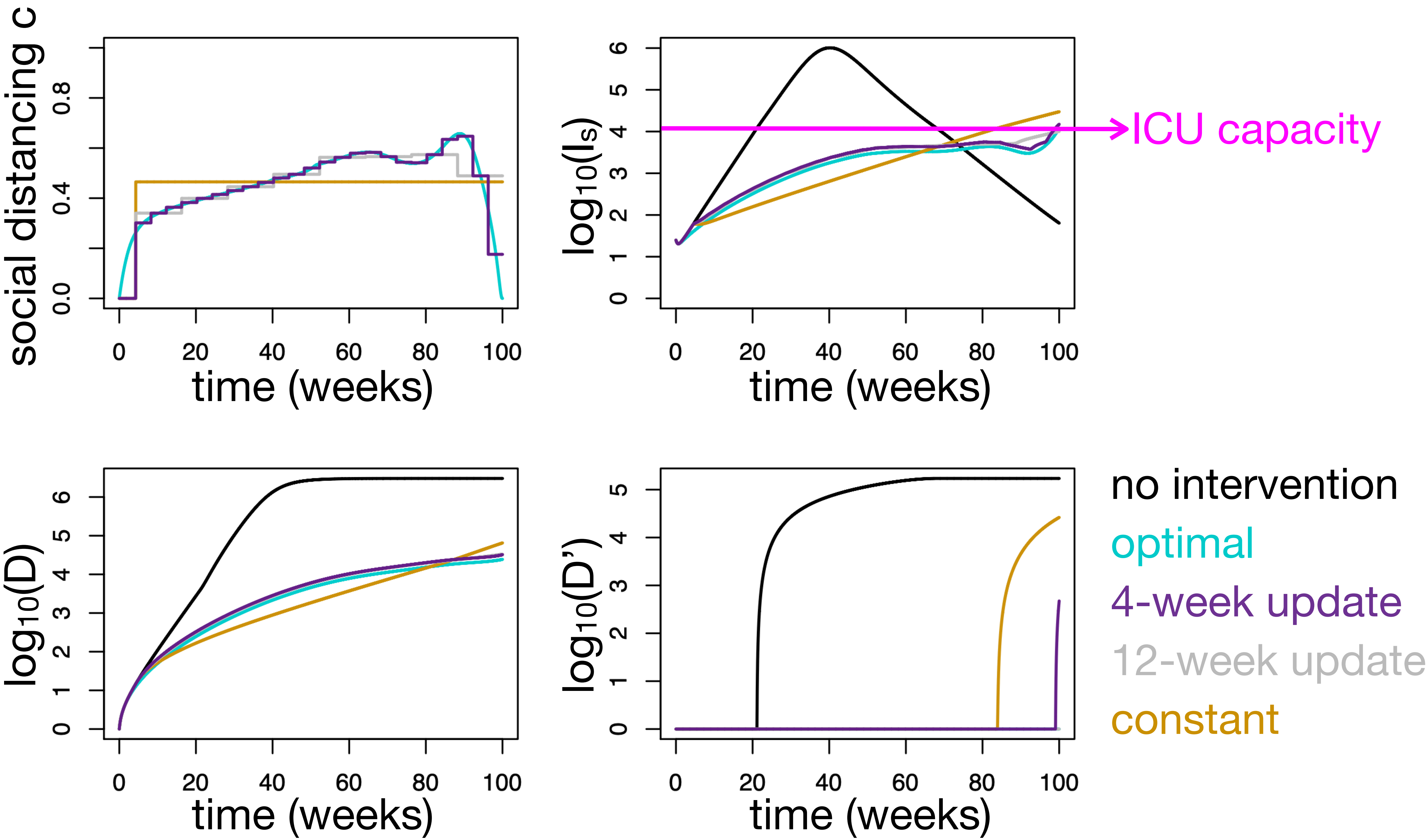
Math Model Nat Pheno: 10.1101/2020.04.02.20049189

Results

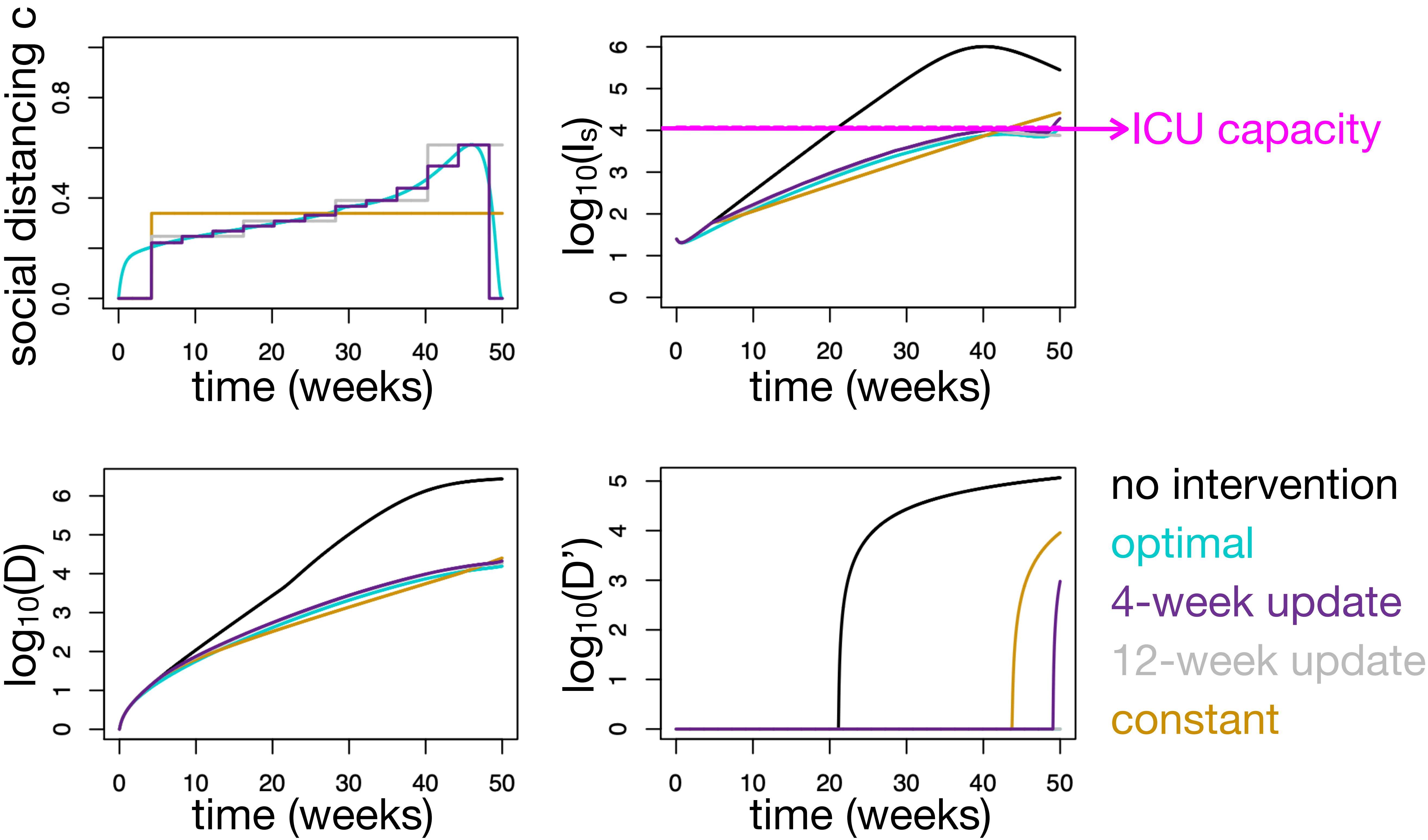
Submitted to *Math Model Nat Pheno*:

