

The spatio-temporal spread of infectious pathogens: lessons learned from COVID-19

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Thank you

for receiving me in your homes/offices and to ..

- many people over the years, including most recently
 - Pierre-Yves Boëlle (IPLESP, Sorbonne Université, Paris)
 - Evan Milliken (University of Louisville)
 - Stéphanie Portet (U of M)
- based also on earlier work with Nicolas Bajeux, S. Portet and James Watmough
- PHAC external modelling group members for discussions

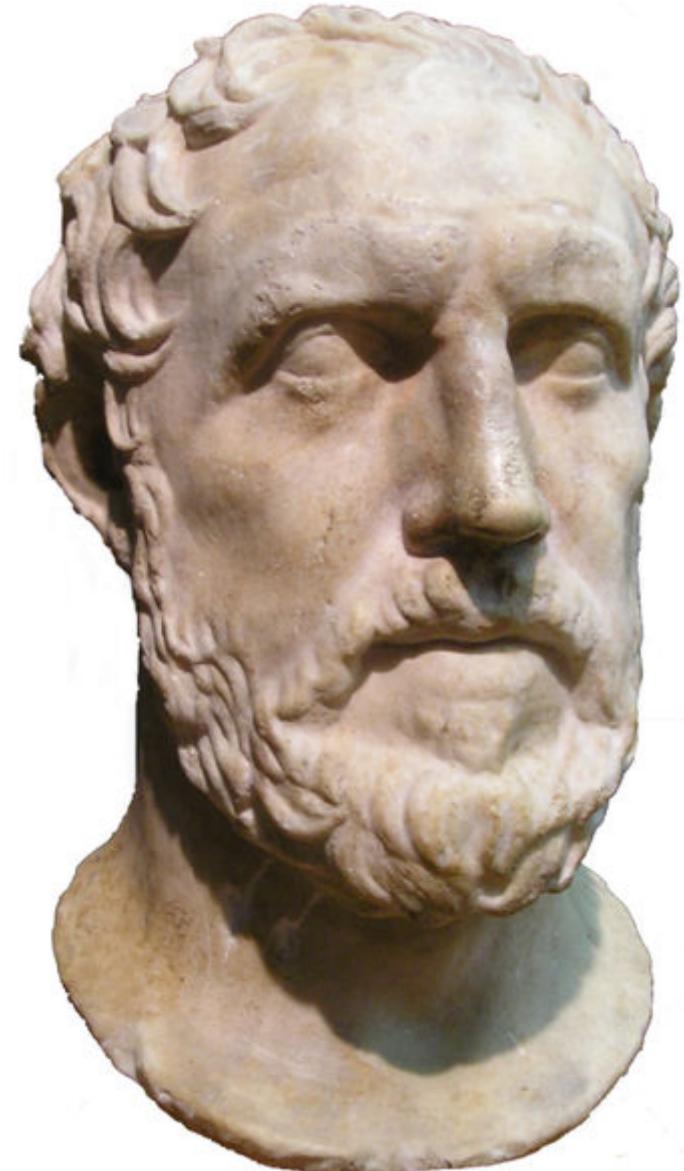
Funding NSERC and CIHR

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Pathogens have been mobile for a while

It first began, it is said, in the parts of Ethiopia above Egypt, and thence descended into Egypt and Libya and into most of the [Persian] King's country. Suddenly falling upon Athens, it first attacked the population in Piraeus [...] and afterwards appeared in the upper city, when the deaths became much more frequent.

Thucydides (c. 460 BCE - c. 395 BCE)
History of the Peloponnesian War



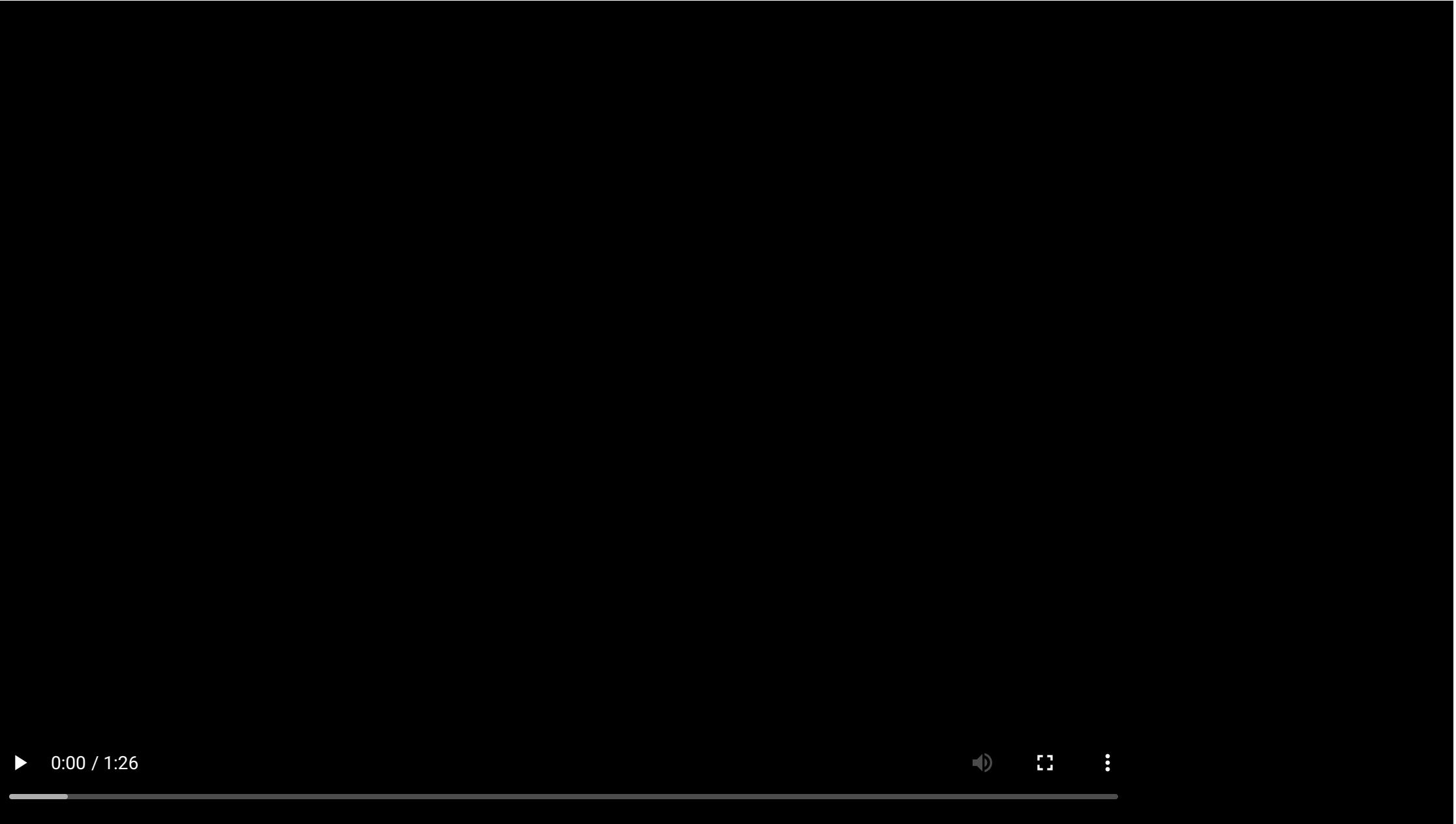
Outline

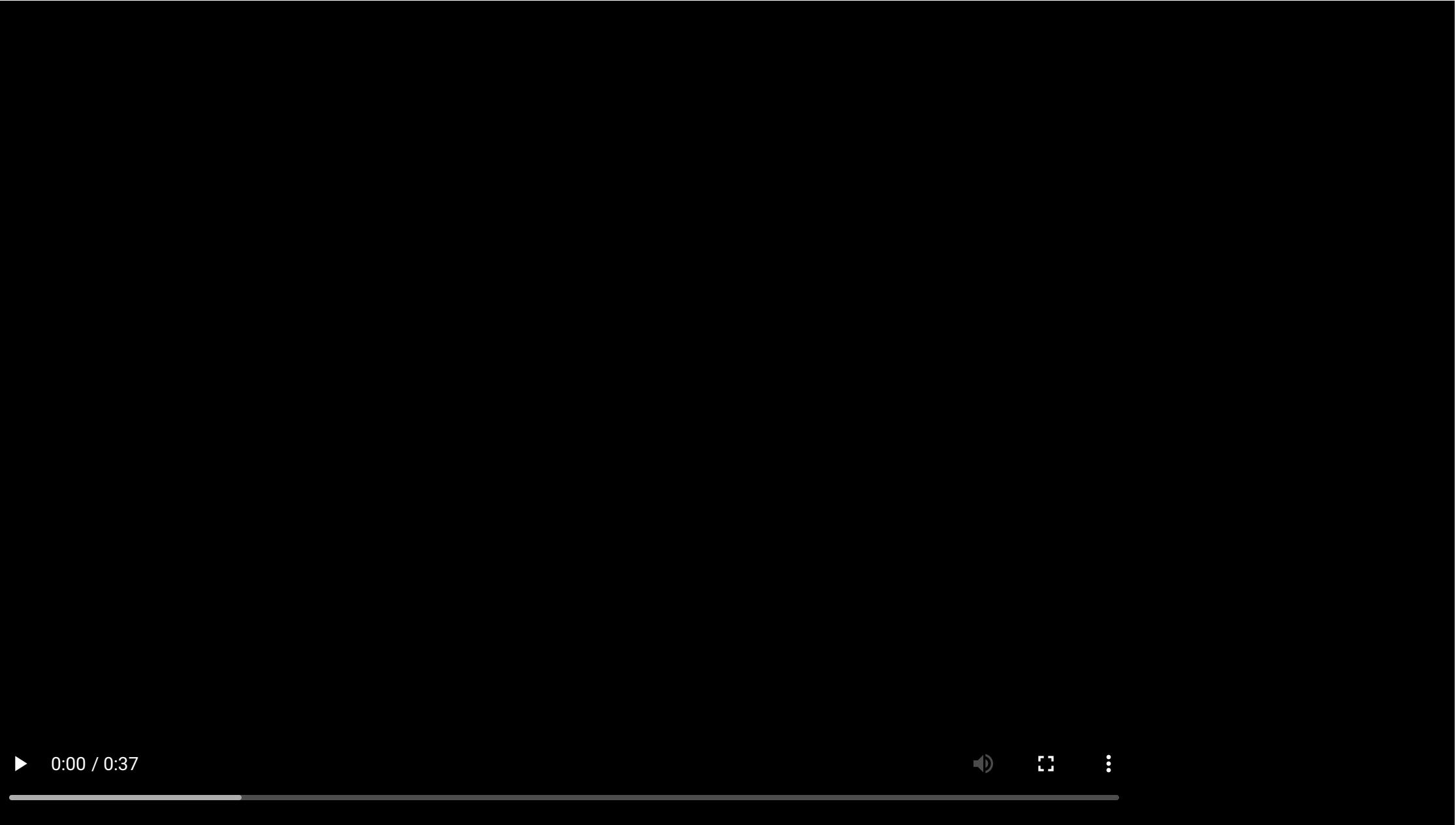
- Movement and the spatialisation of an epidemic
- The initial spread of COVID-19
- Role of transport restrictions
- Role of quarantine

Movement and the spatialisation of an epidemic

Following 2 slides

- S (blue), I (red), R (green) model
- Individuals spatially located
- Interaction radius to model local movement
- When contacts occur, each contact is infecting with indicated $\mathbb{P}.$ so binomial
- Infecting contact to an R is "lost"
 - First slide: fixed infectious period of 5 days
 - Second slide: infectious period in $\mathcal{U}(3, 10)$ days





This is good for diseases of (not winged) animals

- Range is typically not huge
- Disease moving between species see patchiness of the support bridged by variety of ranges in the different species