10.1101/2020.04.02.20049189

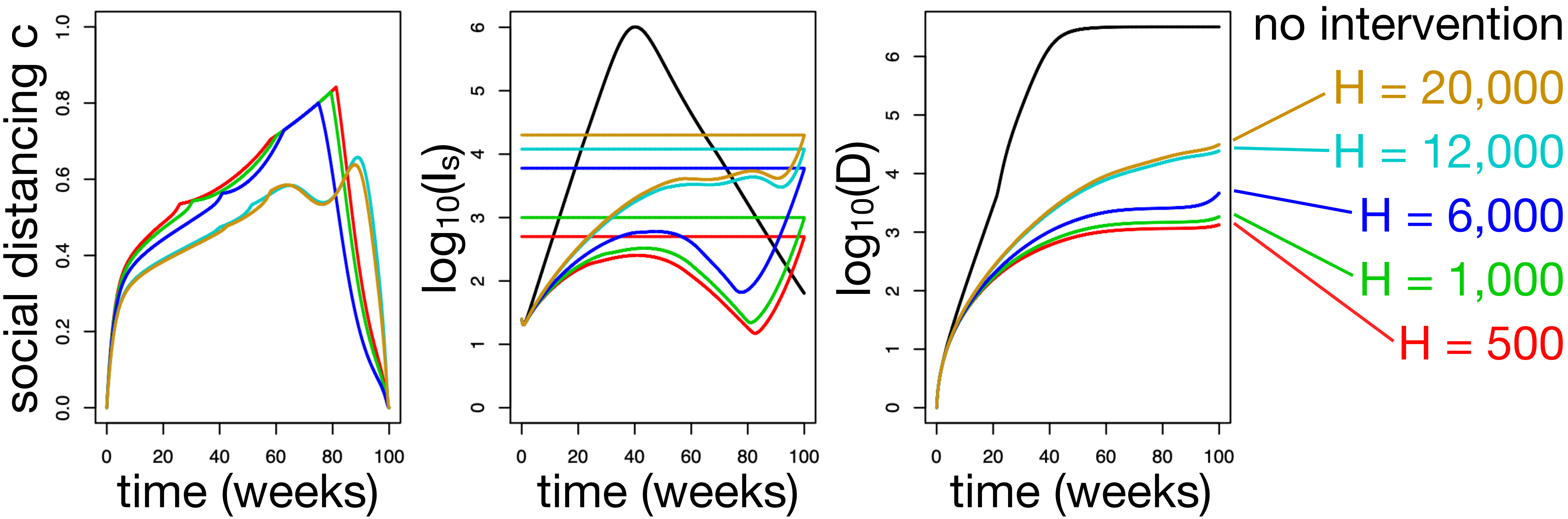
Time horizon: 100 weeks



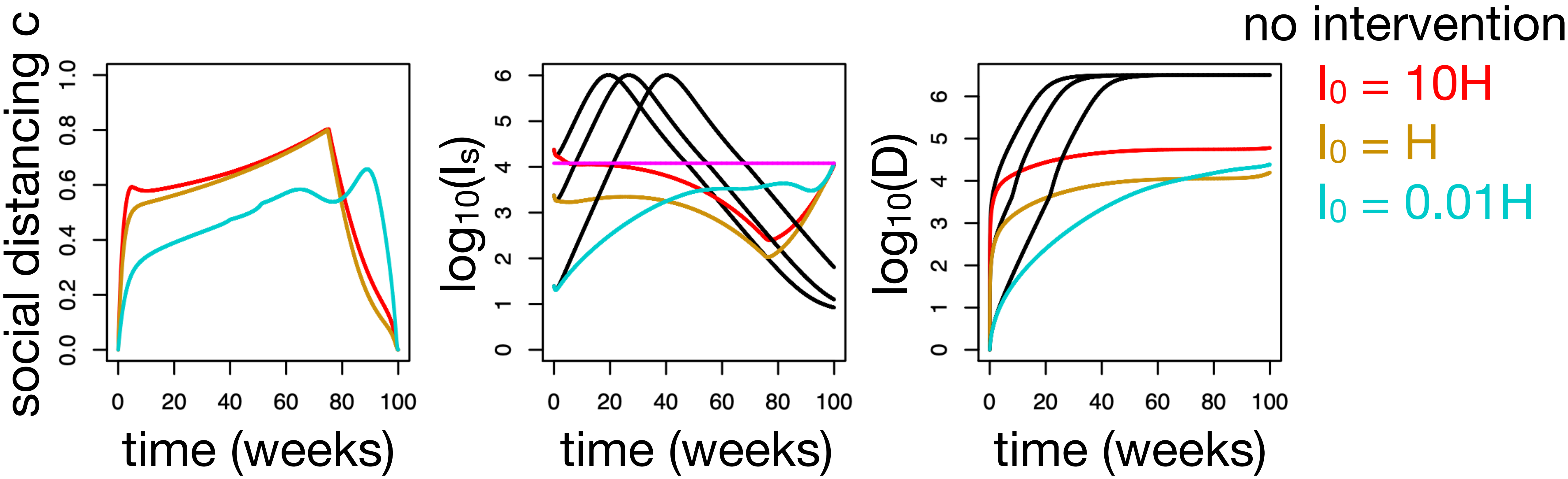
Time horizon: 50 weeks



Effect of ICU maximum capacity



Effect of initial outbreak size

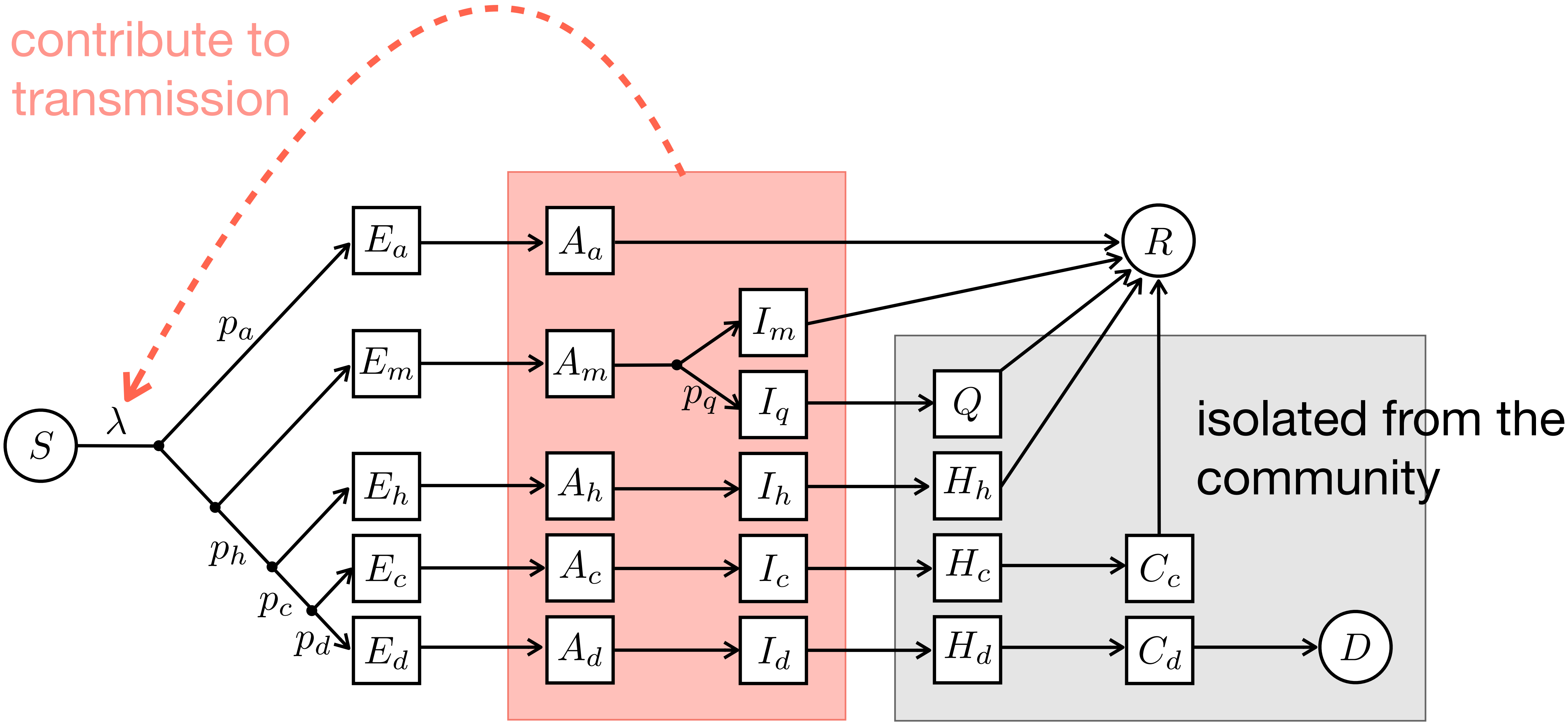


Host and infection age

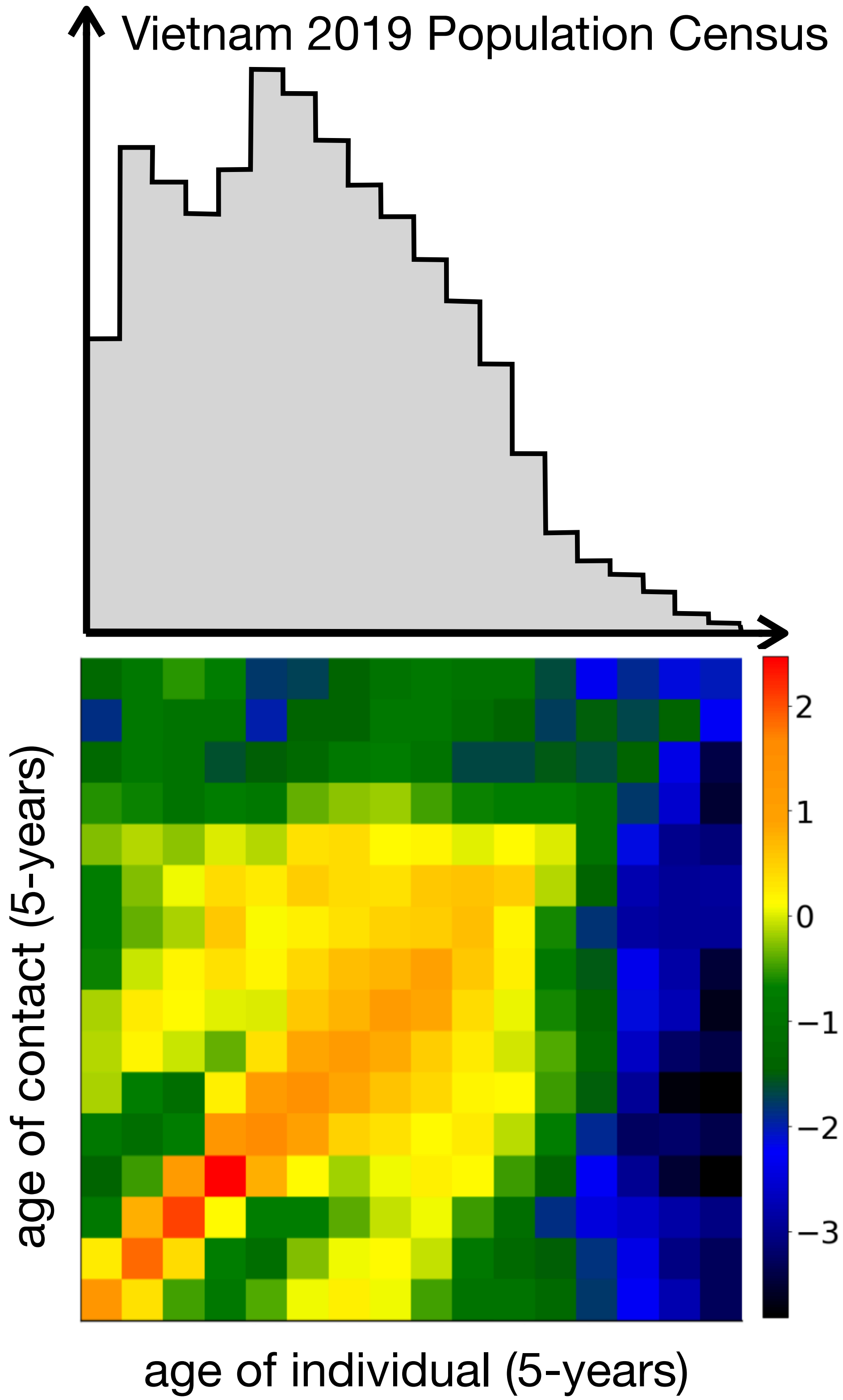
Accepted in *PLoS Comput Biol*:

10.1101/2020.06.23.20138099

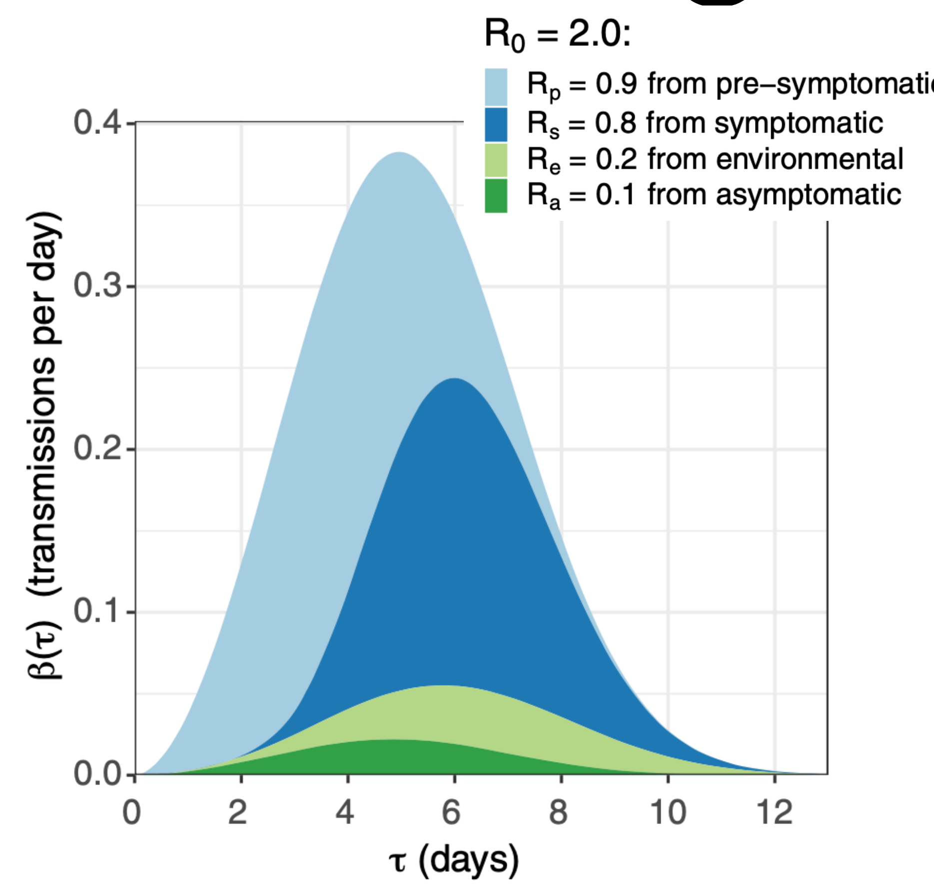
A COVID-19 model



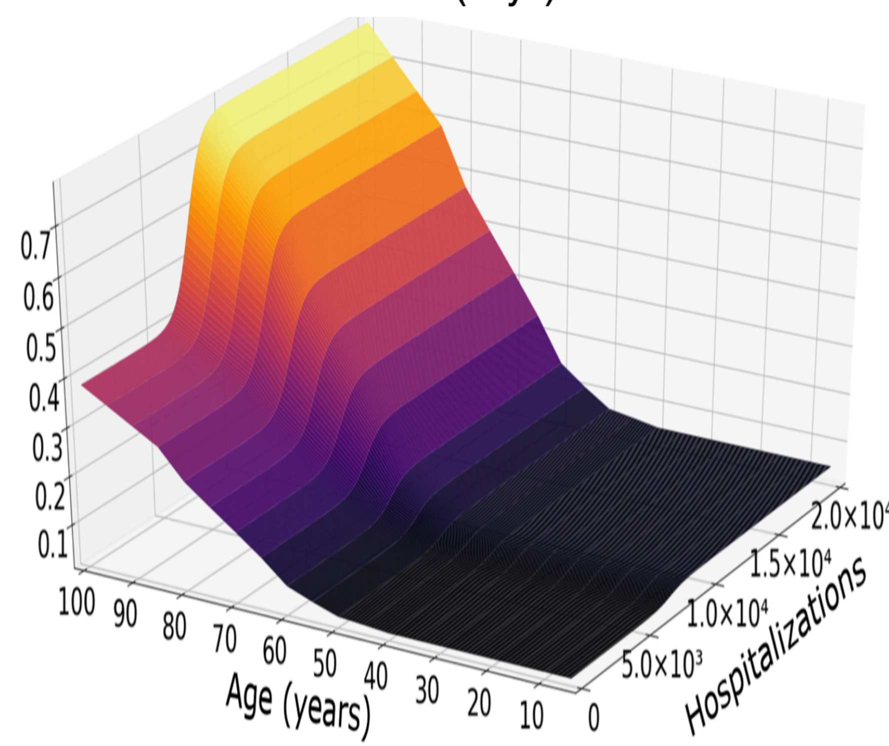
Adding host and infection ages



Prem et al. (2017) PLoS Comput Biol:
10.1371/journal.pcbi.1005697



Ferretti et al. (8 May 2020) Science:
10.1126/science.abb6936



Imperial College COVID-19 Response Team, Report 9
10.25561/77482

Force of infection

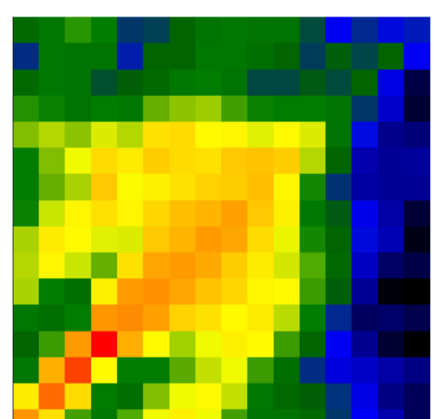
$$\lambda(t,c) = [1 - c(t)] \sum_i [\beta_i^a A_i(t) + \beta_i^s I_i(t)]$$

social distancing

asymptomatic

$$\lambda(t,a,c) = [1 - \boxed{c(t,a)}] \int_0^{a_x} \boxed{K(a,a')} \int_0^\infty \sum_i \boxed{[\beta_i^a(a',i)A_i(t,a',i)} + \boxed{\beta_i^s(a',i)I_i(t,a',i)]}\, \mathrm{d}i \mathrm{d}a'$$

contact rates



symptomatic

age of infection

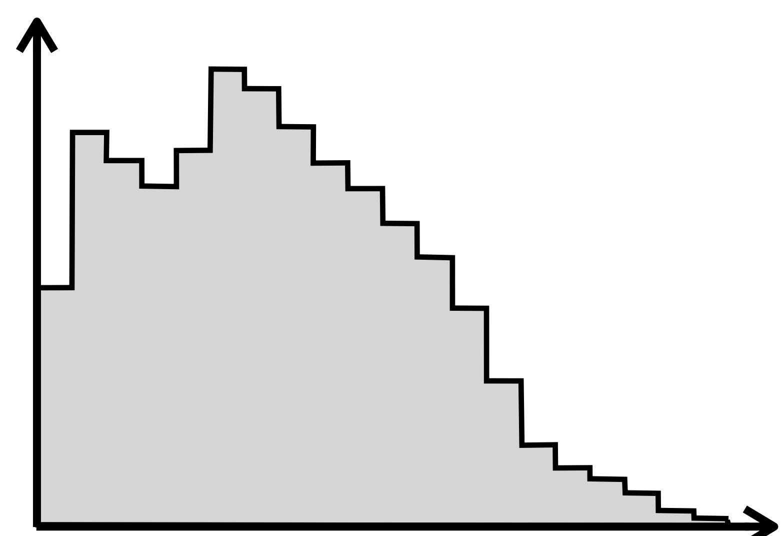
age of host

Objective function

$$M(c) = \int_0^T [D(t,c) + D'(t,c)]\mathrm{d}t + \int_0^T Bc^2(t)\mathrm{d}t$$

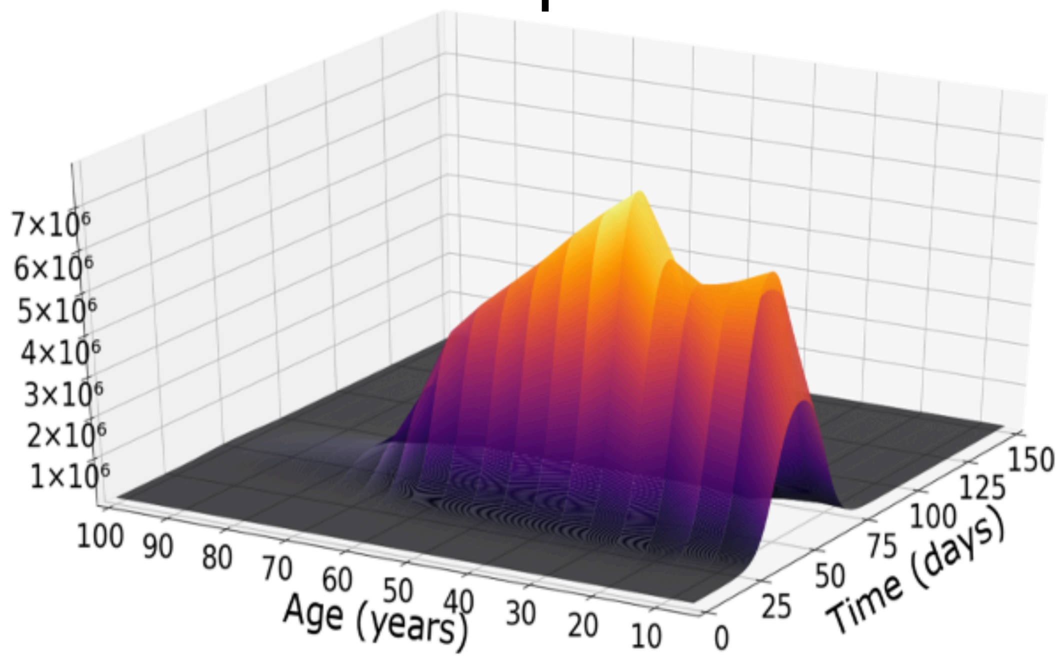
$$M(c) = \int_0^T [D(t,c) + D'(t,c)]\mathrm{d}t + \int_0^T \int_0^{a_x} B(a)c^2(t,a)\mathrm{d}a\mathrm{d}t$$