1990



2000



2010



Model of Lopez, Coutinho, Buratini & Massad (1999)

$$\frac{\partial}{\partial t} S(x, t) = -\lambda(x, t)S(x, t) - \mu S(x, t) + \mu N(x) + \gamma_1 I(x, t)$$

$$\frac{\partial}{\partial t} I(x, t) = \lambda(x, t)S(x, t) - (\mu + \gamma_1 + \gamma_2)I(x, t)$$

$$\frac{\partial}{\partial t} R(x, t) = \gamma_2 I(x, t) - \mu R(x, t)$$

with force of infection

$$\lambda(x, t) = \frac{1}{N} \int_0^L dx' \beta(x, x') I(x', t)$$

and total population along the road

$$N = \int_0^L dx' N(x')$$

Why human diseases differ

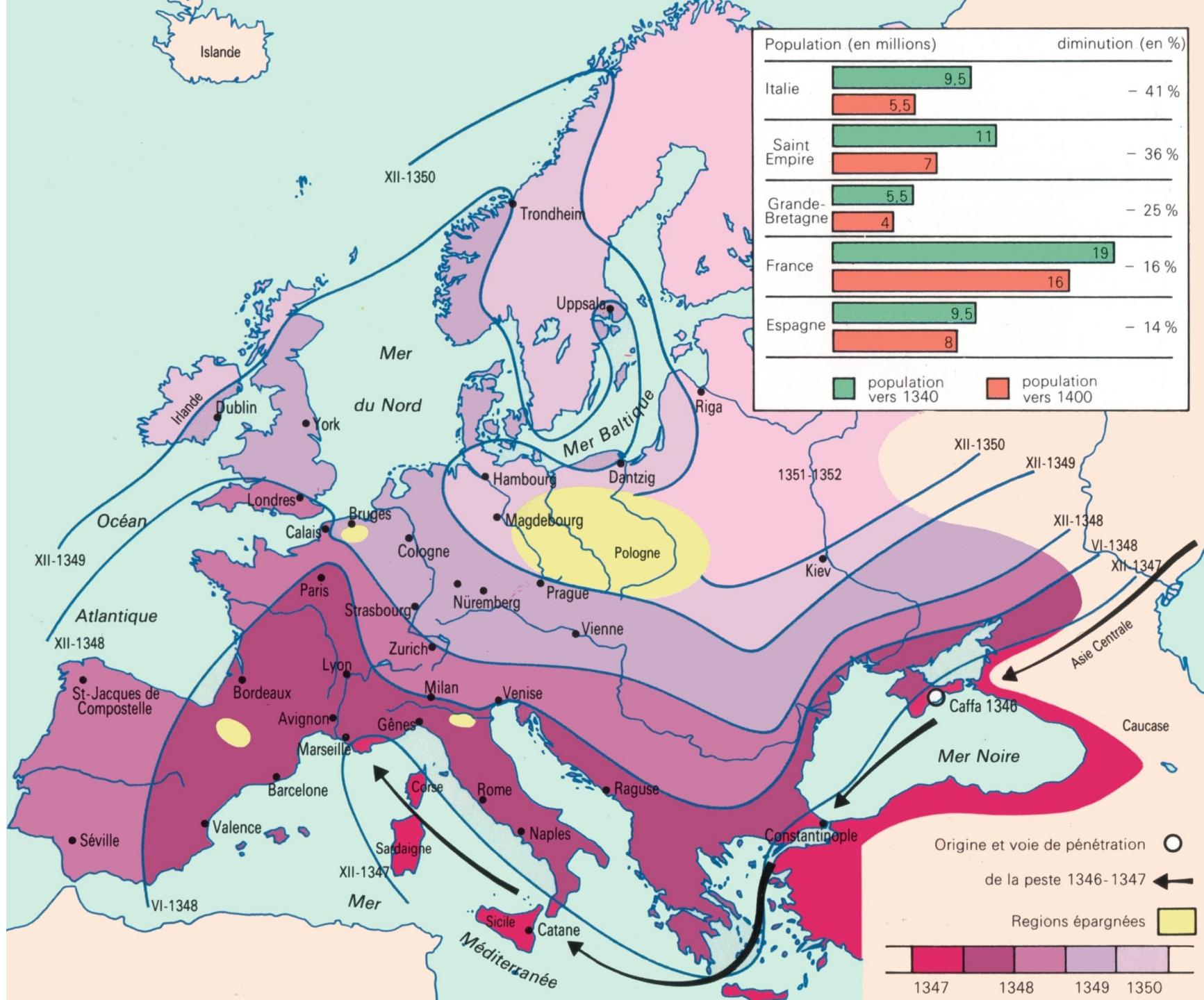
- Pathogens of humans follow .. humans
- Not all humans are mobile, but some humans have for a very long time been more mobile (because of trade)
- Complex spatial patterns have been observed for a long time

First known epidemics (from Wikipedia)

Event	Date	Location	Disease	Death toll (estimate)
Plague of Megiddo	1350 BCE	Megiddo, land of Canaan	Unknown	Unknown
Plague of Athens	429–426 BCE	Greece, Libya, Egypt, Ethiopia	Possibly typhus, typhoid fever or VHF	75,000–100,000
412 BCE epidemic	412 BCE	Greece, Roman Republic	Possibly influenza	Unknown
Antonine Plague	165–180 CE (possibly up to 190 CE)	Roman Empire	Possibly smallpox	5–10 million
Jian'an Plague	217 CE	Han dynasty	Possibly typhoid fever or VHF	Unknown
Plague of Cyprian	250–266 CE	Europe	Possibly smallpox	Unknown
Plague of Justinian				15–100 million (25–60%)

A.D.1212





Human epidemics have evolved..

- because human mobility has changed a lot:
 - Range has vastly increased
 - Time to range has diminished
 - Duration of travel has decreased (on average)
 - Fraction of population able to undertake travel has increased



Jeanne d'Albret
(1528-1572)
Queen of Navarre (1555-1572)



Henri IV
(1553-1610)
King of Navarre (1572-1610)
King of France (1589-1610)



Cosy turtle shell crib in Pau
(then capital of Béarn & Navarre)



ONLY 15 DAYS
Liverpool to Winnipeg
PROVINCE OF MANITOBA.

MANITOBA offers the most easily accessible and the most promising and productive Lands of any Colonial Province in the world. Situated in a pure, healthy climate, under a free form of government, and within close proximity by direct rail communication to the great centres of th^e Continent, which afford ready markets for Live Stock, Grain, and other products.

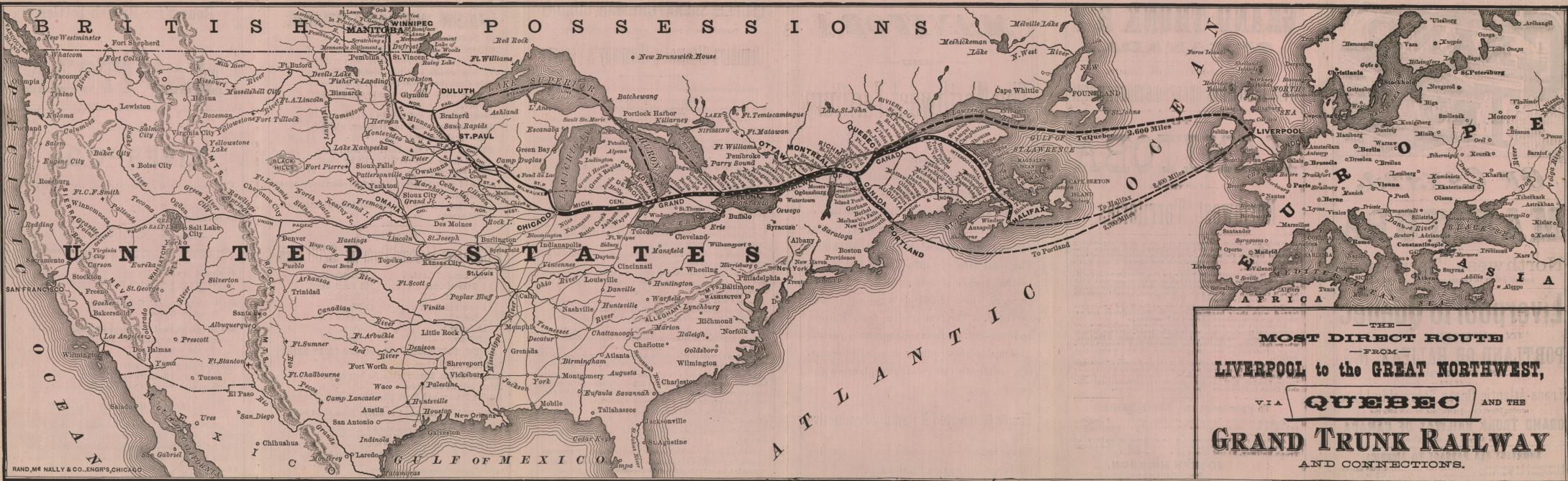
**THE LAND IS PRAIRIE
 NOT BUSH LAND,**

UNITED STATES
AND THE NORTHWEST TERRITORIES.

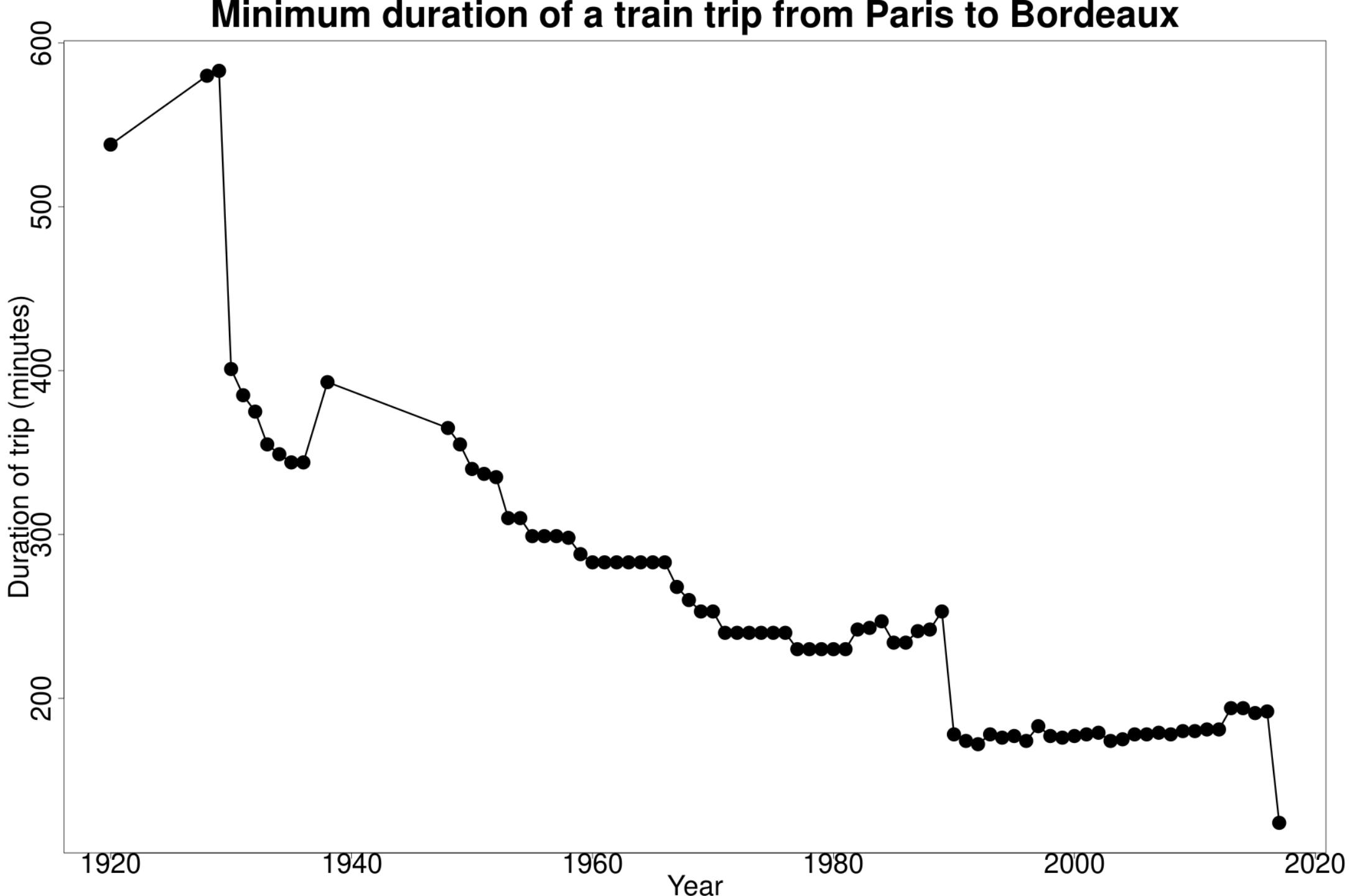
Total area of Lands fit for cultivation is estimated at 375,184,000 acres, of which 10,660,369 acres are already surveyed.