with $$B(a) = \frac{B^* S_0(a)}{\int_0^{a_x} S_0(u)\mathrm{d}u}$$

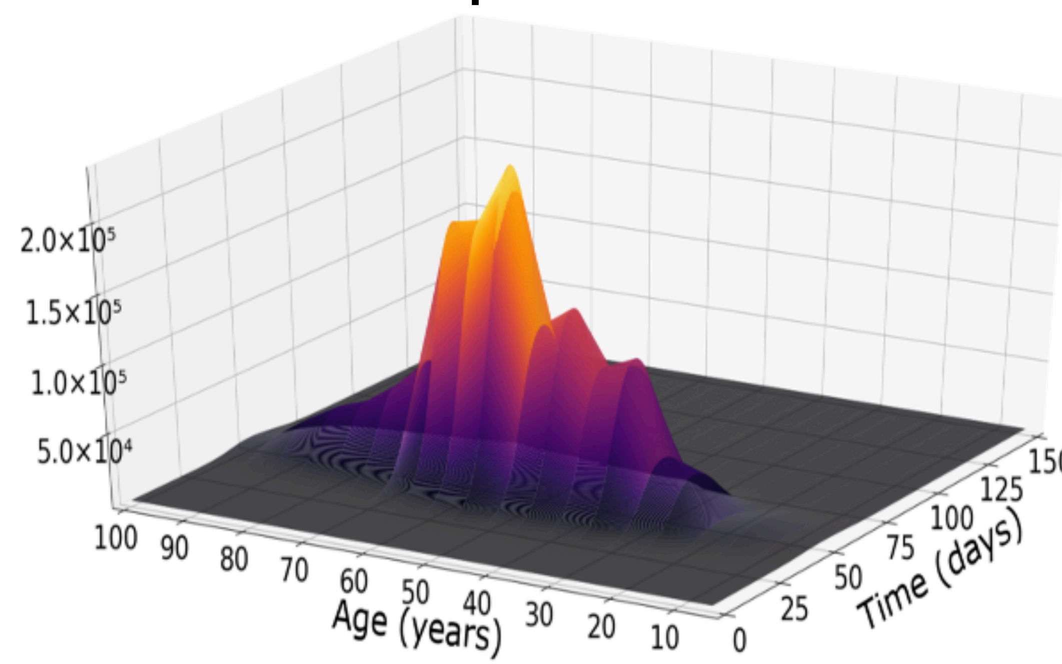


Dynamics without intervention

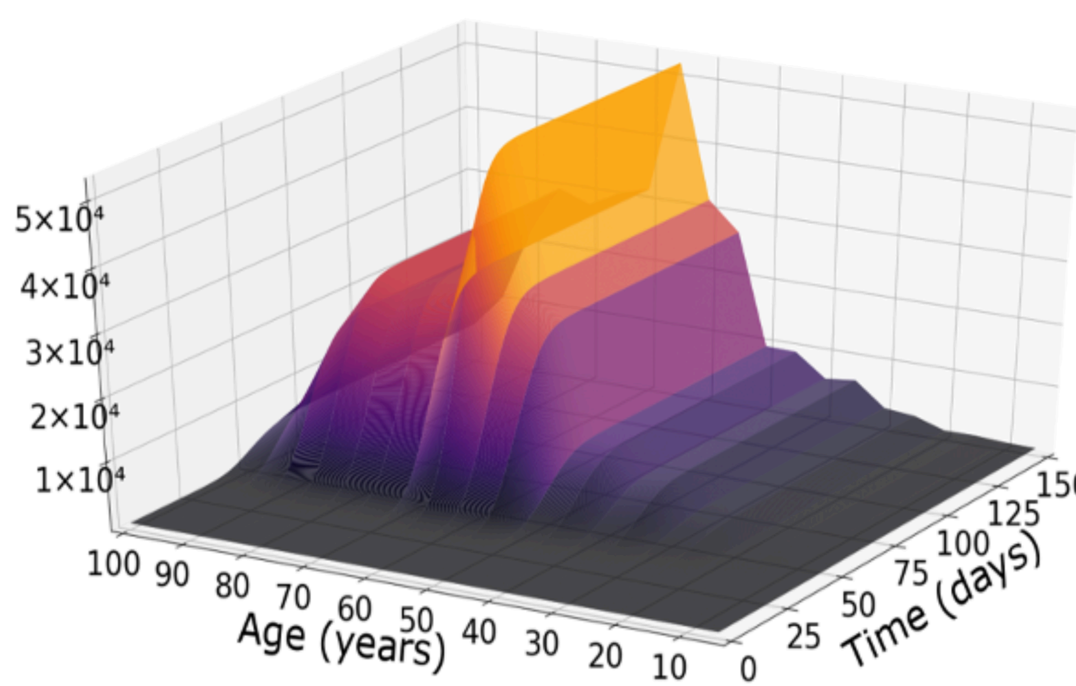
non-hospitalized



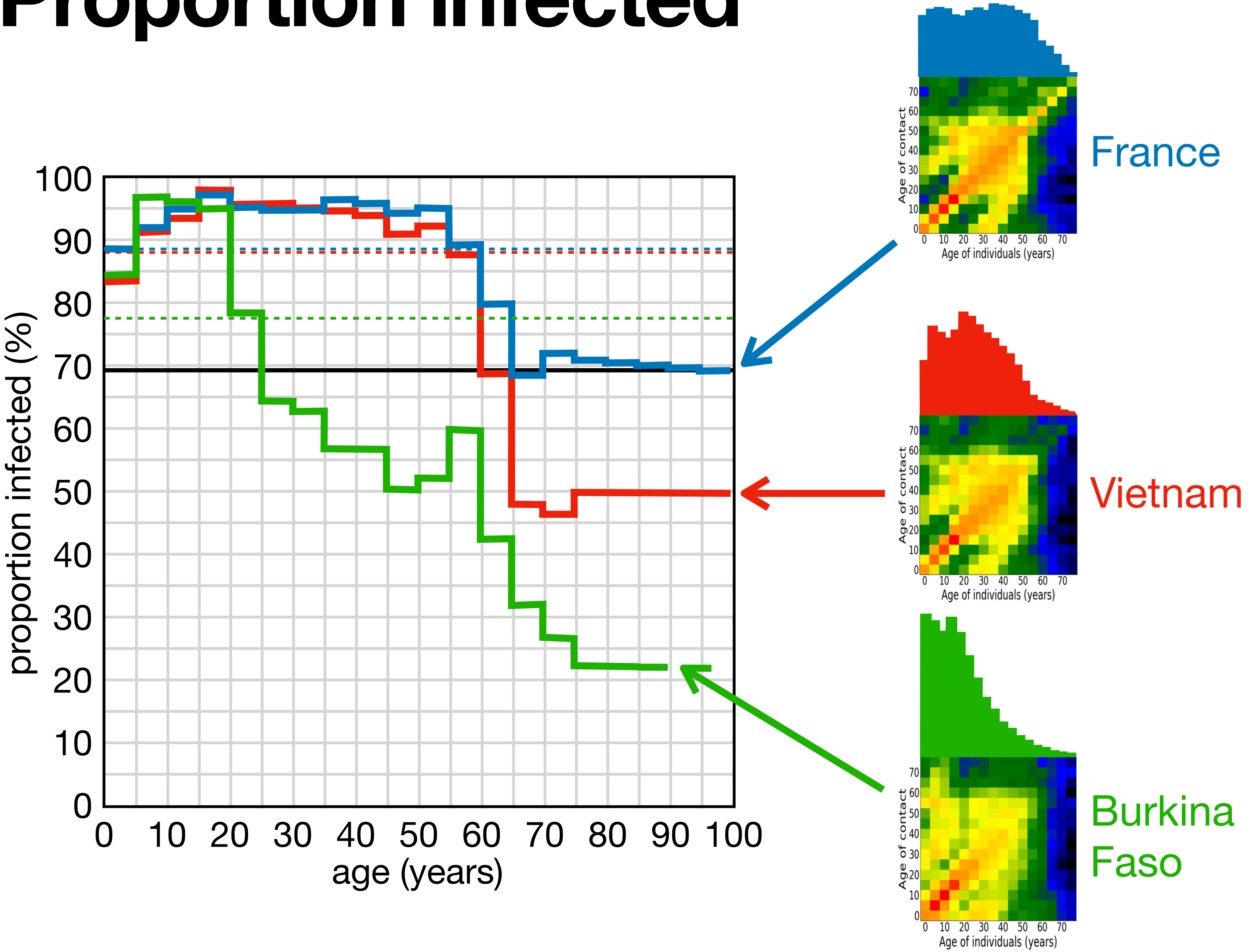
hospitalized



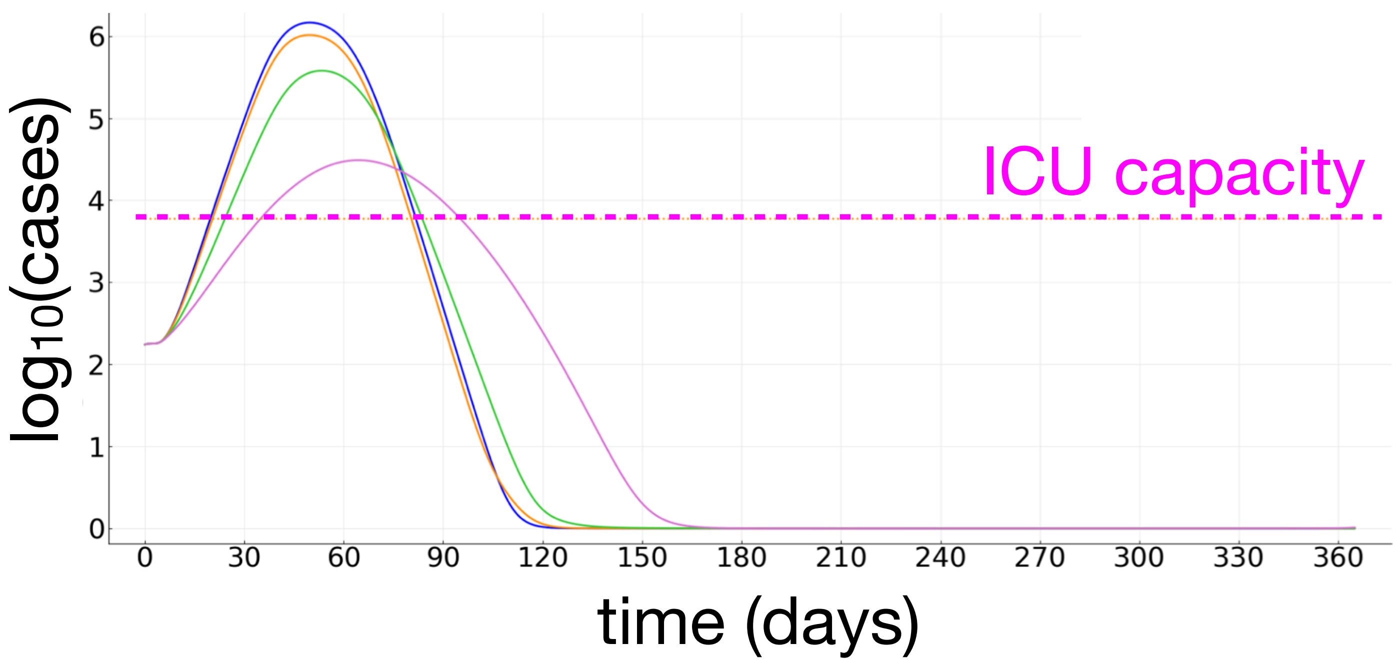
cumulative deaths

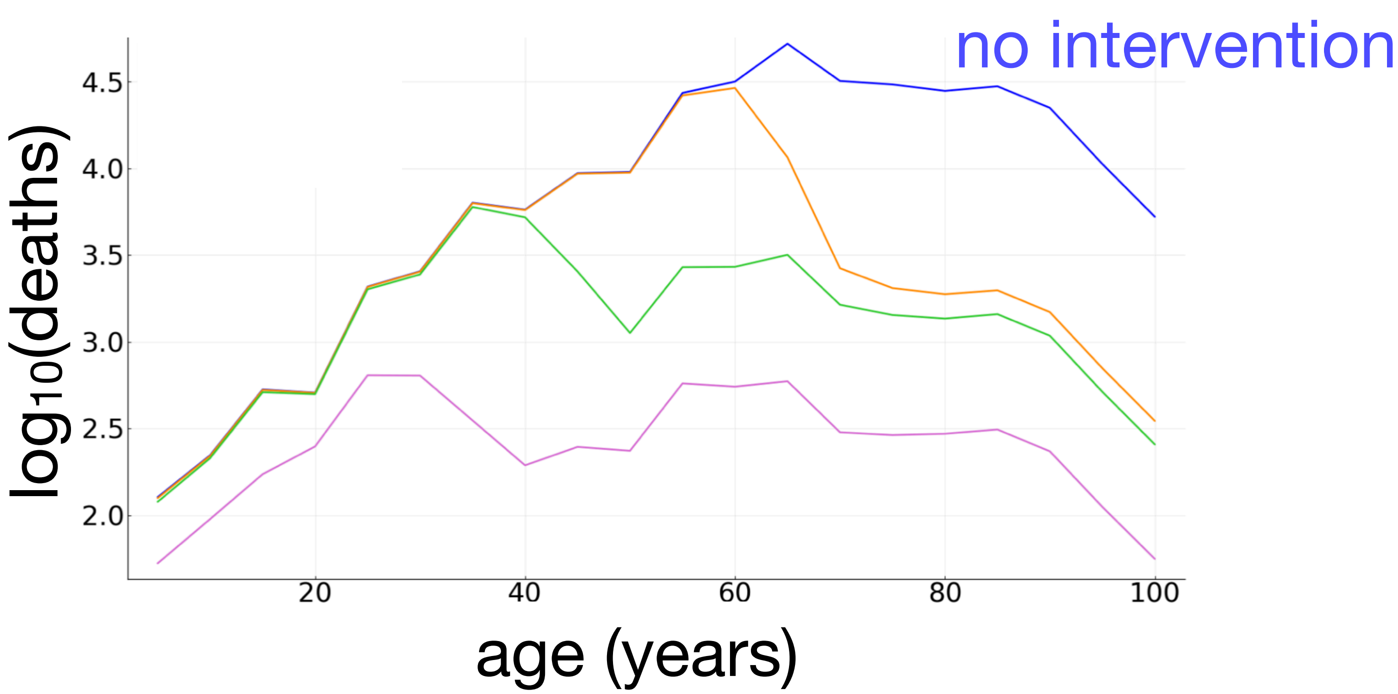


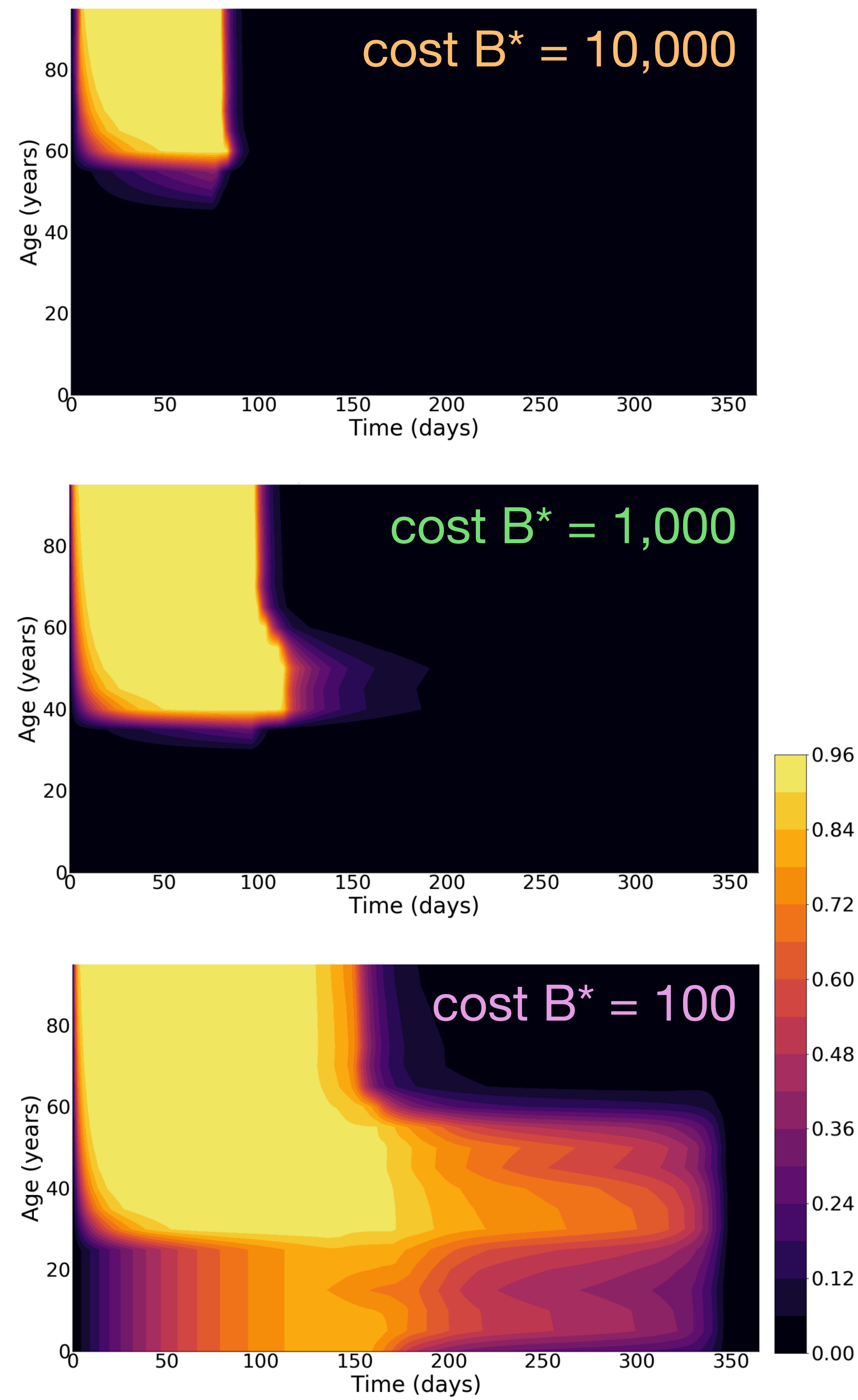
Proportion infected



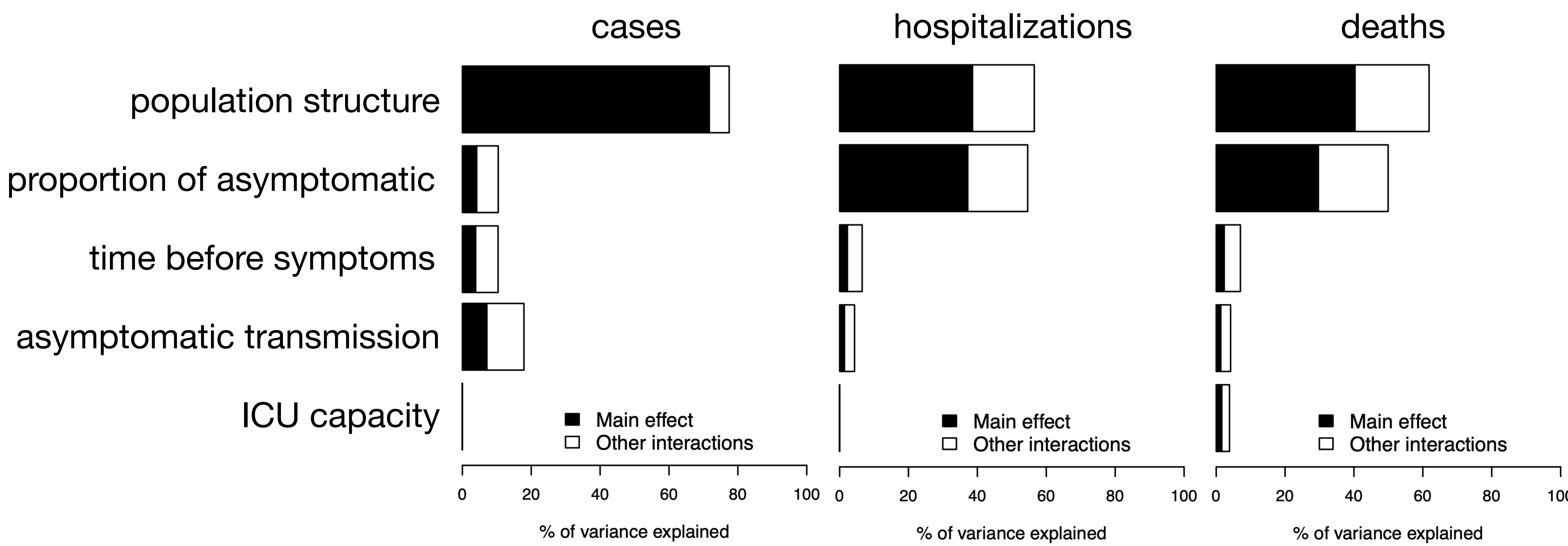
Optimal control







Model sensitivity



Space

Work in progress

Human mobility data

censuses and surveys
transport services
mobile phone providers