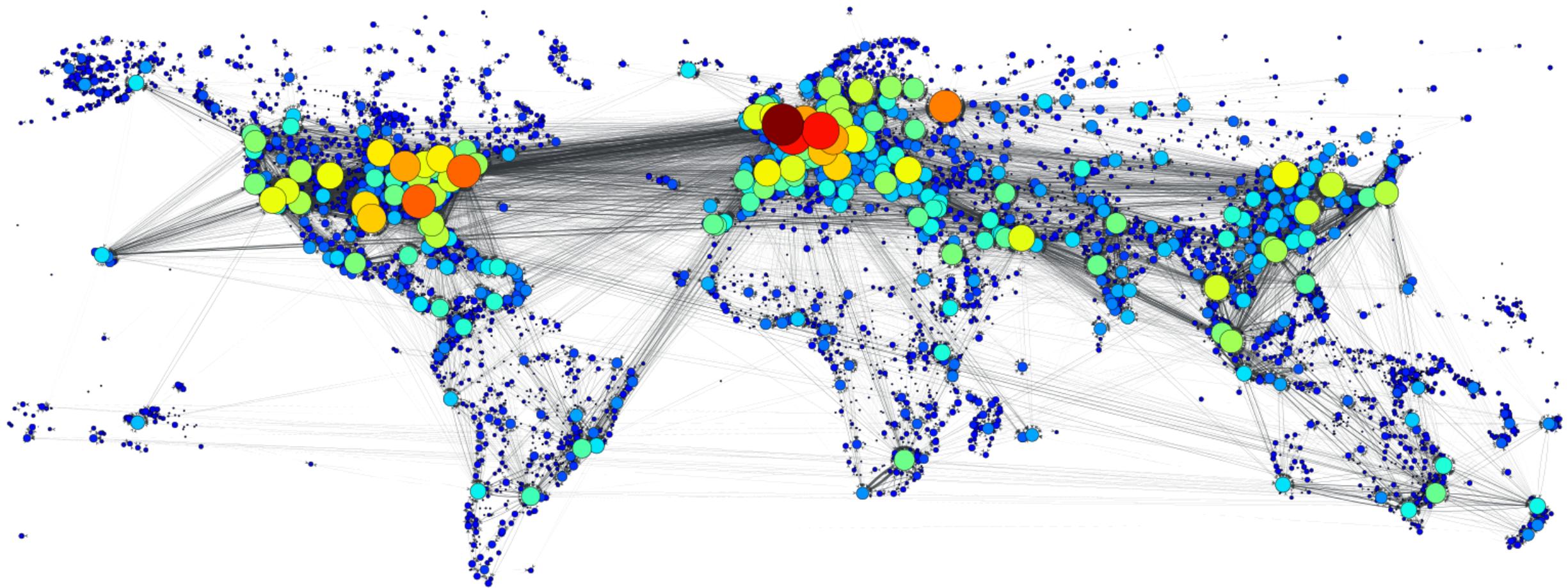
THE DOMINION HOMESTEAD LAW

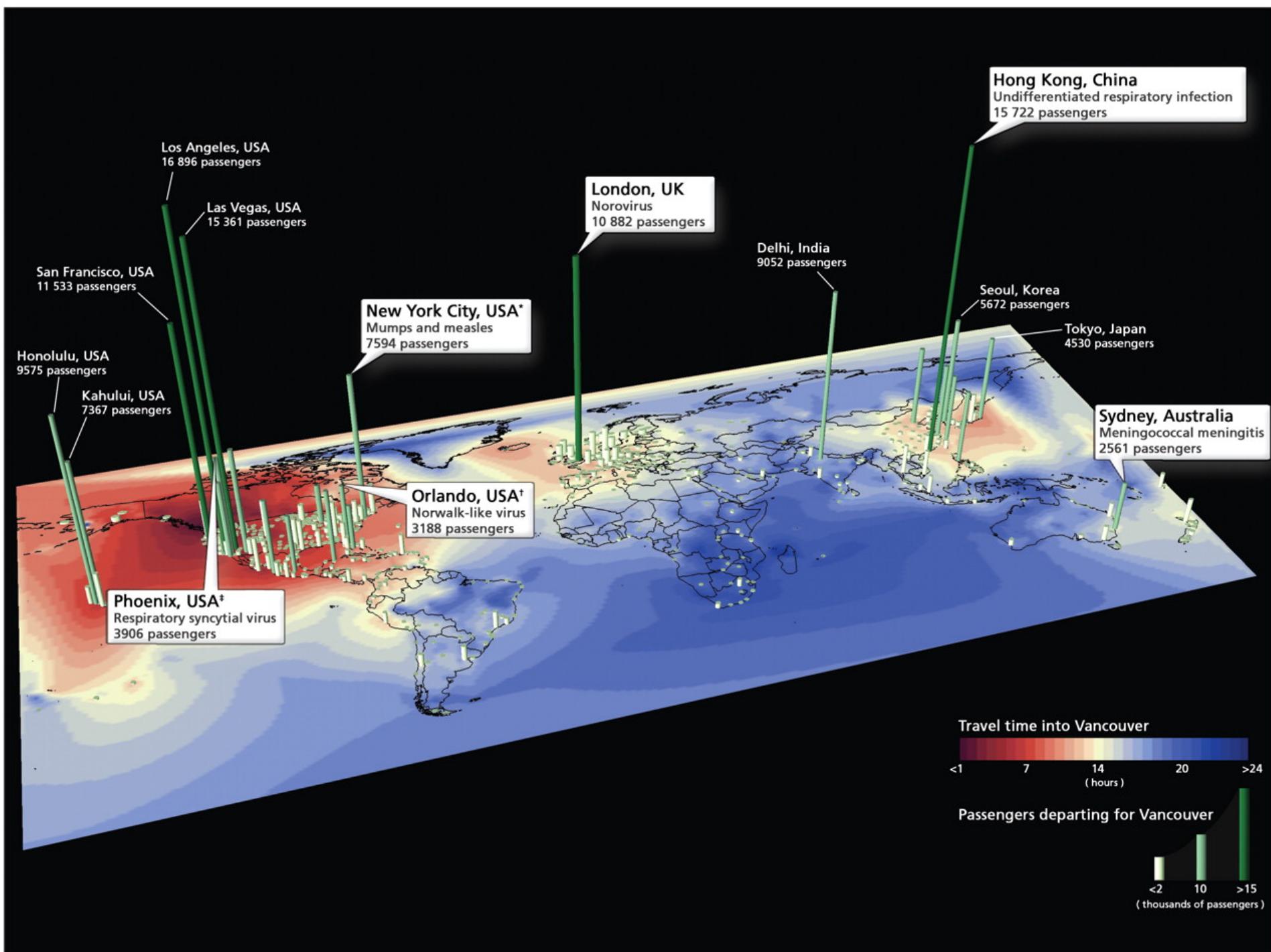
Is one of the most liberal character. Every actual settler is entitled to enter one quarter section of 160 acres as a Homestead, for which a patent is given on proof of three years residence and cultivation. He may, however, apply for a patent before the expiration of six years, in which case he will receive a patent for which he will pay him on payment of \$1.00 per acre, and when he has completed his Homestead duties he will receive a patent for the same land, and also a patent for the timber on it at the expiration of six years, on proof of having planted the same trees in four years subsequent to year of entry. The ordinary Dominion Lands are open for entry in tracts of One dollar per acre, payable in Cash, Scrip, or Military Bounty Warrants.



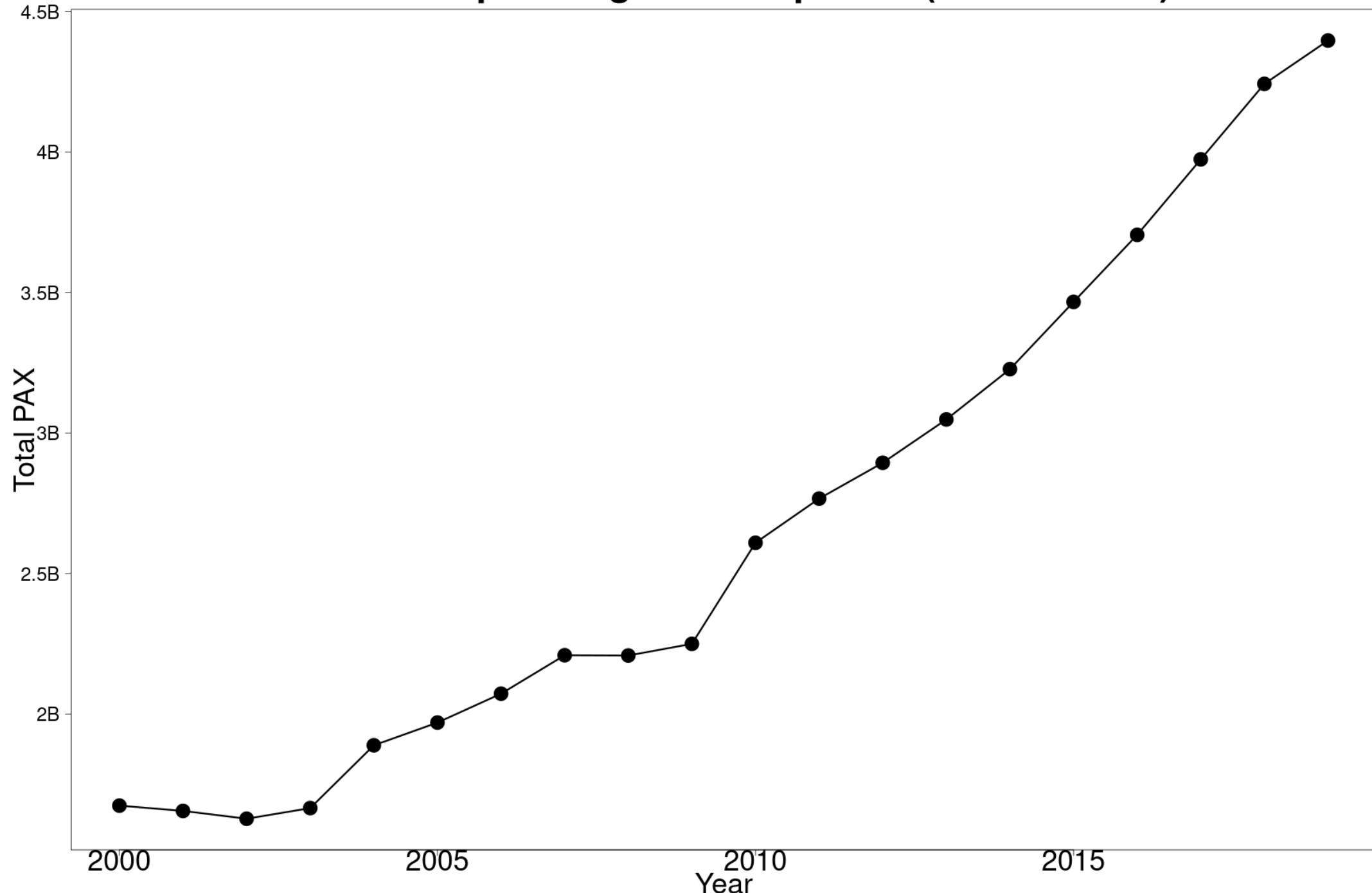
THE MOST DIRECT ROUTE
FROM
LIVERPOOL to the GREAT NORTHWEST,
VIA QUEBEC AND THE
GRAND TRUNK RAILWAY
AND CONNECTIONS.





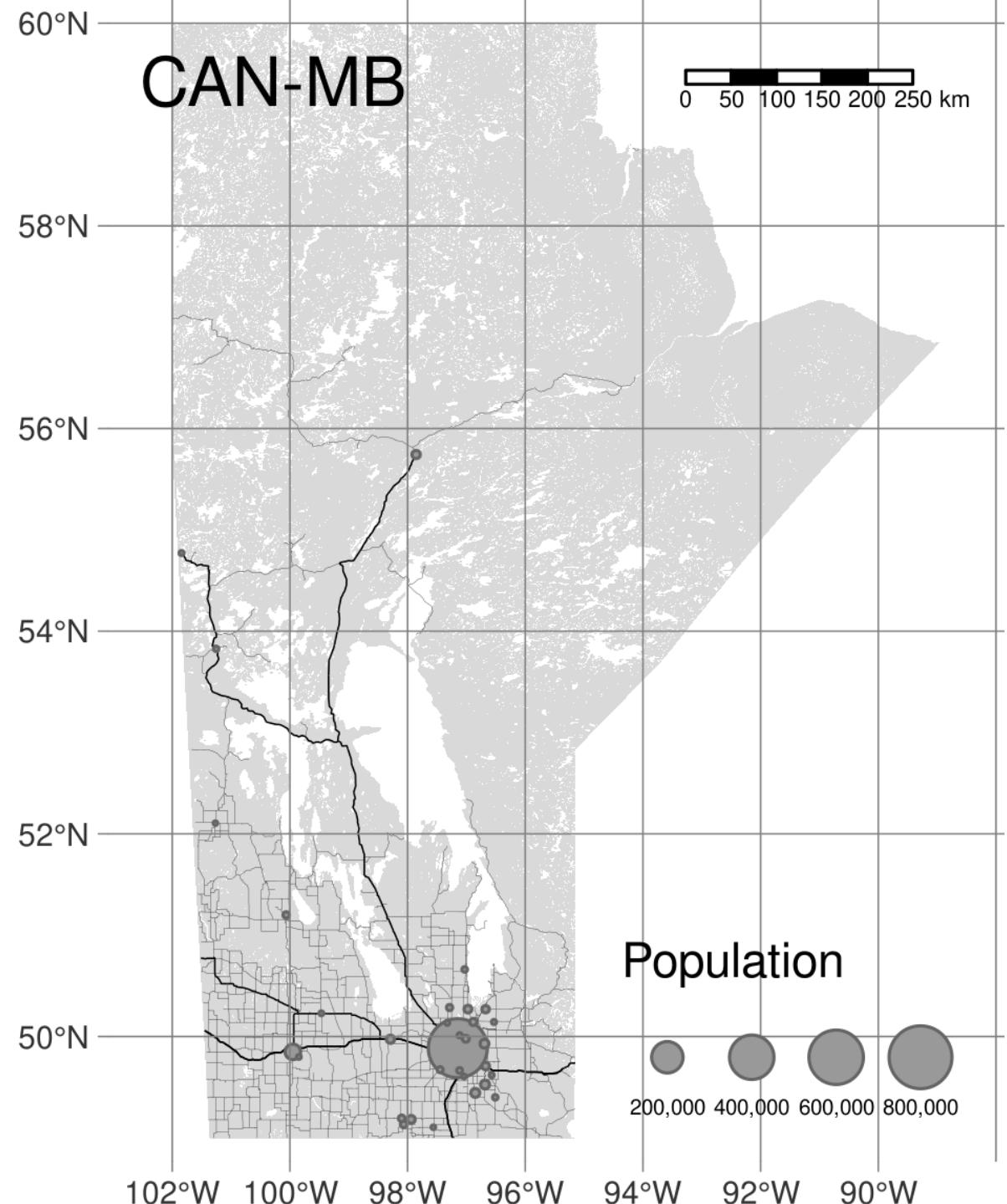
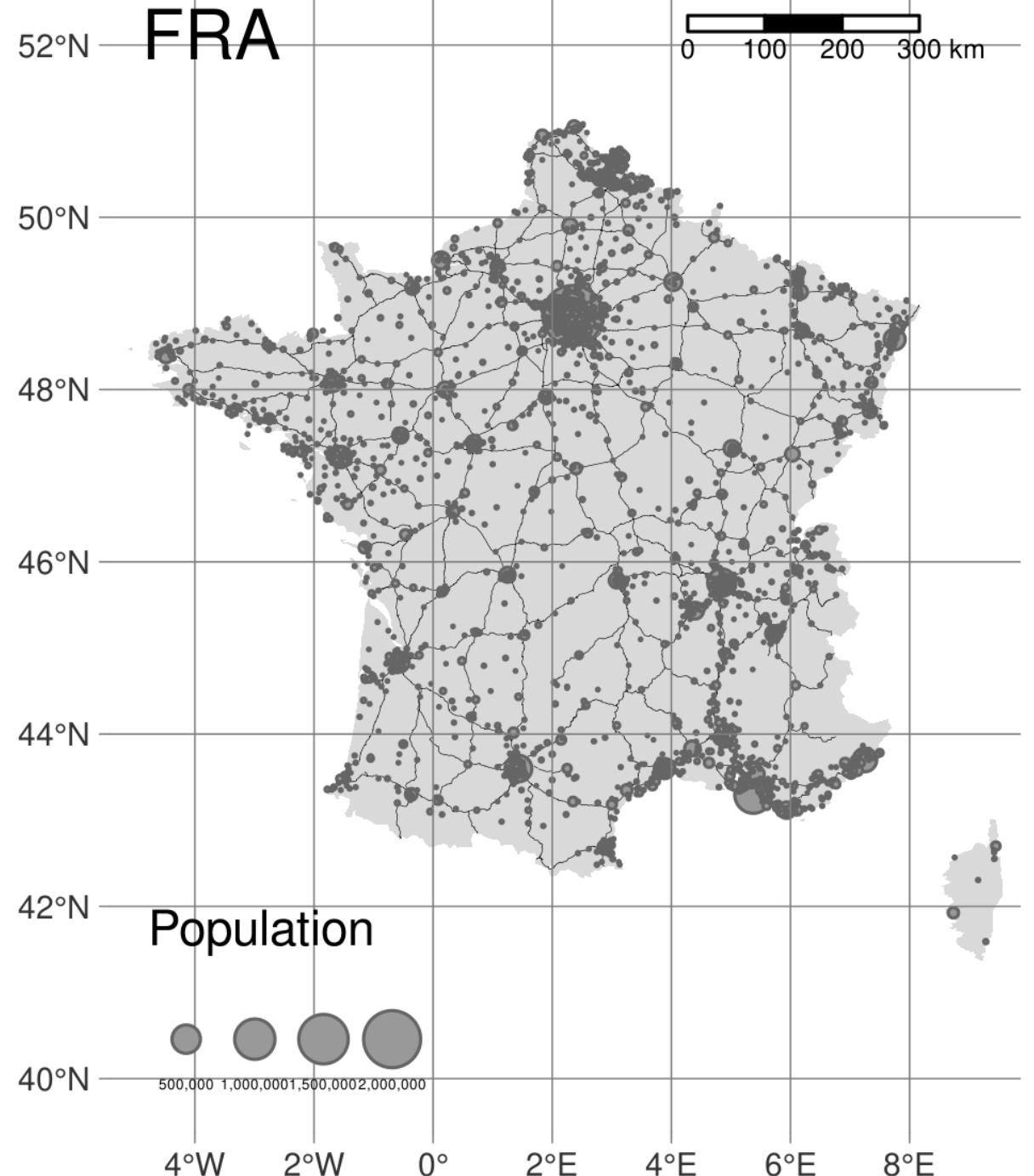


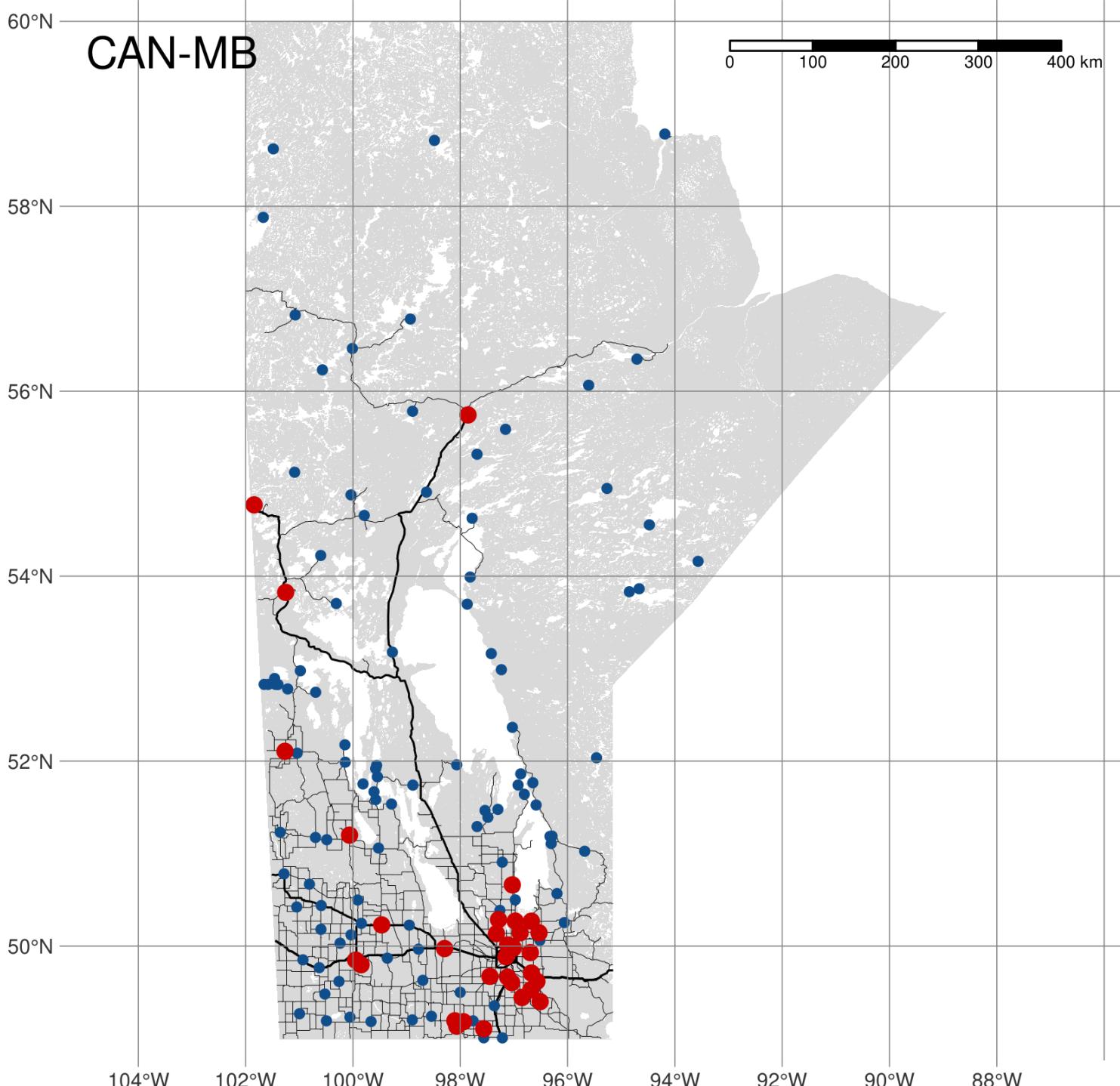
Number of passengers transported (all countries)

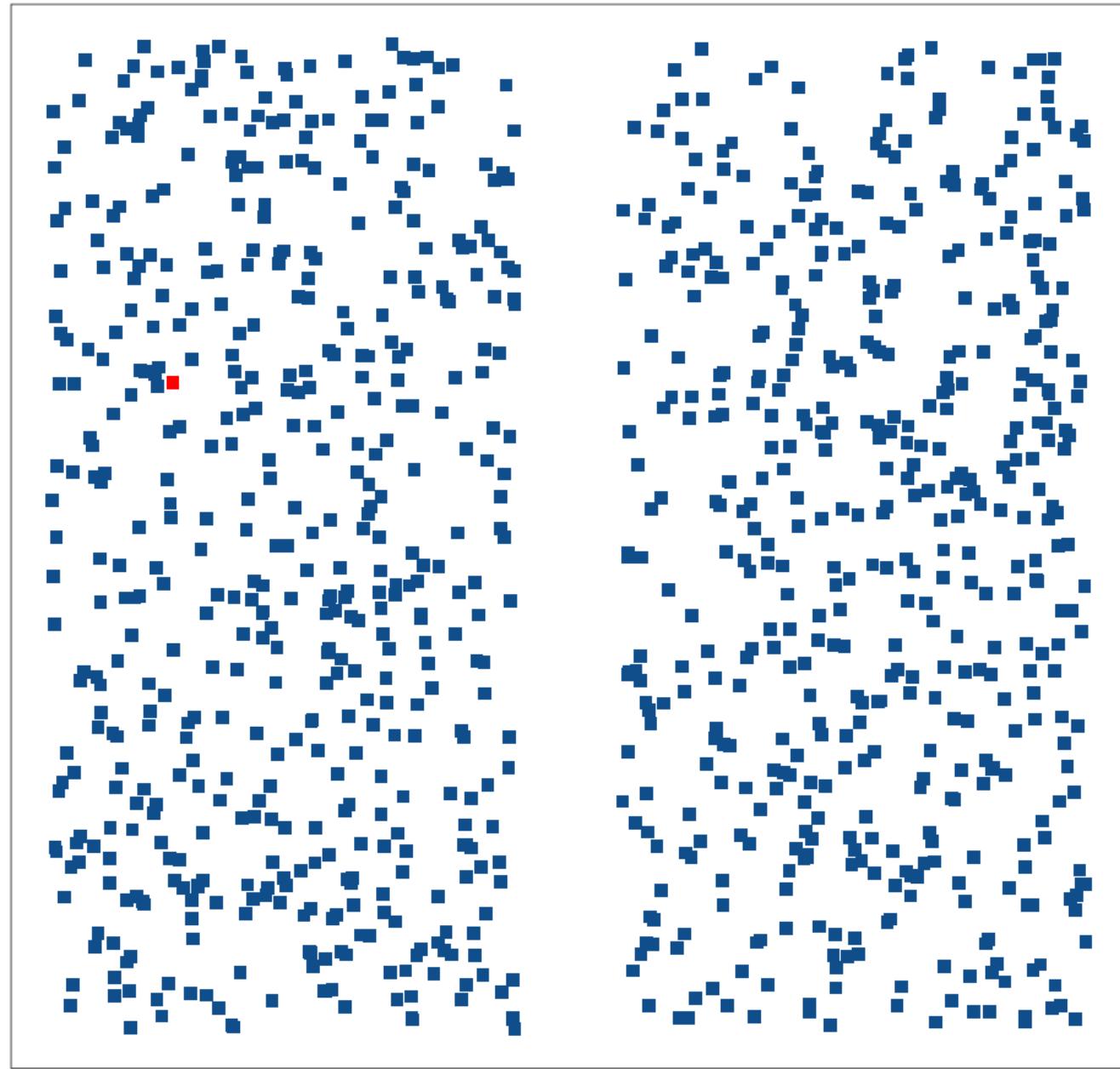


The human world is fragmented

- Political divisions: nation groups (e.g., EU), nations, provinces/states, regions, counties, cities..
- With increasing administration, movement between jurisdictions might become more complicated
- Data is also integrated at the jurisdicinal level
- Long range mobility is a bottom→top→top→bottom process ("moving between cones")
- Mobility in bottom layer is on a more continuous support than higher levels
- Situation is highly variable even at the country level

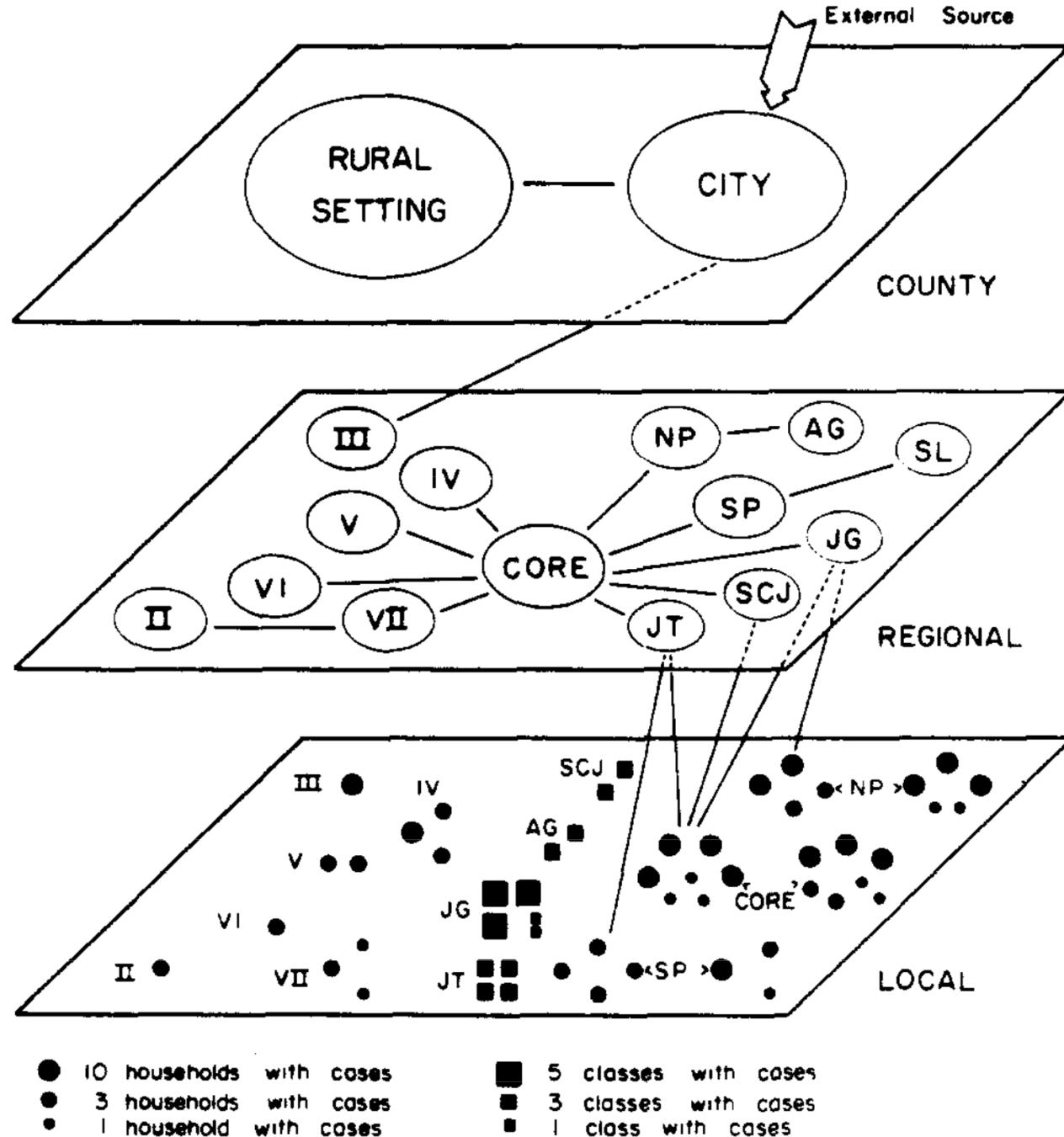






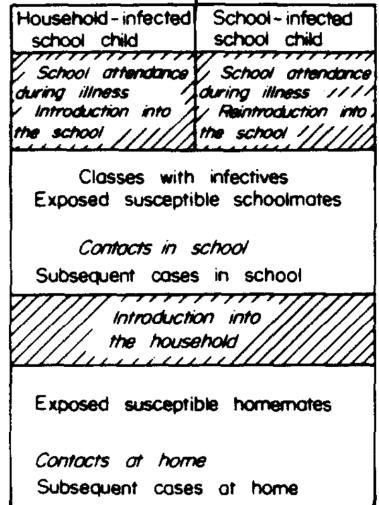
Cones of resolution

= various levels or scales of the functional or spatial aspects of a diffusion process. Scale (cone of resolution) takes on two dimensions: *functional* (decisions made by different groups of individuals) and *spatial* (manifestations of these decisions as observed in a spatial context)