GPS devices
social media services

Differ respective to:

- spatial resolution and coverage
- temporal resolution and coverage
- population representativeness and coverage
- ease of use

Mobility inferences remain consistent across data sources (10.1371/journal.pone.0105184)

Facebook *data for good* project

- > 14 year-old
- registered to Facebook
- using the Facebook smartphone App
- location history and background location collection turned on
- no individual variables available (demographic, socio-economic)
- anonymized user ID

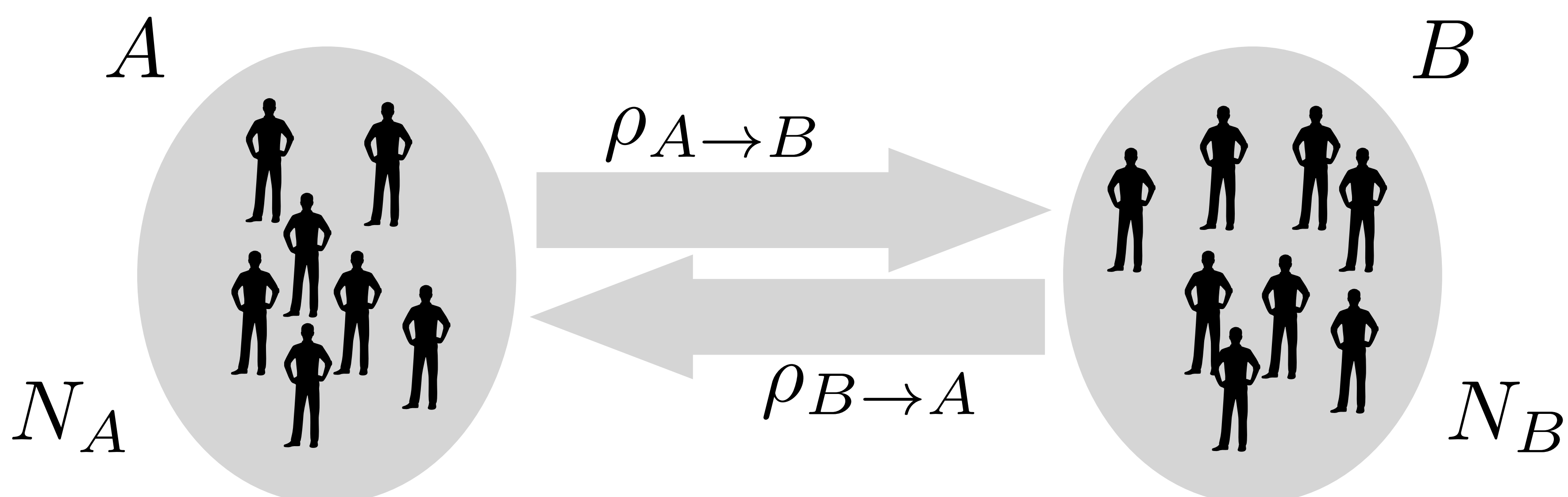
Low coverage of the total population: 10-20% max

Many biases: poorer and older are under-represented

Processed aggregated data sets

“Colocation” data

For meta-population analyses



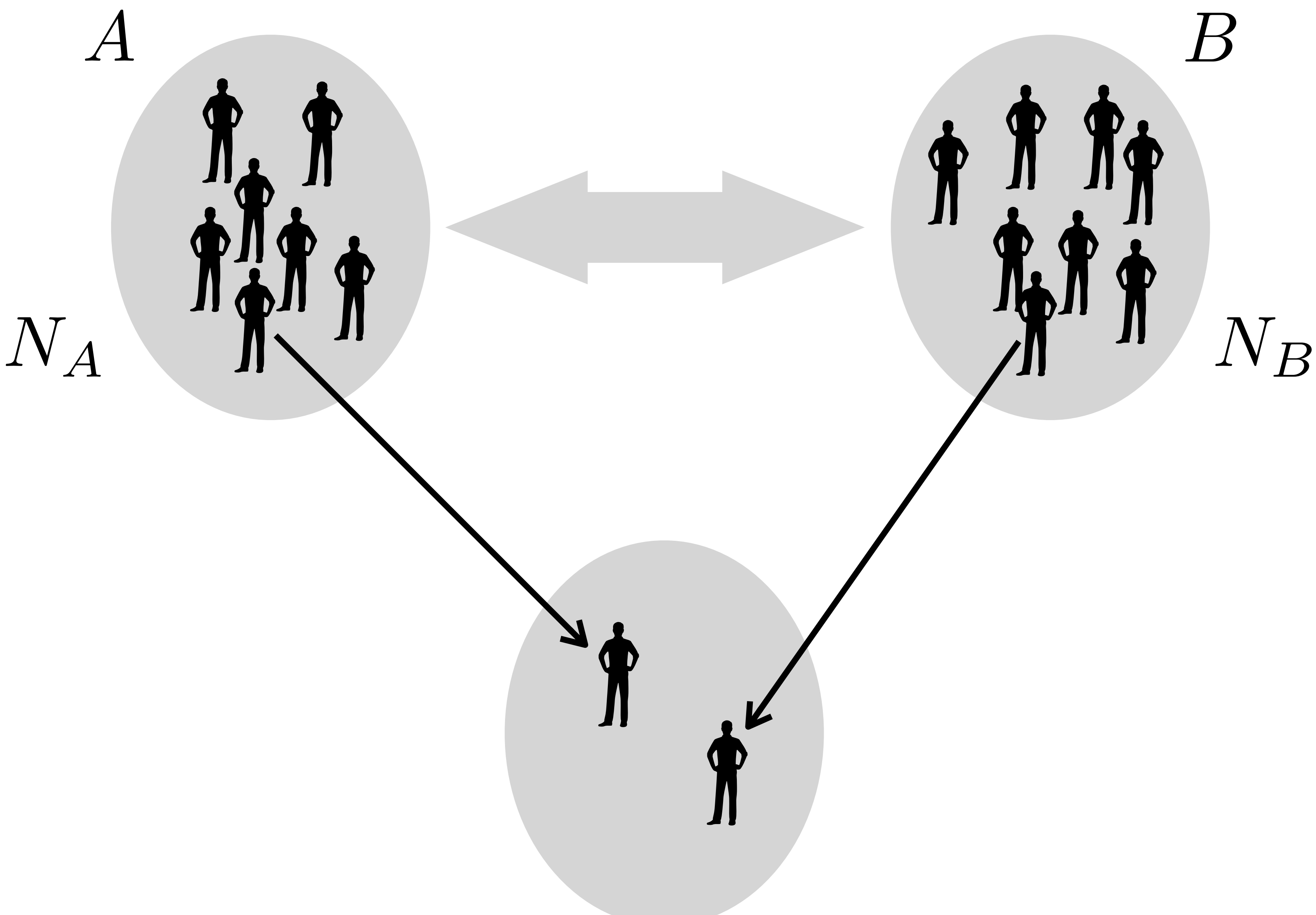
LETTERS

Aggregated mobility data could help fight COVID-19

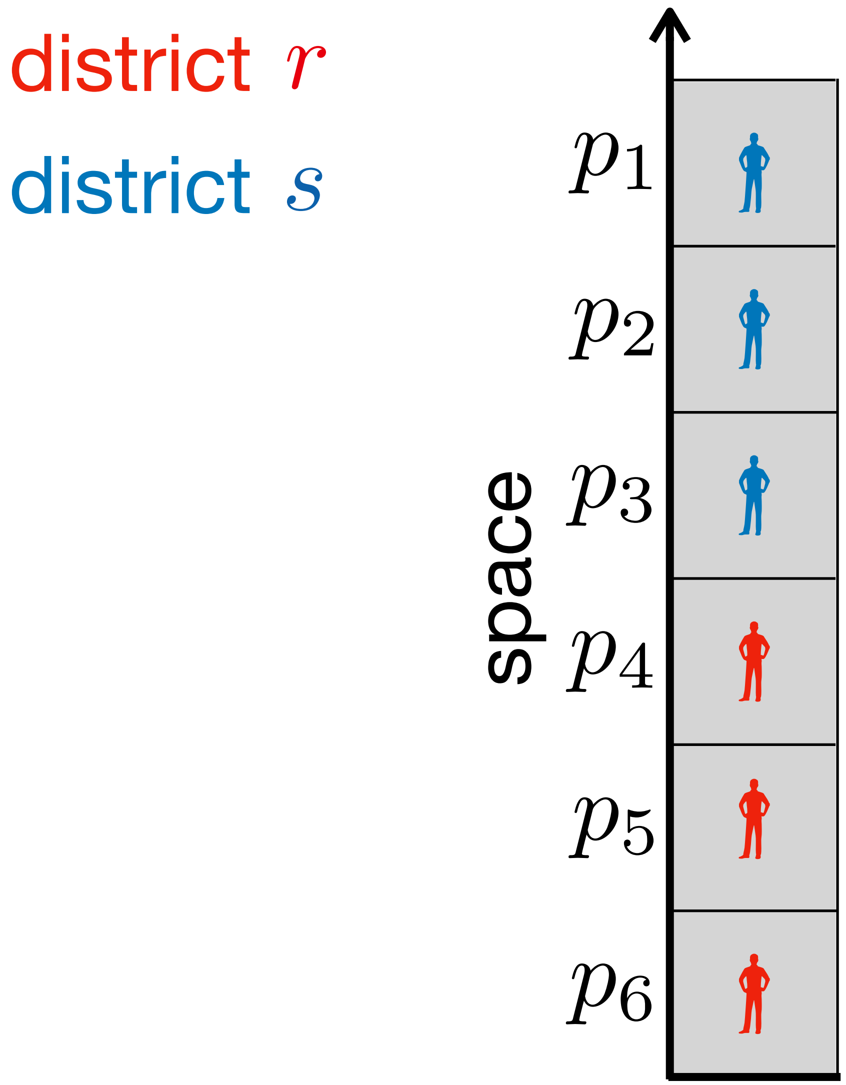
Caroline O. Buckee[1,*], Satchit Balsari[2], Jennifer Chan[3,4], Mercè Crosas[5], Francesca Dominici[6], Urs Gasser[7], Yonatan H. Grad[1], Bryan Grenfell[8], M. Elizabeth Halloran[9,10], Moritz U. G. Kraemer[11,12], Marc Lipsitch[1], C. Jessica E. Metcalf[8], Lauren Ancel Meyers[13], T. Alex Perkins[14], Mauricio Santillana[15,12], Samuel V. Scarpino[16], Cecile Viboud[17], Amy Wesolowski[18], Andrew Schroeder[19]

Science, 10 Apr 2020, Vol. 368, Issue 6487, pp. 145-146 DOI: 10.1126/science.abb8021