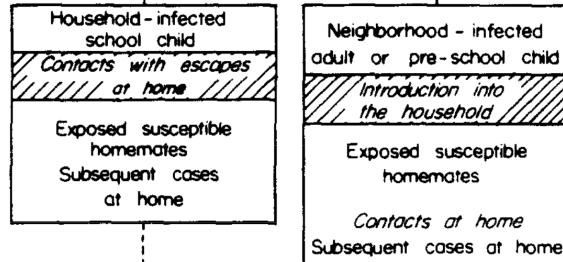


FUNCTIONAL PERSPECTIVE

PROPAGATOR SUPPORTED DIFFUSION

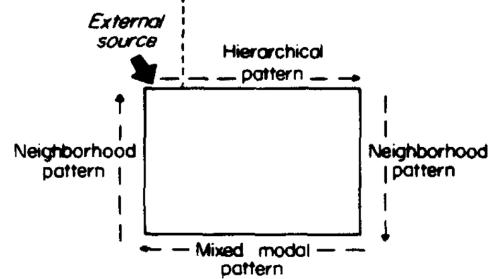


NON - PROPAGATOR SUPPORTED DIFFUSION

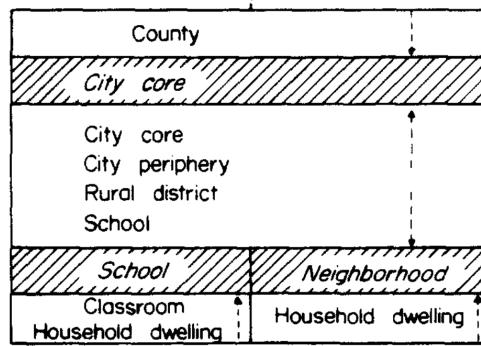


SPATIAL PERSPECTIVE

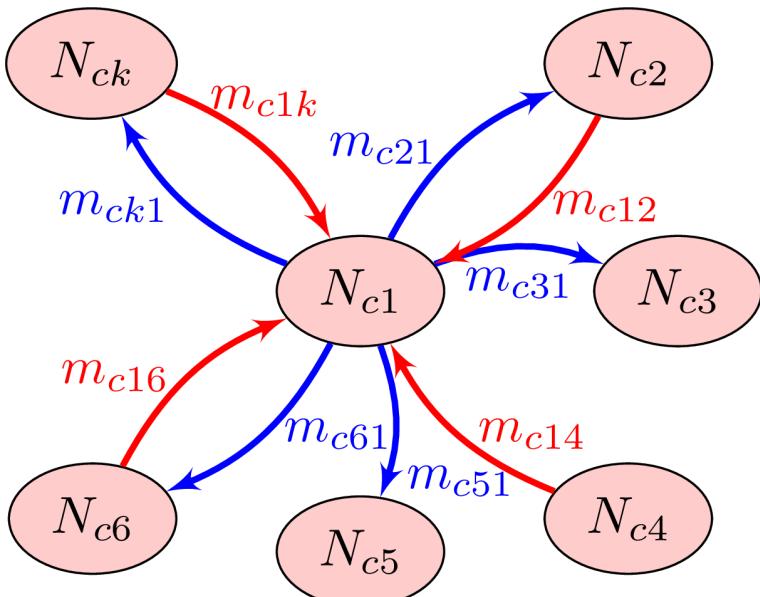
SPATIAL FORM



SPATIAL SCALE



Modelling heterogeneity using metapopulations



Movement for compartment c in patch 1

$$N'_{c1} = \sum_{p \in \mathcal{L} \setminus \{1\}} m_{c1p} N_{cp} - N_{c1} \sum_{p \in \mathcal{L} \setminus \{1\}} m_{cp1}$$

or

$$N'_{c1} = \sum_{p \in \mathcal{L}} m_{c1p} N_{cp} \text{ assuming } m_{c11} = - \sum_{p \in \mathcal{L} \setminus \{1\}} m_{cp1}$$

In each patch, put a system describing the evolution of the number of individuals in each compartment present

Assume **uninfected** (s) and **infected** (i) compartments \mathcal{U} and \mathcal{I} . For all $j \in \mathcal{U}, k \in \mathcal{I}$ and $\ell \in \mathcal{L}$

$$s'_{j\ell} = f_{j\ell}(S_\ell, I_\ell) + \sum_{q \in \mathcal{L}} m_{j\ell q} s_{jq}$$

$$i'_{k\ell} = g_{k\ell}(S_\ell, I_\ell) + \sum_{q \in \mathcal{L}} m_{k\ell q} i_{kq}$$

f and g describe interactions between compartments in a given location. Might involve more than S_ℓ, I_ℓ , but always local (ℓ)

Sums describe movement of (individuals from) compartments between locations

Describing movement - The movement matrix

Movement from location $q \in \mathcal{L}$ to location $p \in \mathcal{L}$ occurs at rate m_{Xpq} for individuals in compartment X

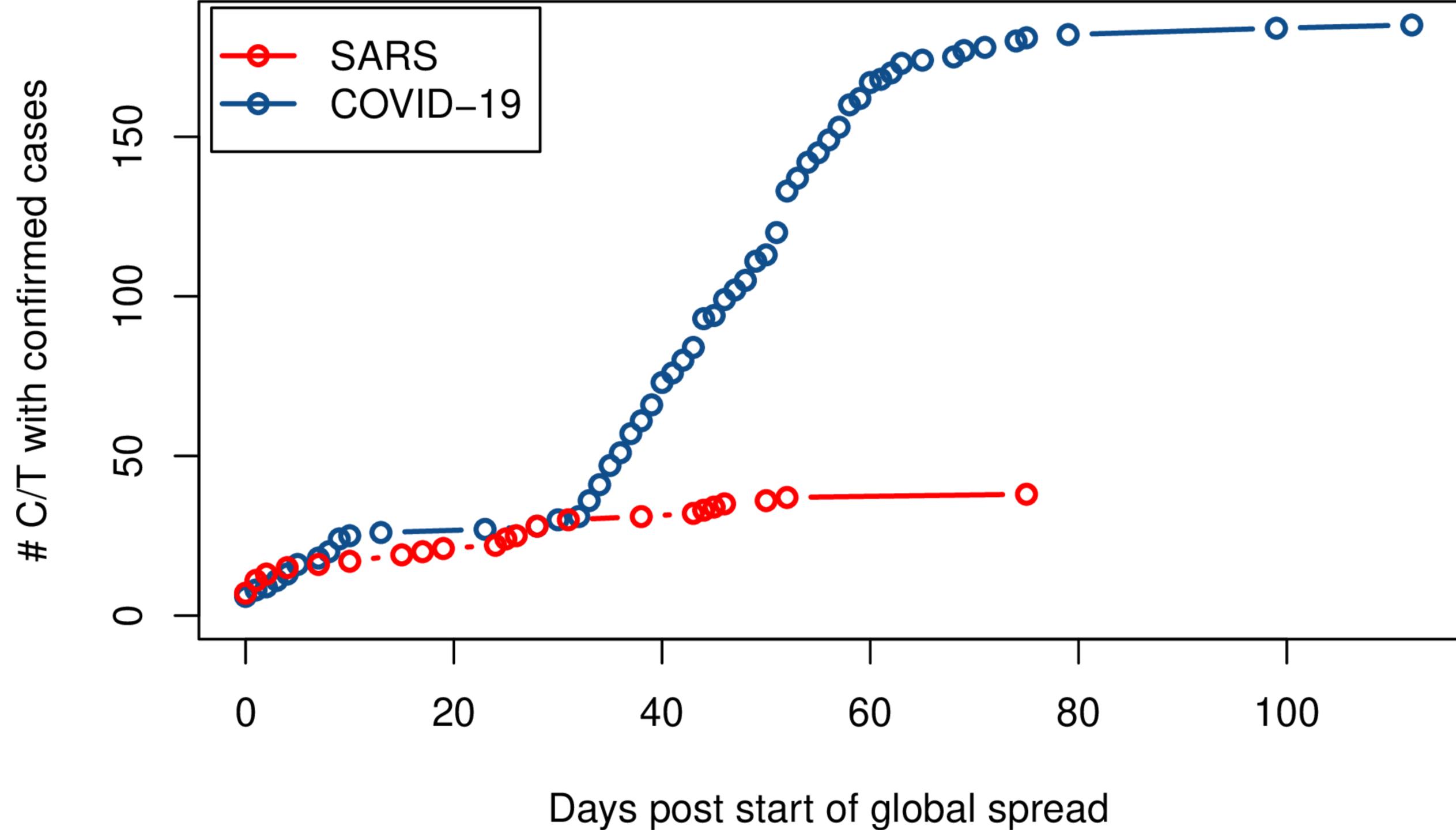
Movement matrix for compartment X :

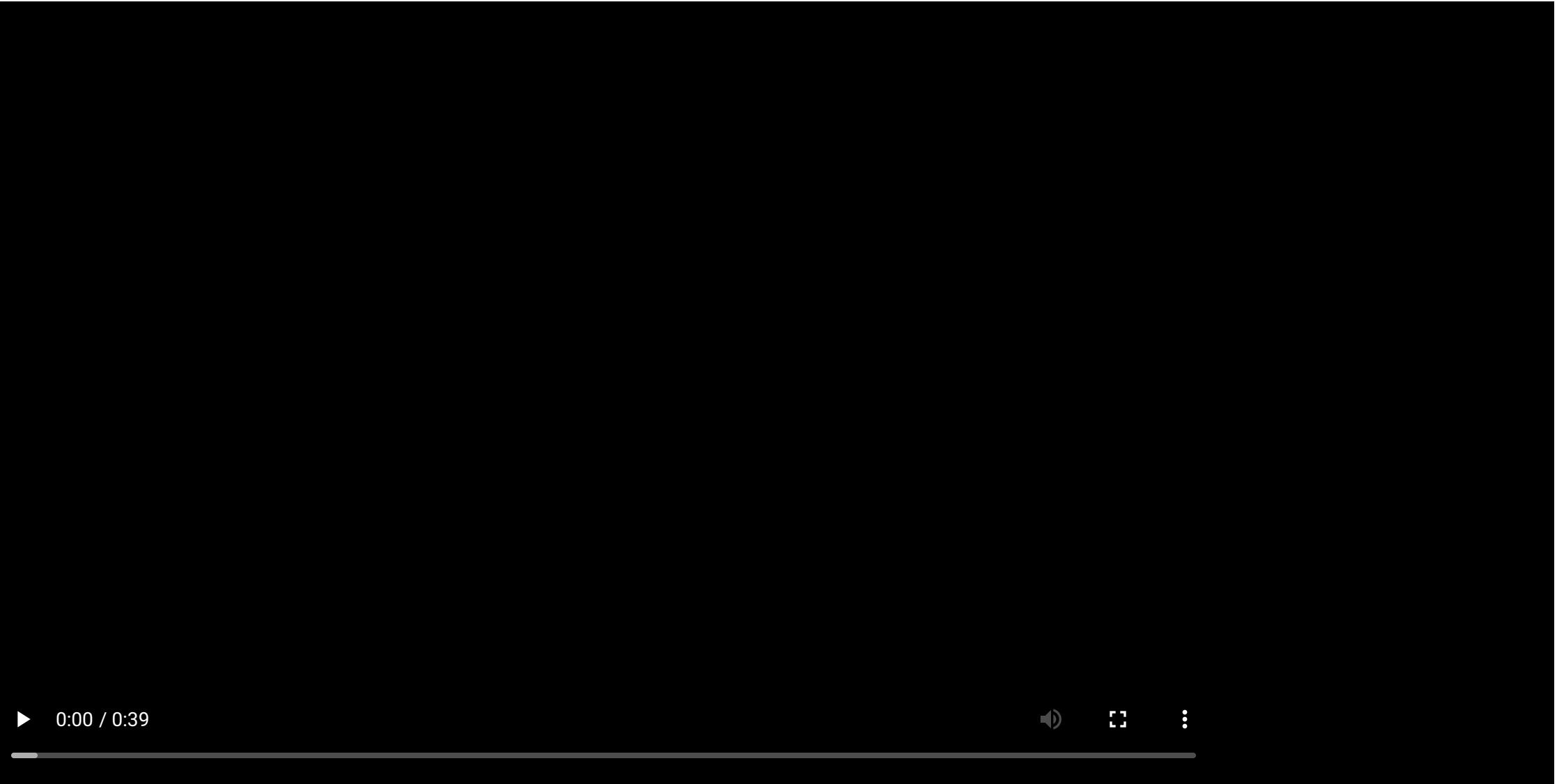
$$\mathcal{M}^X = \begin{pmatrix} -\sum_{q \in \mathcal{L}, q \neq p} m_{Xq1} & m_{X12} & \cdots & m_{X1|\mathcal{L}|} \\ m_{X21} & -\sum_{q \in \mathcal{L}, q \neq p} m_{Xq2} & & m_{X2|\mathcal{L}|} \\ m_{X|\mathcal{L}|1} & m_{X|\mathcal{L}|2} & & -\sum_{q \in \mathcal{L}, q \neq p} m_{Xq|\mathcal{L}|} \end{pmatrix}$$

The initial spread of COVID-19

First detections outside China

Date	Location	Note
13 Jan.	Thailand	Arrived 8 Jan.
16 Jan.	Japan	Arrived 6 Jan.
20 Jan.	Republic of Korea	Airport detected on 19 Jan.
20 Jan.	USA	Arrived Jan. 15
23 Jan.	Nepal	Arrived 13 Jan.
23 Jan.	Singapore	Arrived 20 Jan.
24 Jan.	France	Arrived 22 Jan.
24 Jan.	Vietnam	Arrived 13 Jan.
25 Jan.	Australia	Arrived 19 Jan.
25 Jan.	Malaysia	Arrived 24 Jan.





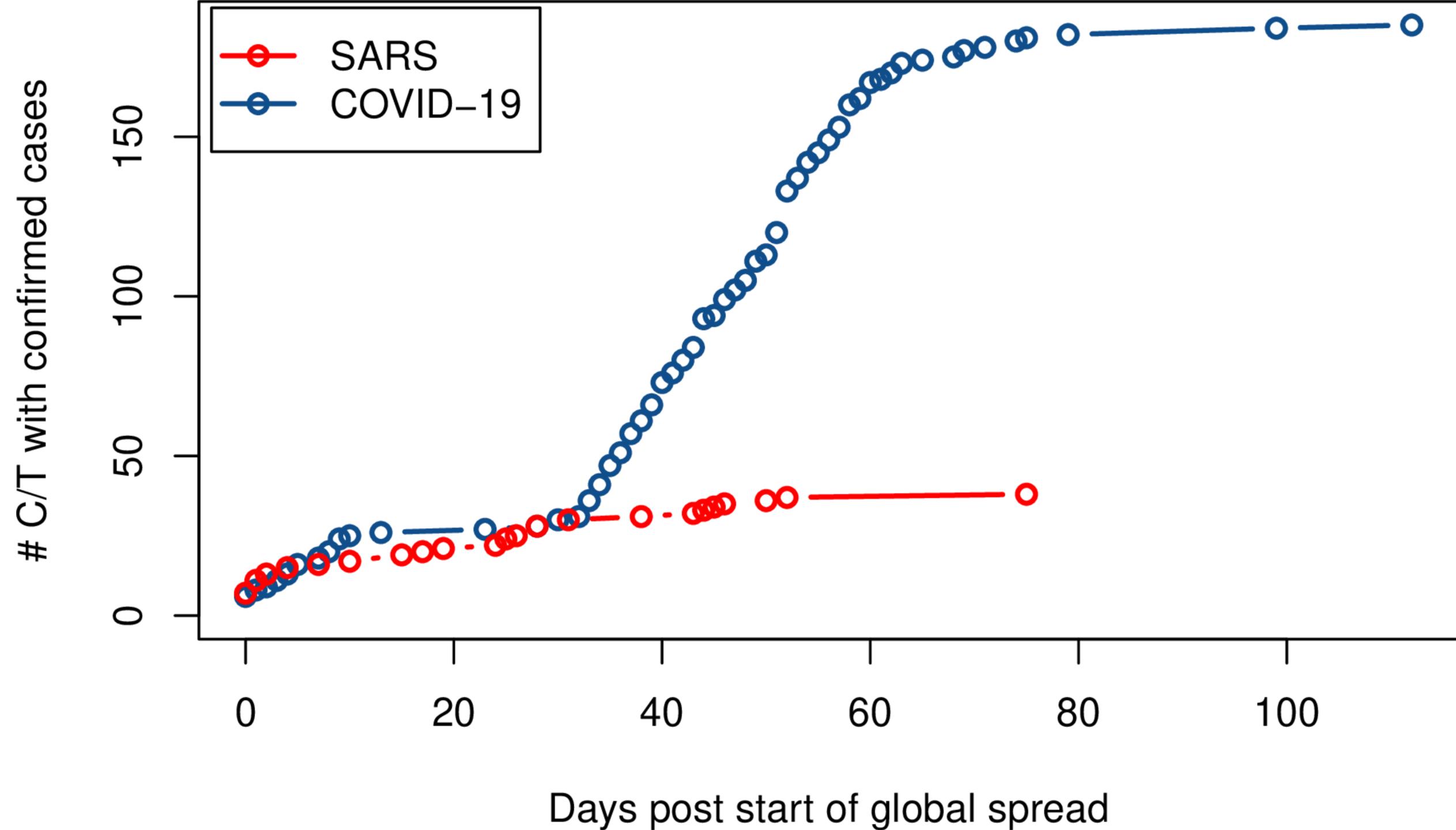
Case importations

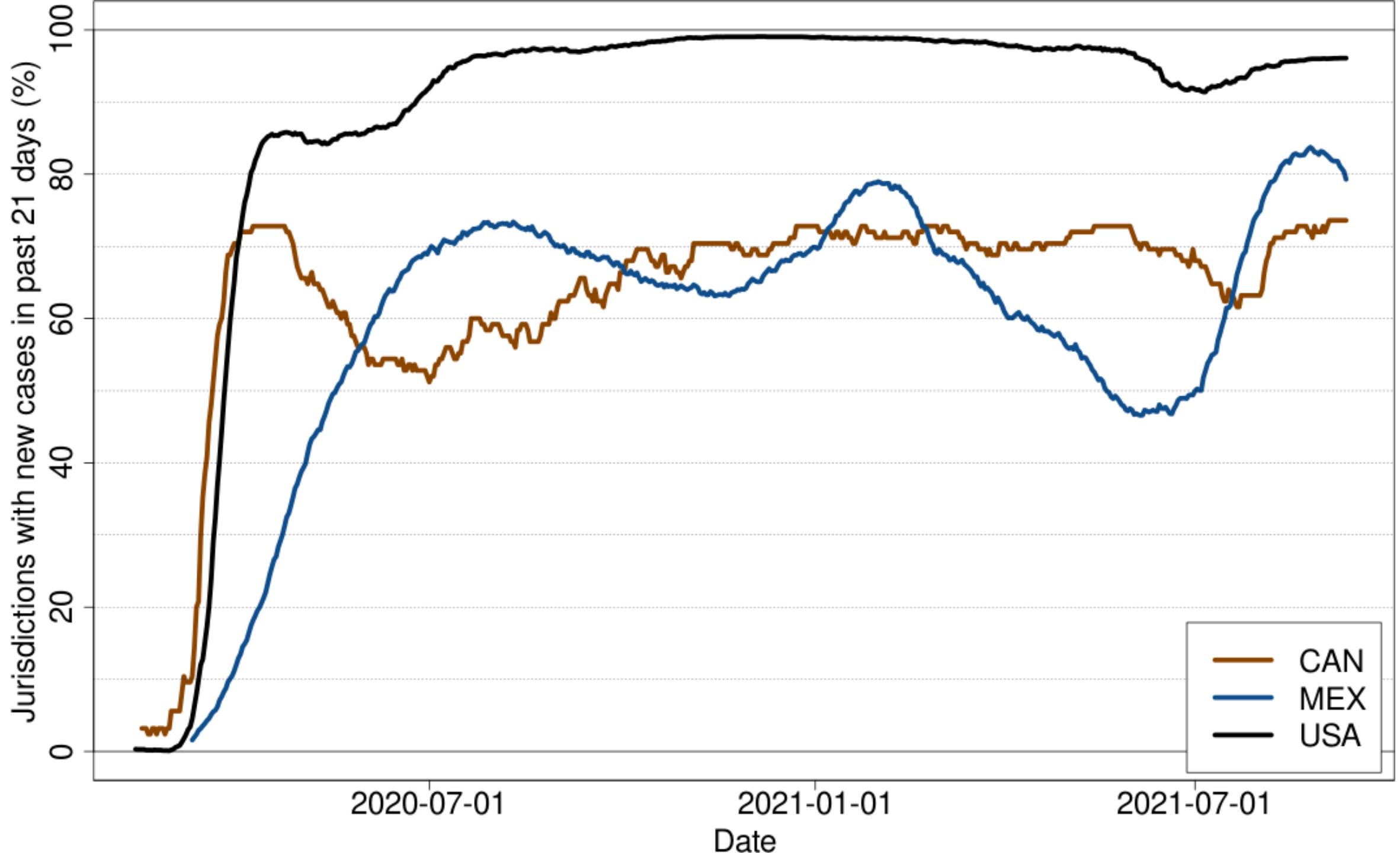
J. Arino & S. Portet. A simple model for COVID-19. *Infectious Disease Modelling*, 2020

J. Arino, N. Bajeux, S. Portet & J. Watmough. Quarantine and the risk of COVID-19 importation. *Epidemiology & Infection*, 2020

Importations

- In Ecology, importations are called *introductions* and have been studied for a while, because they are one of the drivers of evolution and, more recently, because of *invasive species*
- An importation occurs when an individual who acquired the infection in a jurisdiction makes their way to another jurisdiction while still infected with the disease
- Geographies greatly influence reasoning
 - At the country level, importations quickly become less relevant
 - Consider an isolated location of 500 people.. disease may become extinct then be reimported