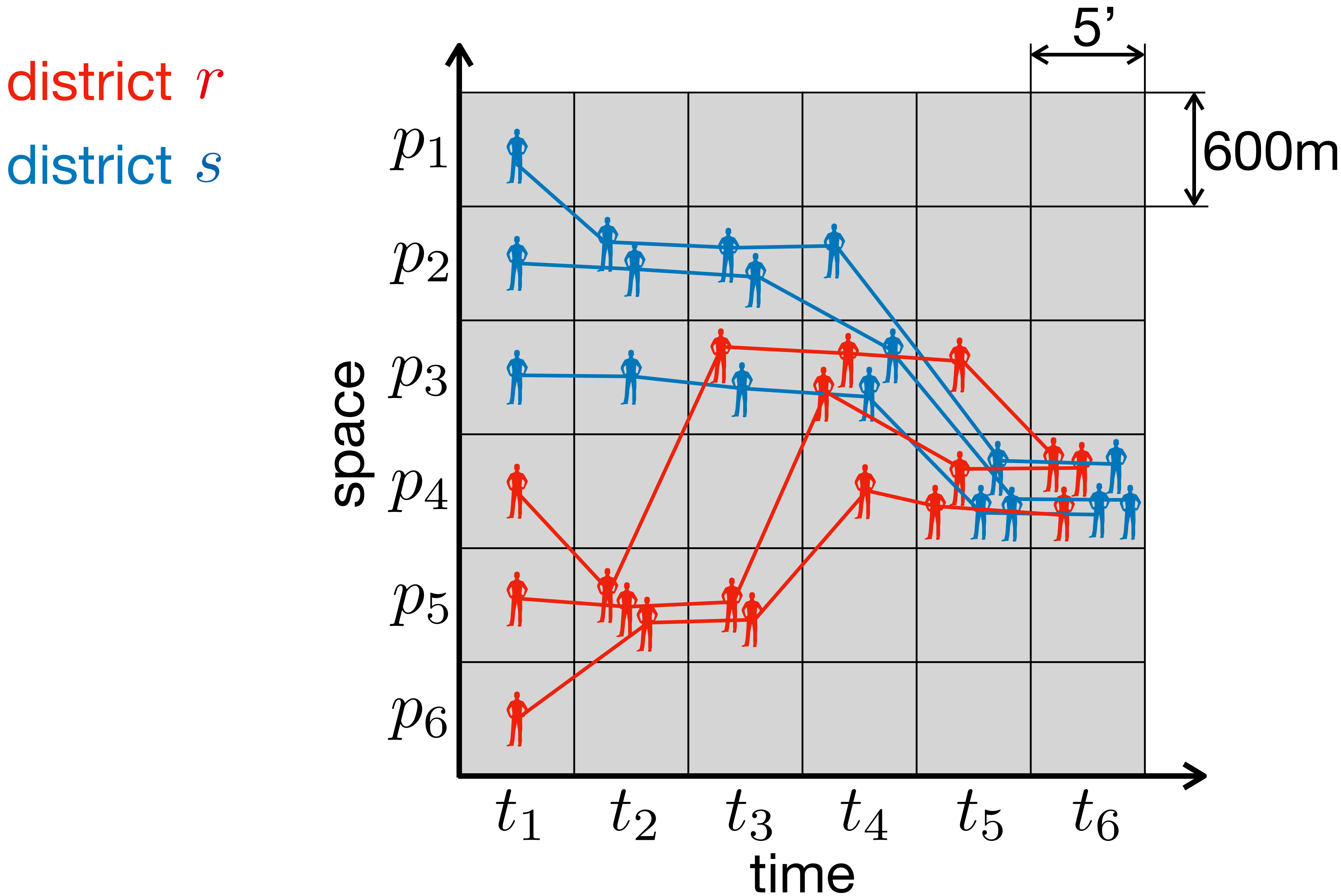
Colocation ≠ movement



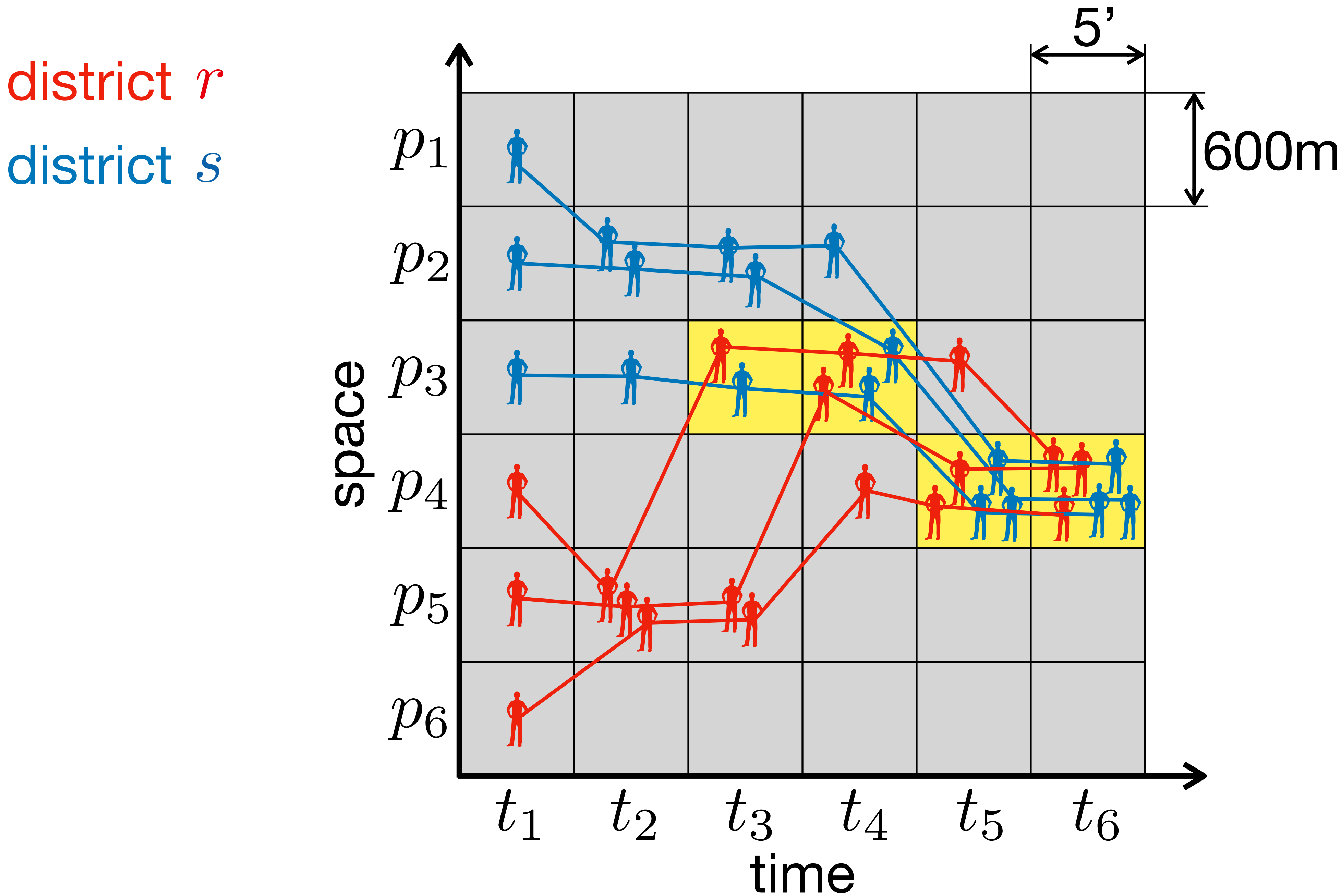
Number of weekly colocations



Number of weekly colocations



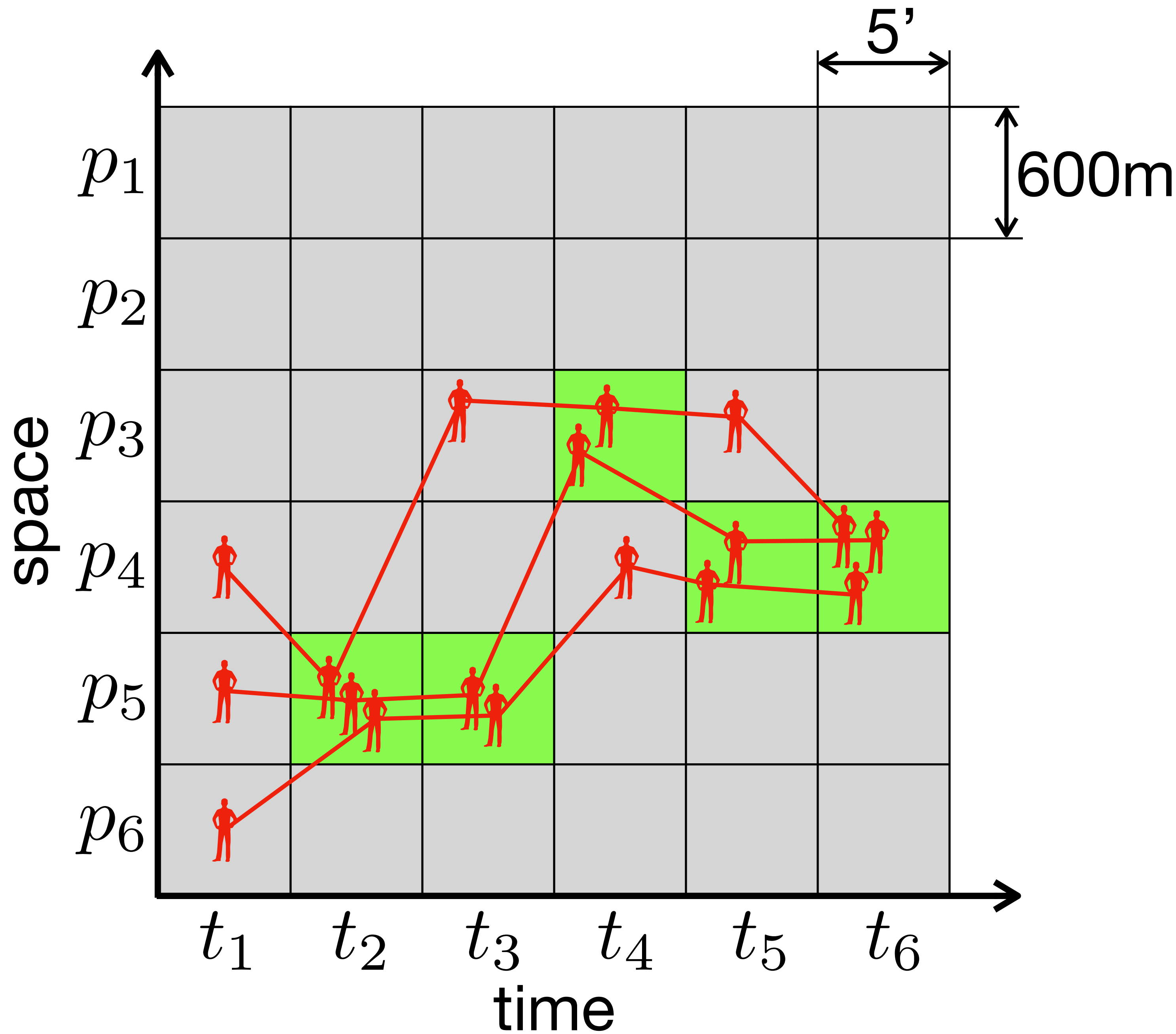
Number of weekly colocations



$$m_{rs} = \sum_{ij} X_{ijr} X_{ijs} = 1 \times 1 + 2 \times 2 + 2 \times 3 + 3 \times 3 = 20$$

Number of weekly colocations

district r



$$m_{rs} = \sum_{ij} X_{ijr}(X_{ijr} - 1) = 3 \times 2 + 2 \times 1 + 2 \times 1 + 2 \times 1 + 3 \times 2 = 18$$

Weekly probability of colocation

total number of realized colocations

$$p_{rs} = \frac{m_{rs}}{2016 \times n_r n_s}$$

maximum possible total number of colocations

7 days / 5'

$$p_{ss} = \frac{m_{ss}}{2016 \times n_s(n_s - 1)}$$

Colocation data

Spatial unit: district (698 in Vietnam)