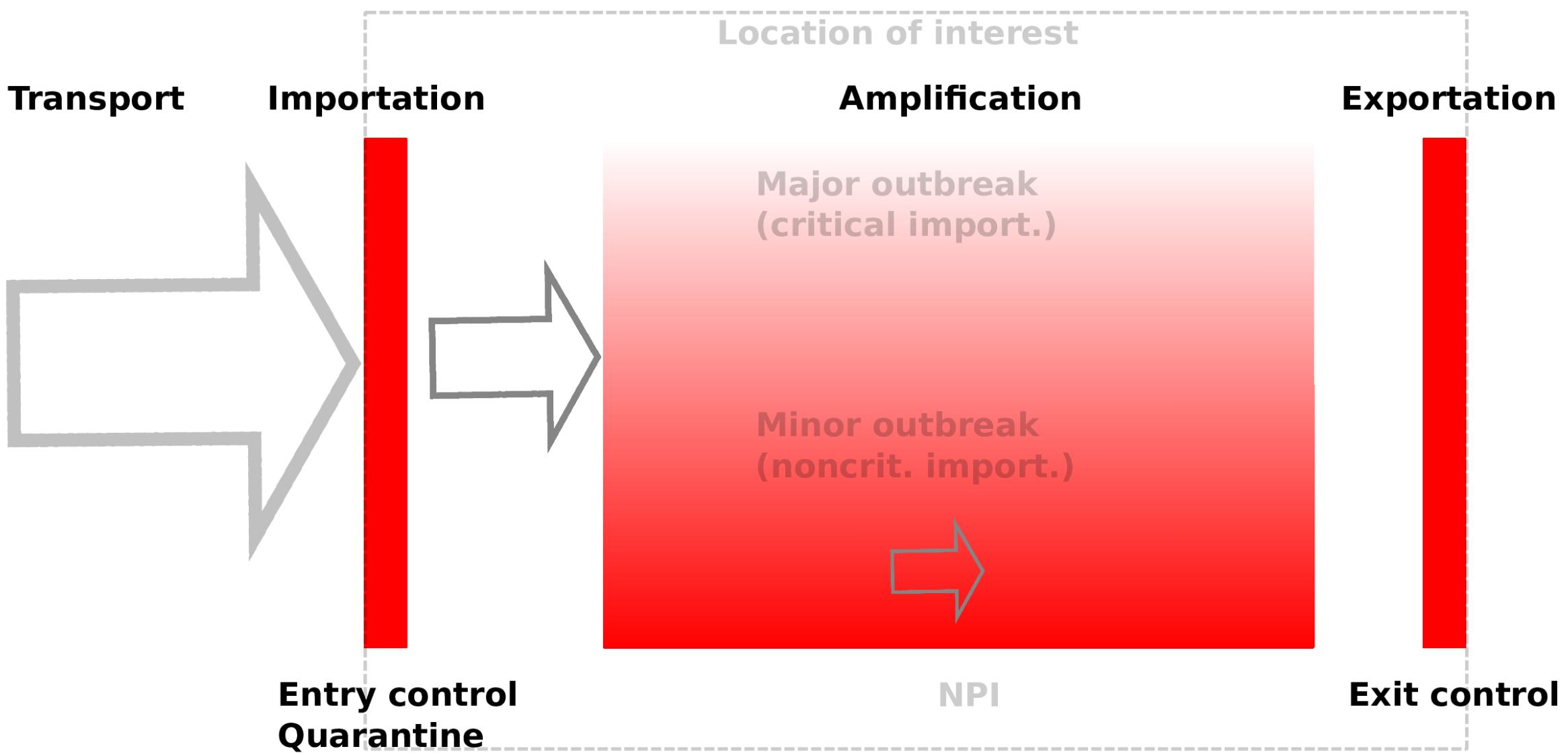


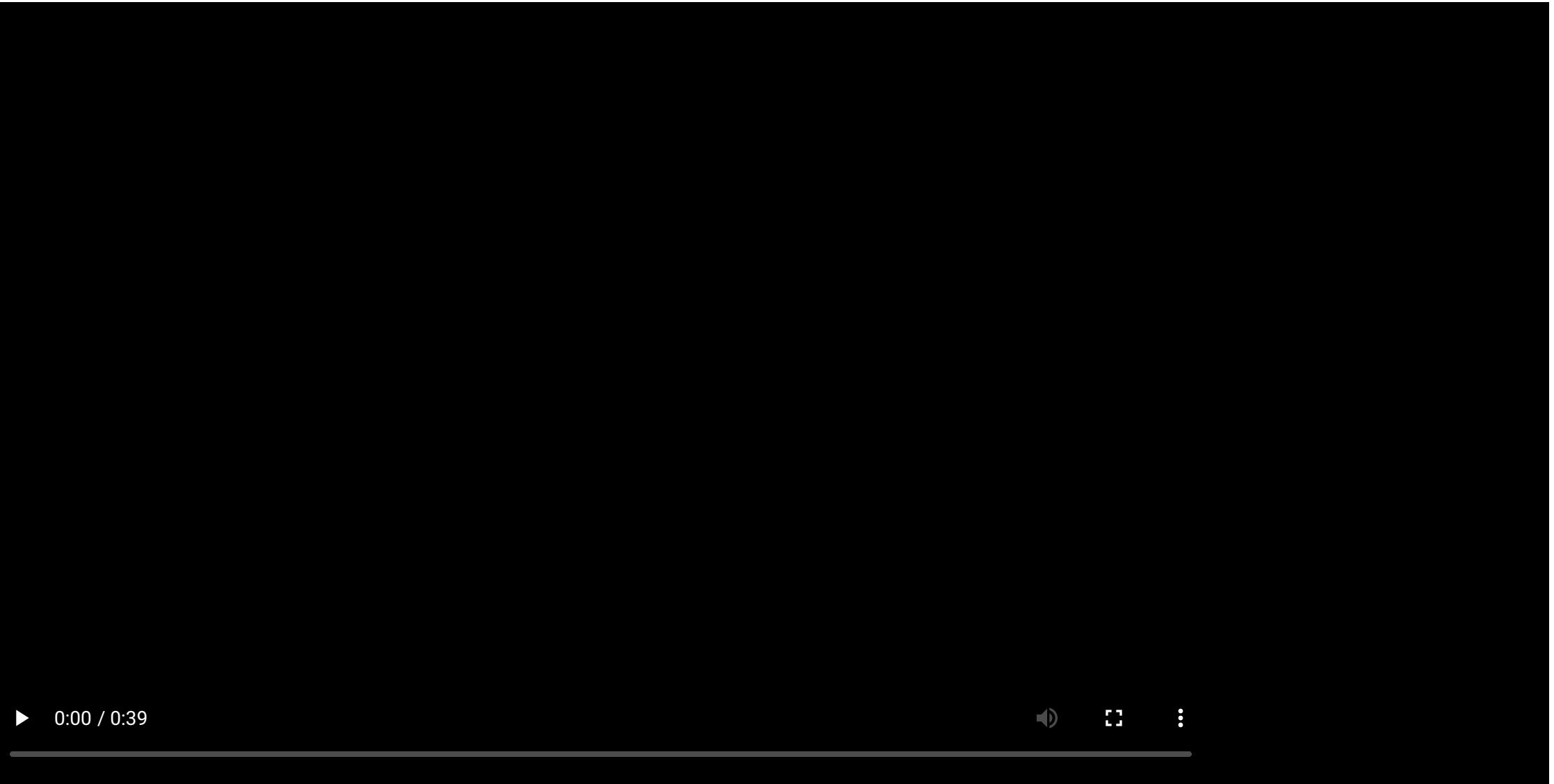


Phase

Epidemiology

Management



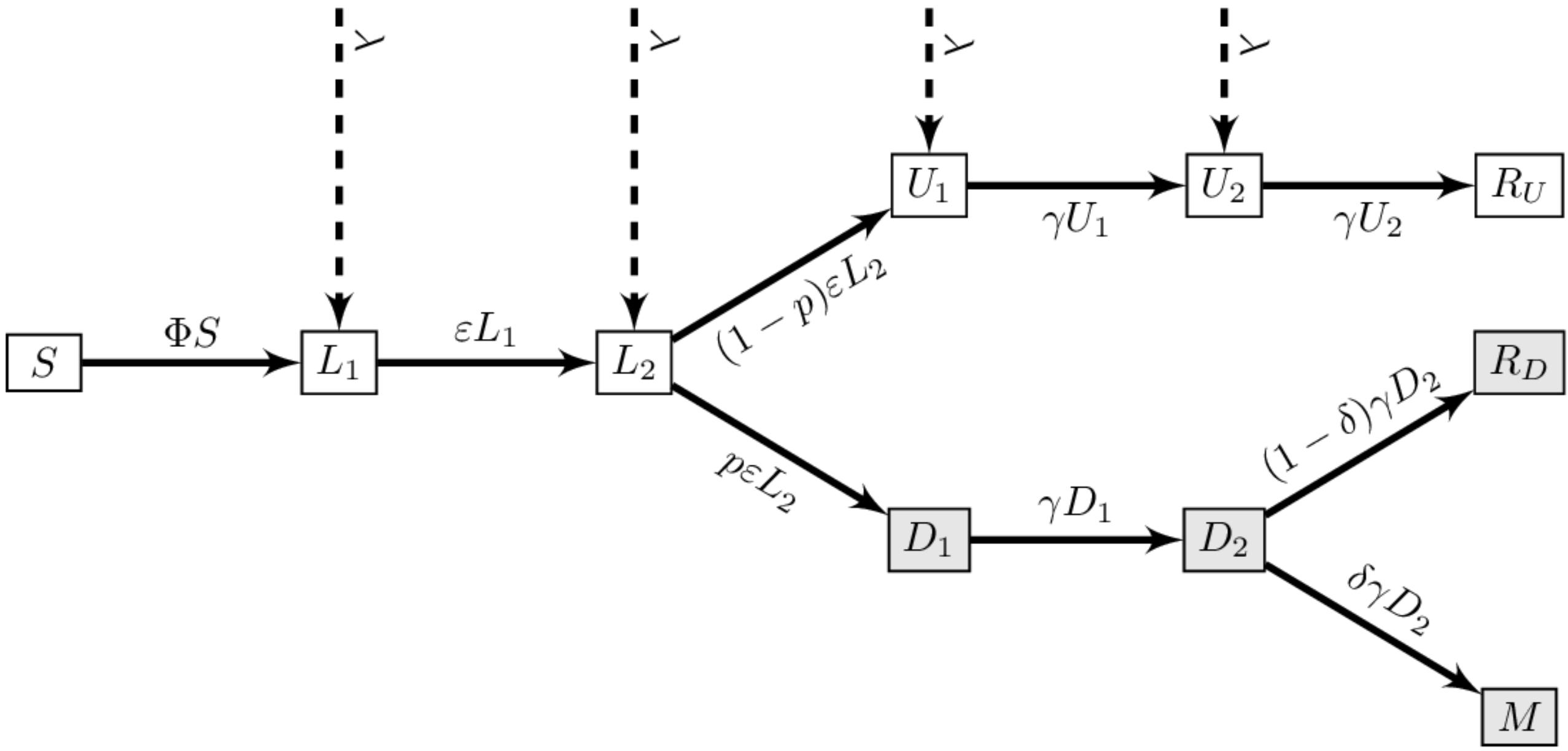


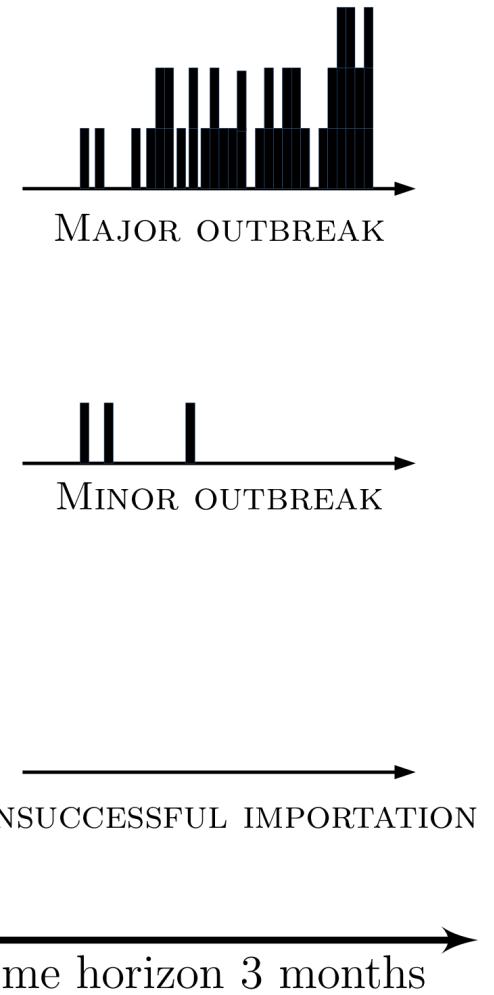
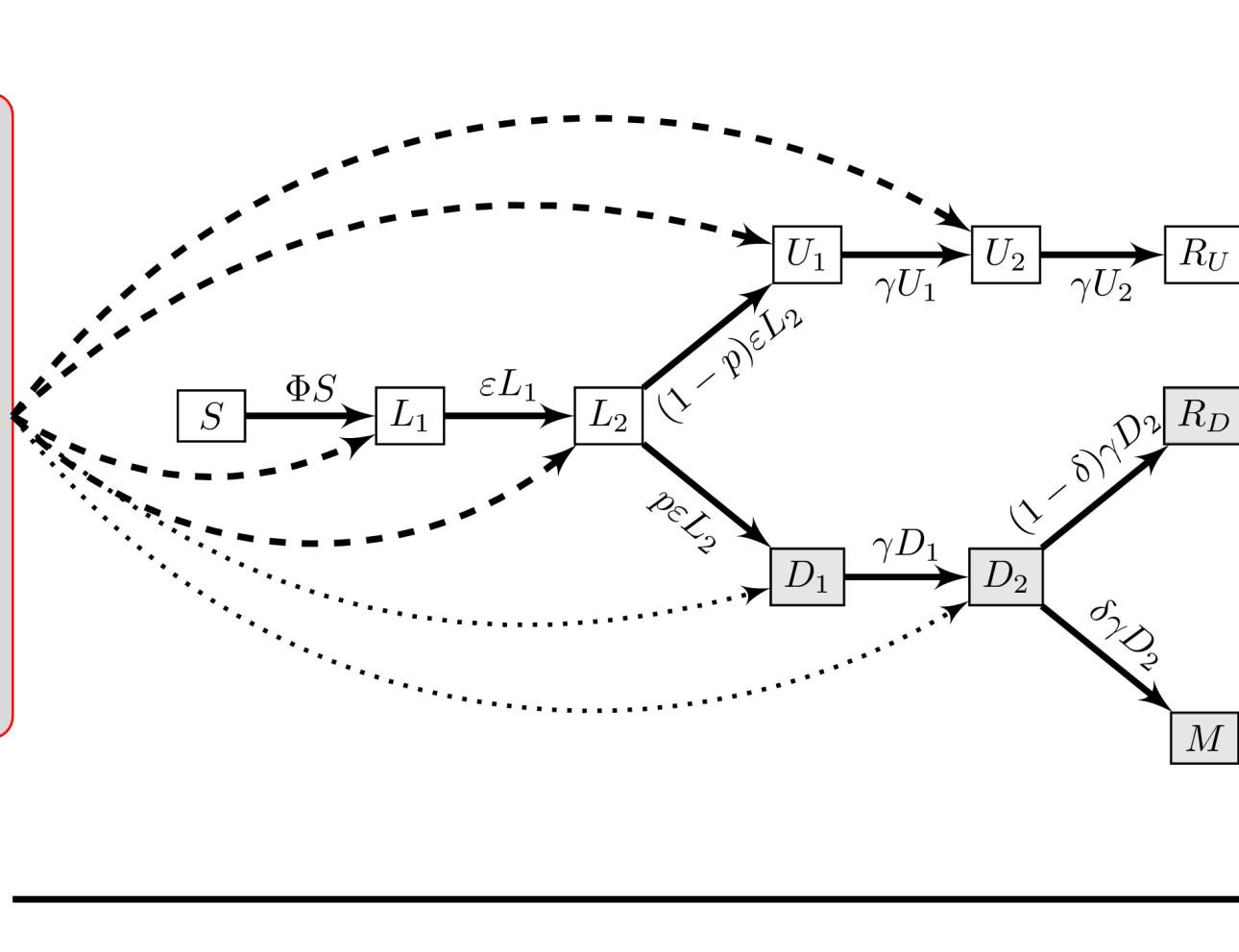
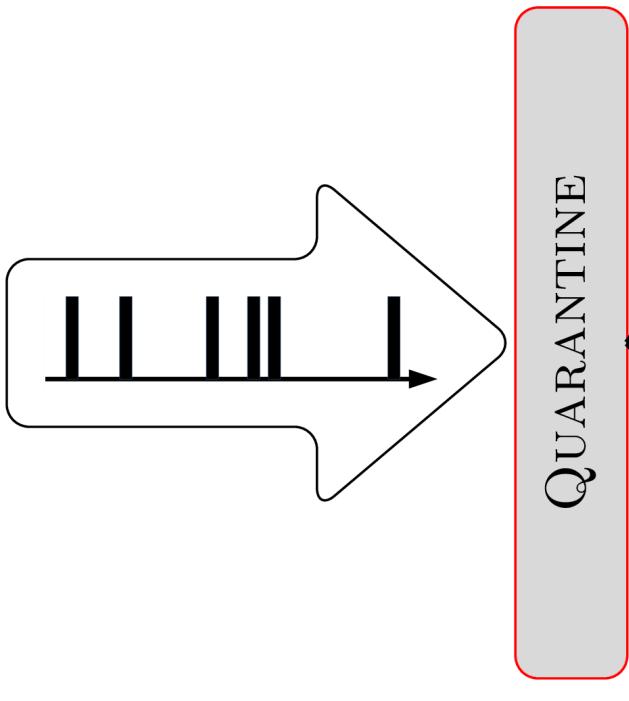
Our base model for considering COVID-19 uses detection-based compartments