Time unit: week

Colocation inferred using pixel of **600m** and time intervals of **5'**

Residency on week w inferred from
consistent location at night on week w - 1

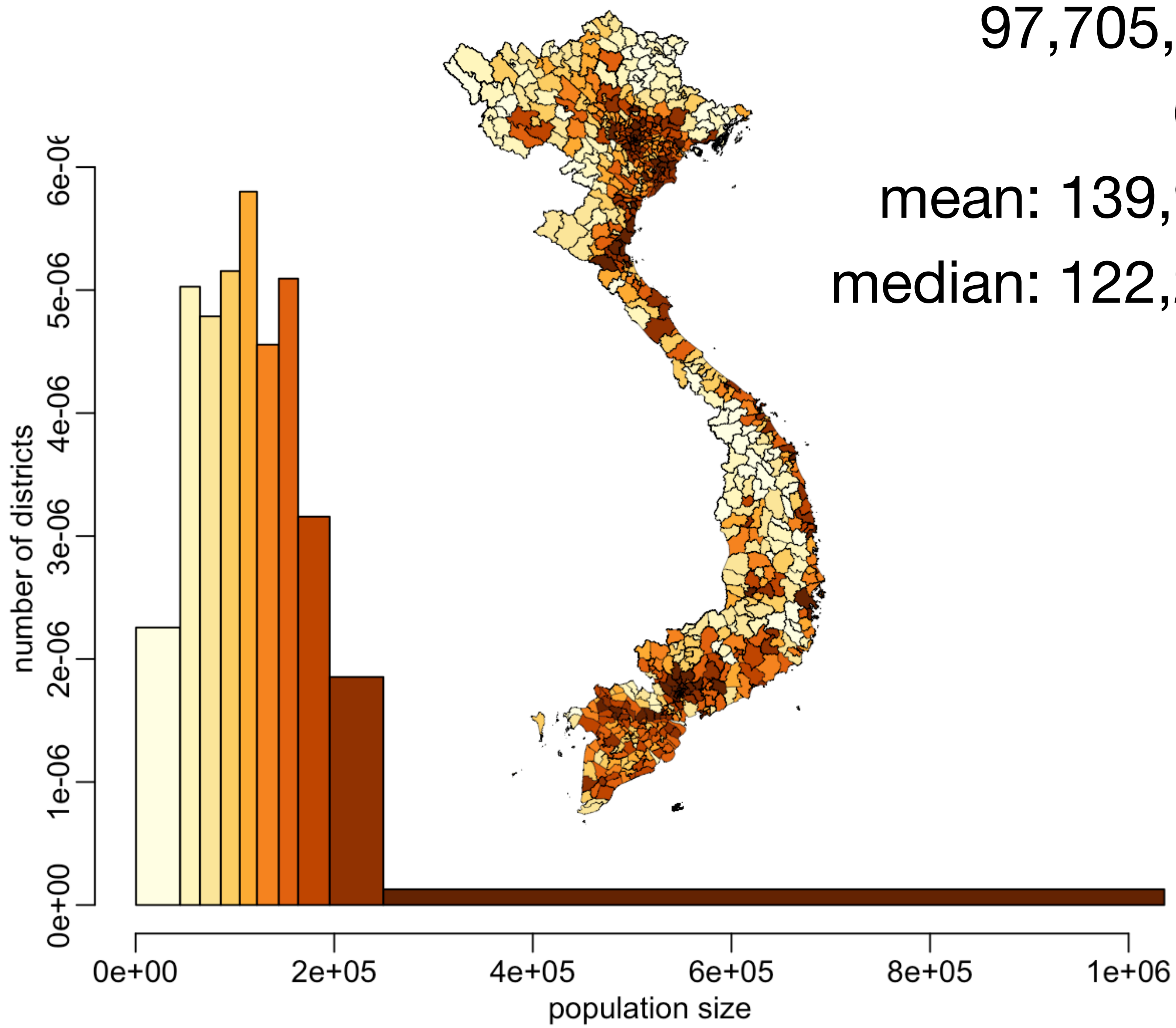
Vietnam 2019 population census

97,705,091 people

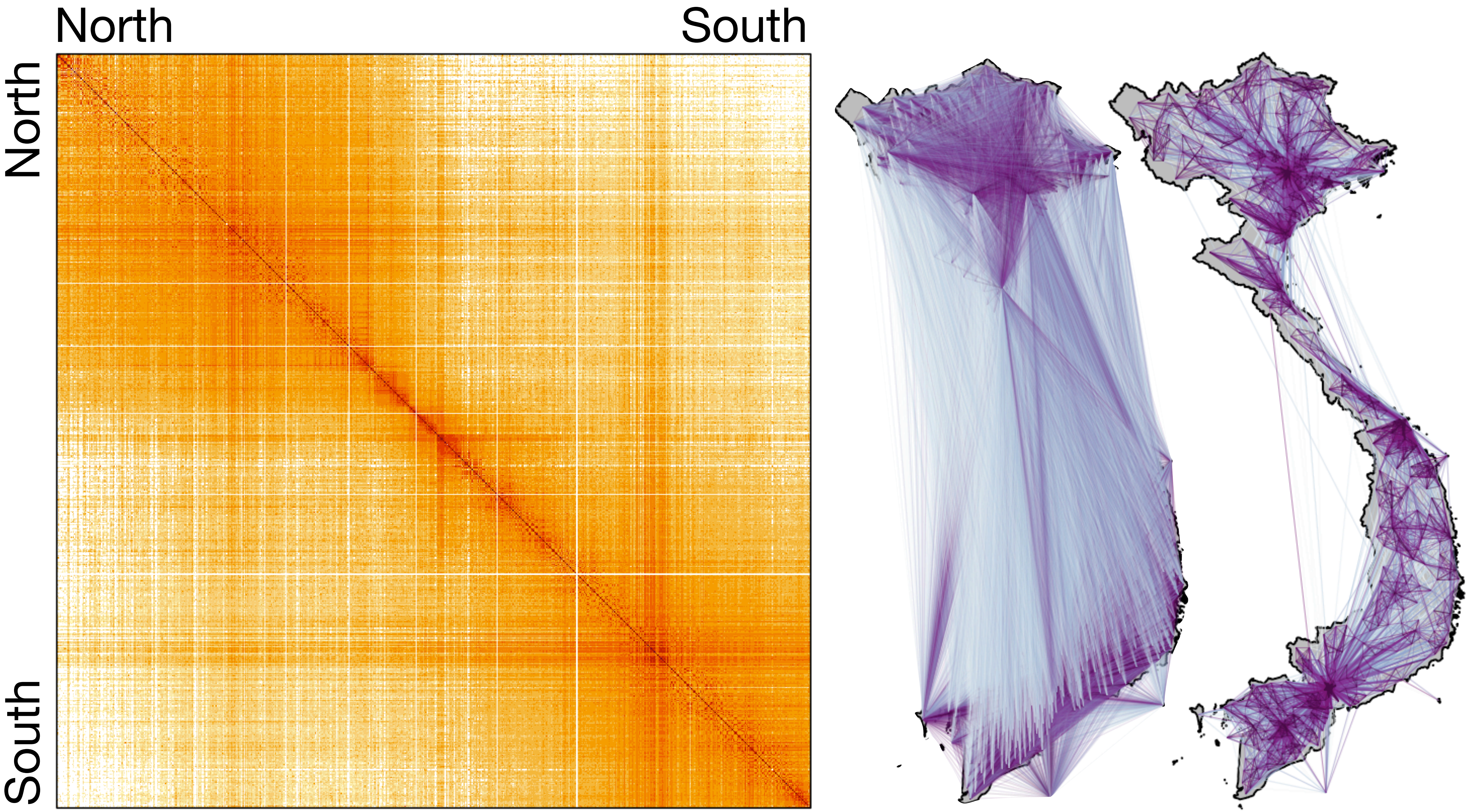
698 districts

mean: 139,979

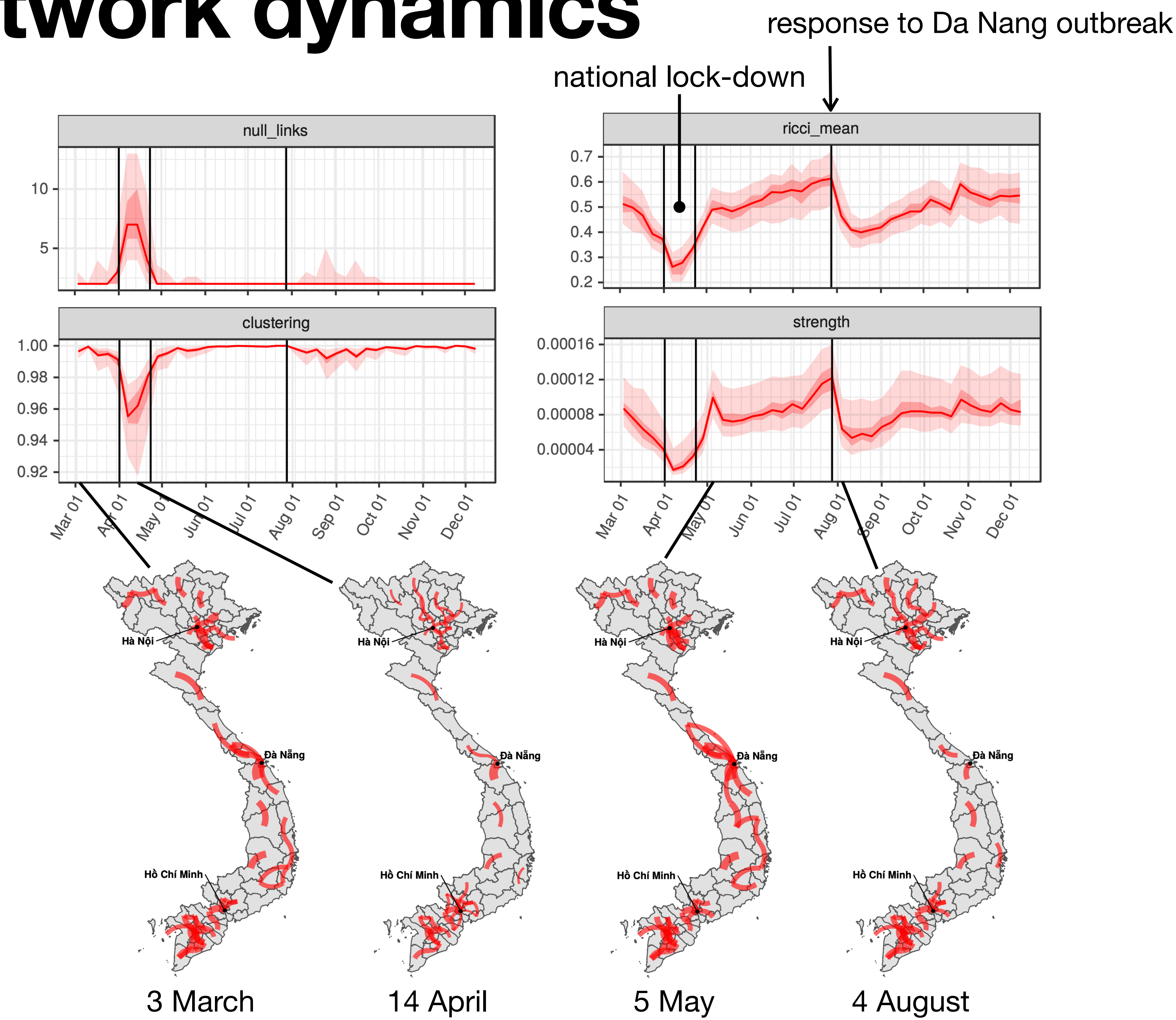
median: 122,217



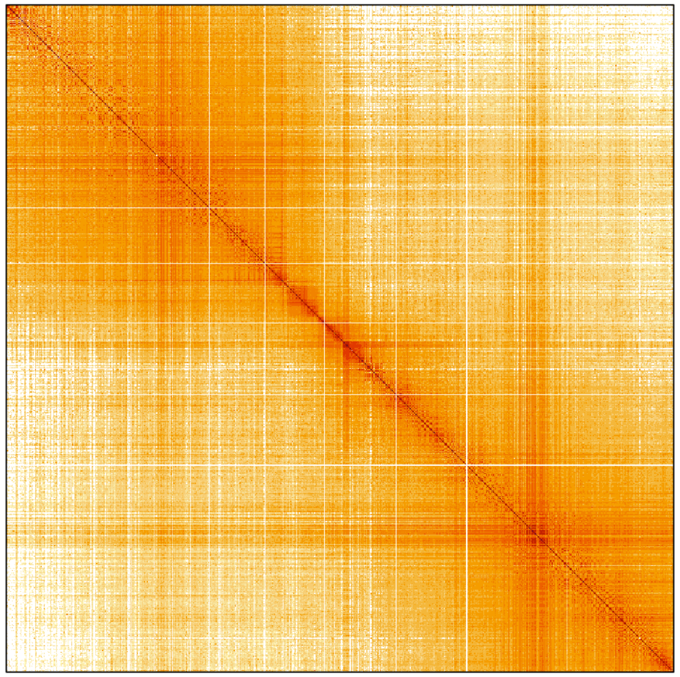
Average colocation Vietnam 2020



Network dynamics



Force of infection



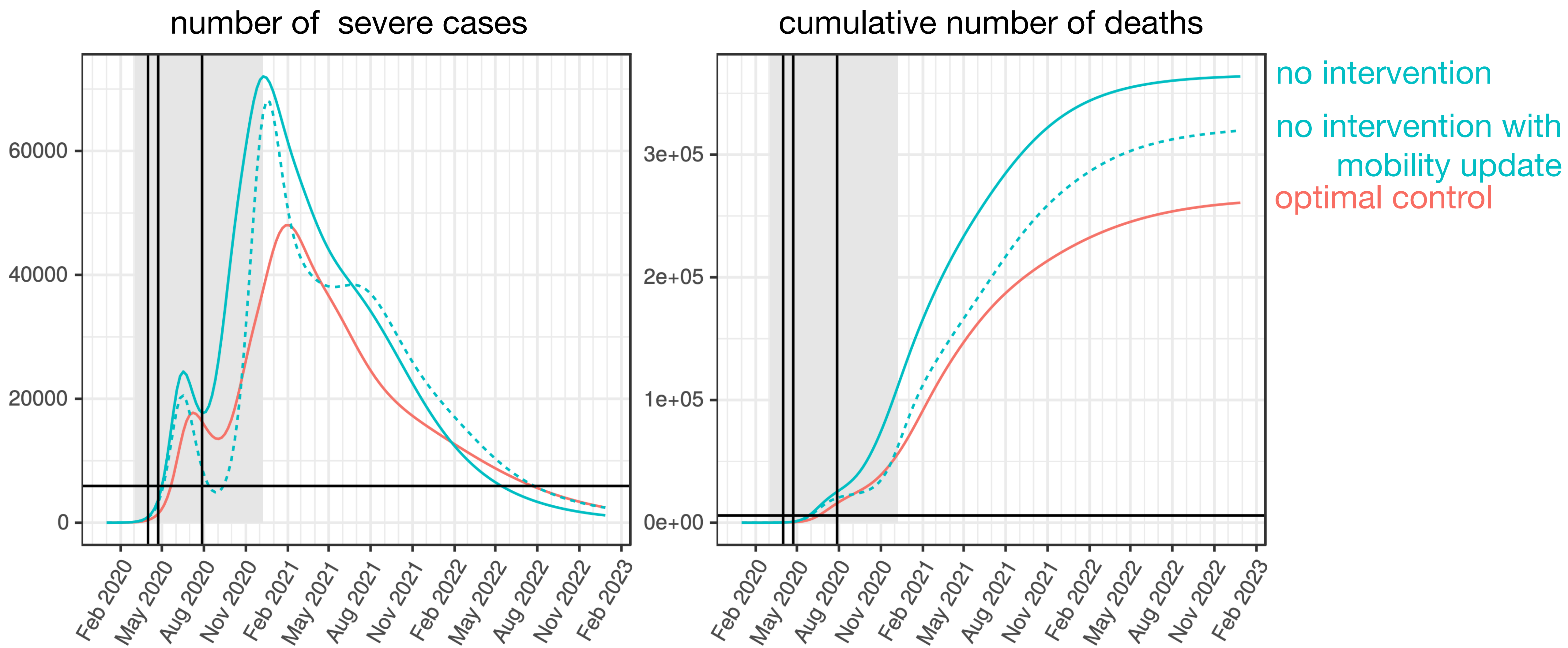
$$\lambda(t, c^b, c^w) = \sum_k \left[(1 - c^b(t)) \sum_{j \neq i} \left[\beta^a_{j,k} A_{j,k}(t) + \beta^s_{j,k} I_{j,k}(t) \right] Kij(t) + \right.$$

$$\left. (1 - c^w(t)) \left[\beta^a_{i,k} A_{i,k}(t) + \beta^s_{i,k} I_{i,k}(t) \right] Kii(t) \right]$$

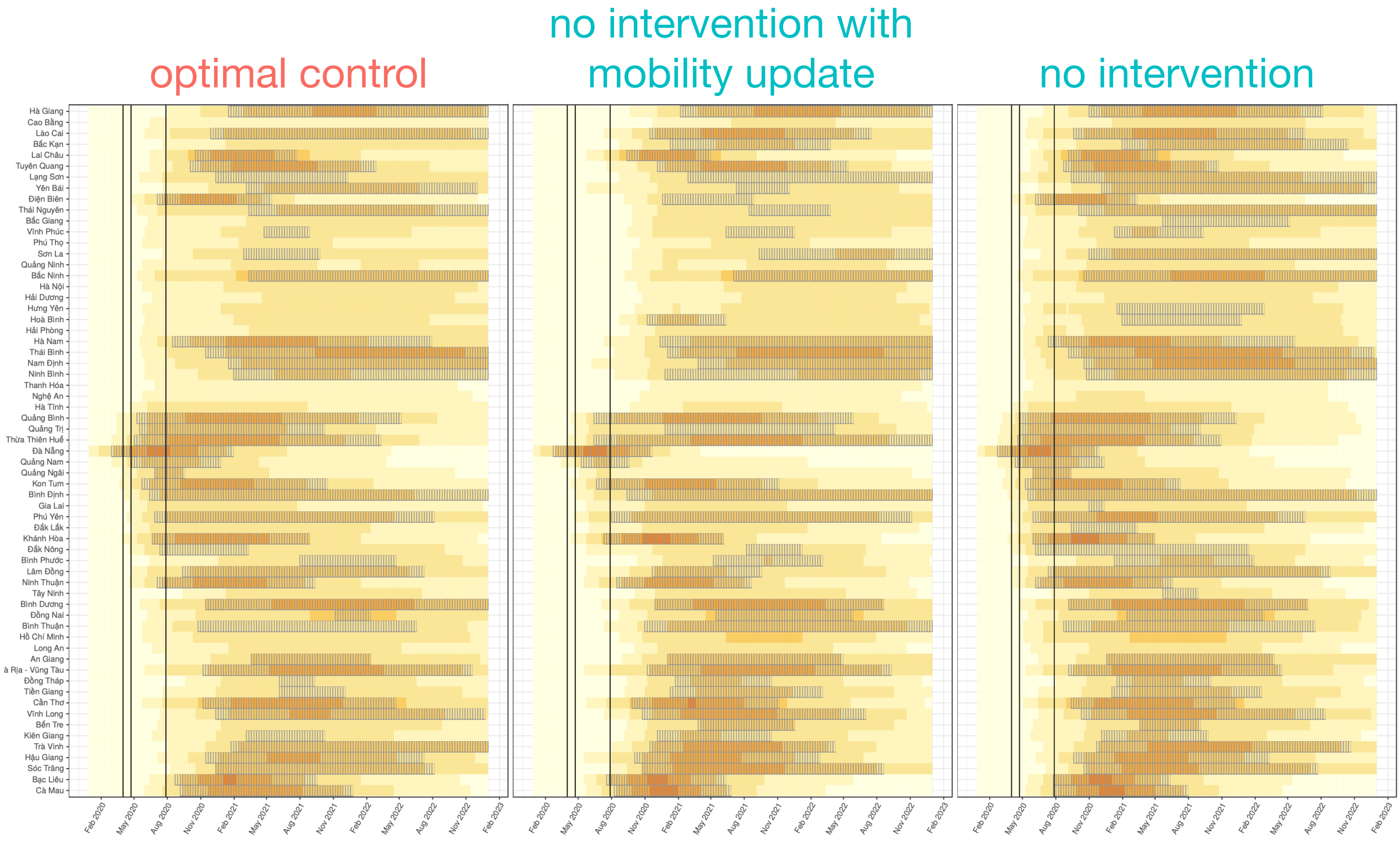
Objective function

$$M(c^b, c^w) = \int_0^T (D(t) + D'(t))\mathrm{d}t + \sum_k \left[B_k^b \int_0^T {c^b}^2(t)\mathrm{d}t + B_k^w \int_0^T {c^w}^2(t)\mathrm{d}t \right]$$

Optimal control



Optimal control



Conclusions

Take-home points

Optimal Control Theory:

- under-used in epidemiology
- potentially very powerful
- practicability not always obvious
- lack of data on the cost function

Emerging infection:

- importance of dynamic modelling

Acknowledgements

Ramsès Djidjou-Demasse (optimal control theory)
Quentin Richard (ages)
Christian Selinger (space)
Pham Quang Thai (NIHE)
Nguyen Cong Khan (NIHE)

The OUCRU COVID-19 Modelling Team
The OUCRU IT