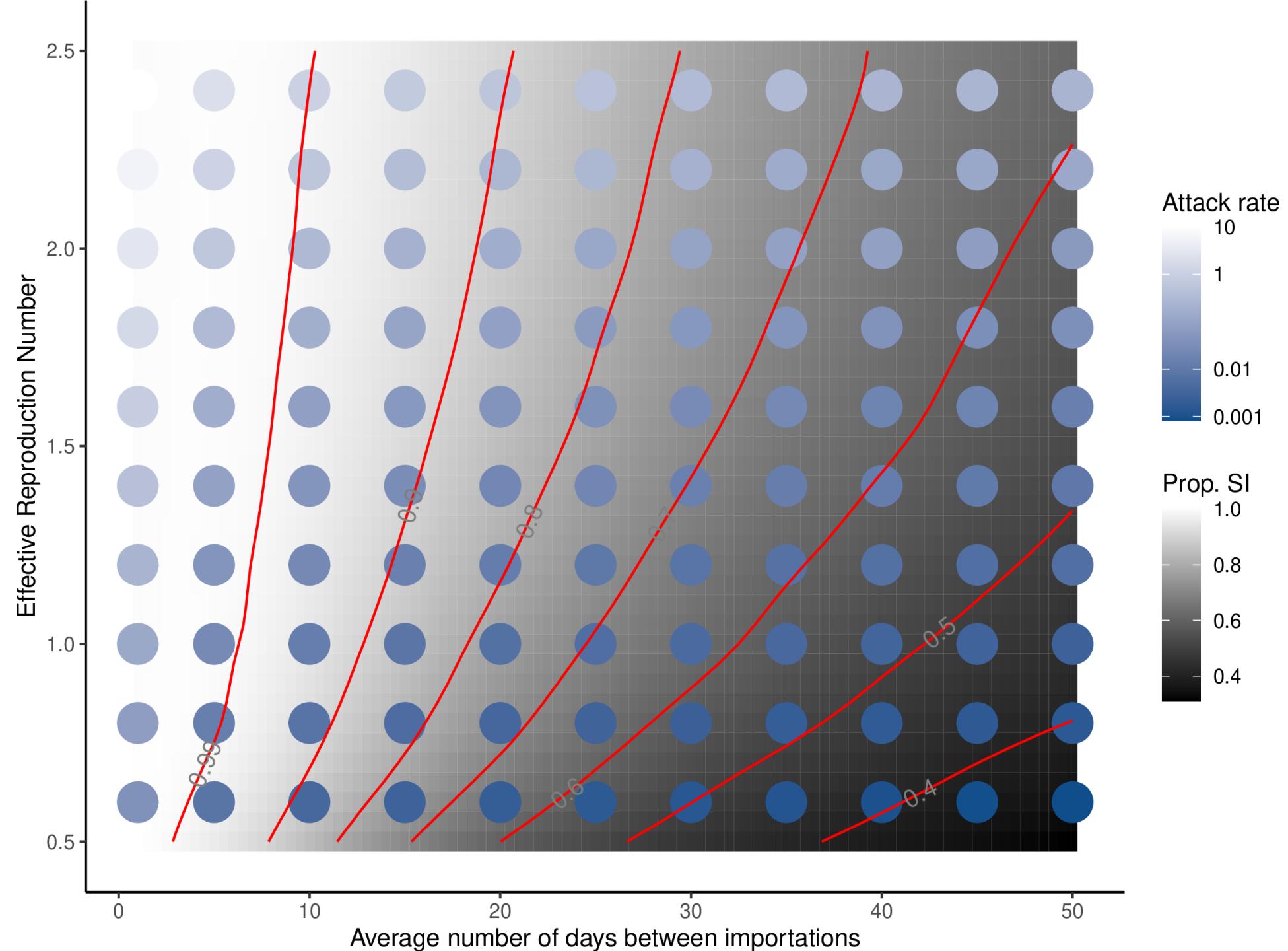
Modify the usual S (*susceptible*), L (*latent*), I (*infectious with symptoms*), A (*infectious without symptoms*) and R (*recovered*)

- D (instead of I) are **detected** (positive tests)
- U (instead of A) are **undetected** (even with symptoms)

p fraction of cases detected *a posteriori* (stricto sensu)







Understanding variant dynamics and how to control it

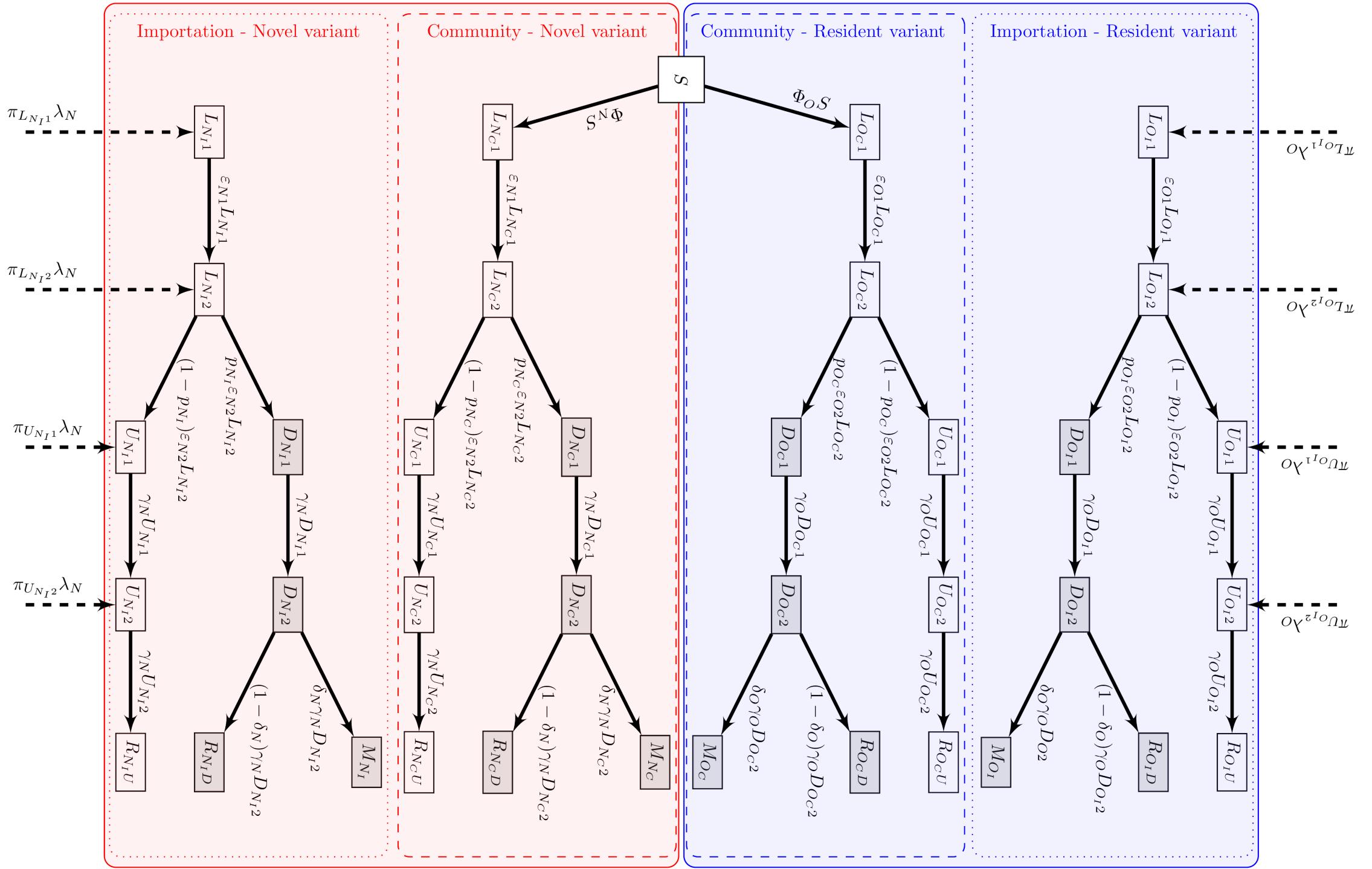
- Suppose a *resident variant* is propagating in a population, say, the original wild type or, now, B.1.1.7
- A *novel variant* comes along, say B.1.617.2 (SARS-CoV-2 Delta) that is more transmissible

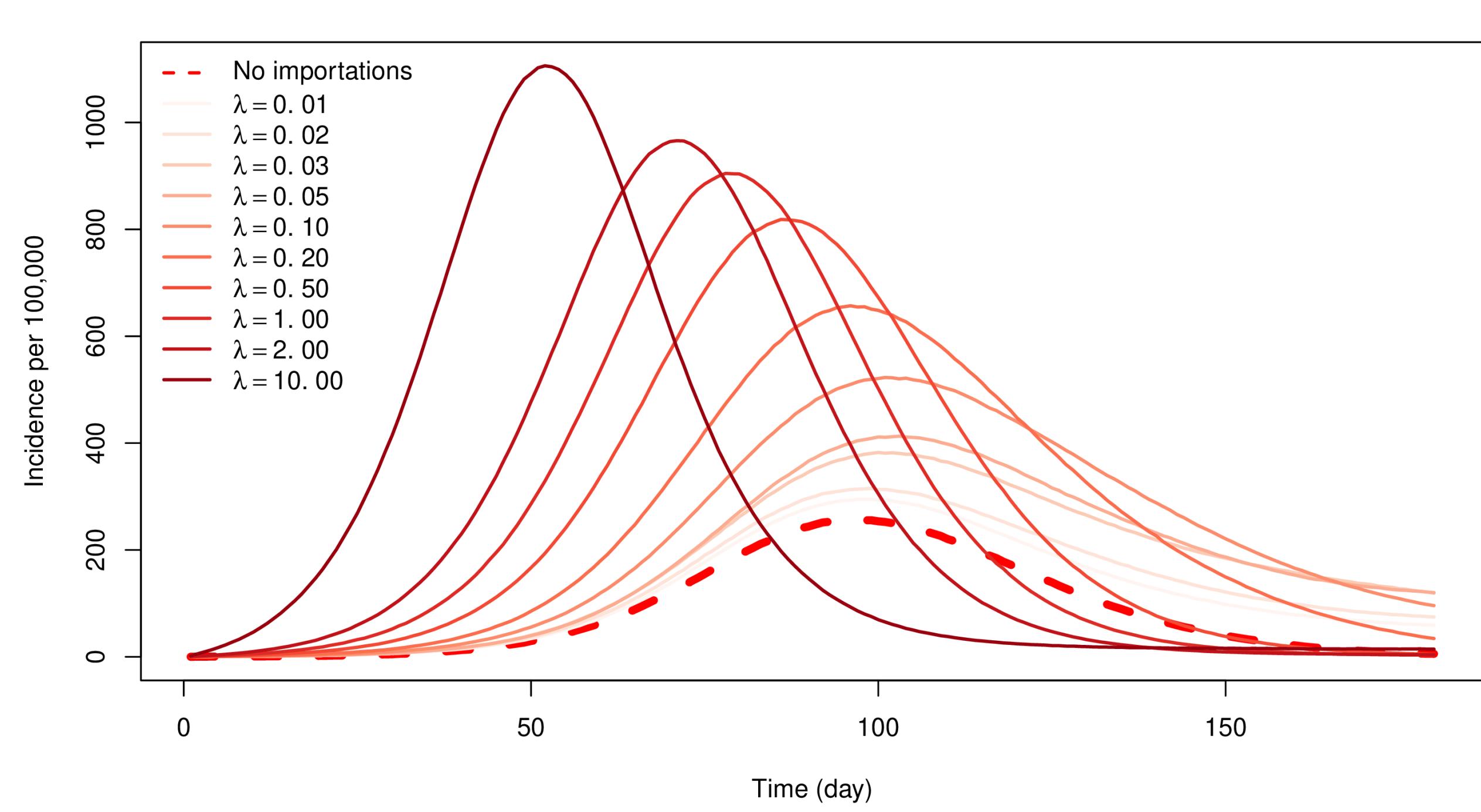
Q:

- How long until novel replaces resident variant in terms of propagation?
- What role do importations play in this?
- How does one diminish role of importations and how useful are measures used to do so?

J. Arino, P.-Y. Boëlle, E.M. Milliken & S. Portet. Risk of COVID-19 variant importation - How useful are travel control measures? *Infectious Disease Modelling*, 2021

S.P Otto, T. Day, J. Arino, C. Colijn *et al.* The origins and potential future of SARS-CoV-2 variants of concern in the evolving COVID-19 pandemic. *Current Biology*, 2021





Travel interruptions



Mur de la Peste in Cabrières-d'Avignon



Progression de la peste

● Foyer (juin 1720)

Espace contaminé

En juin

En août

En septembre

D'octobre à décembre

Été 1721

7 août Date du début de l'épidémie

Axe de propagation

→ Été 1720

→ Automne 1720

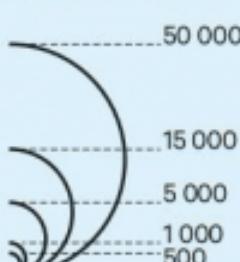
Tentative d'endiguement

— Cordon sanitaire

— Mur de la peste

Mortalité

Nombre de morts :



Taux de mortalité :

Supérieur à 50 %

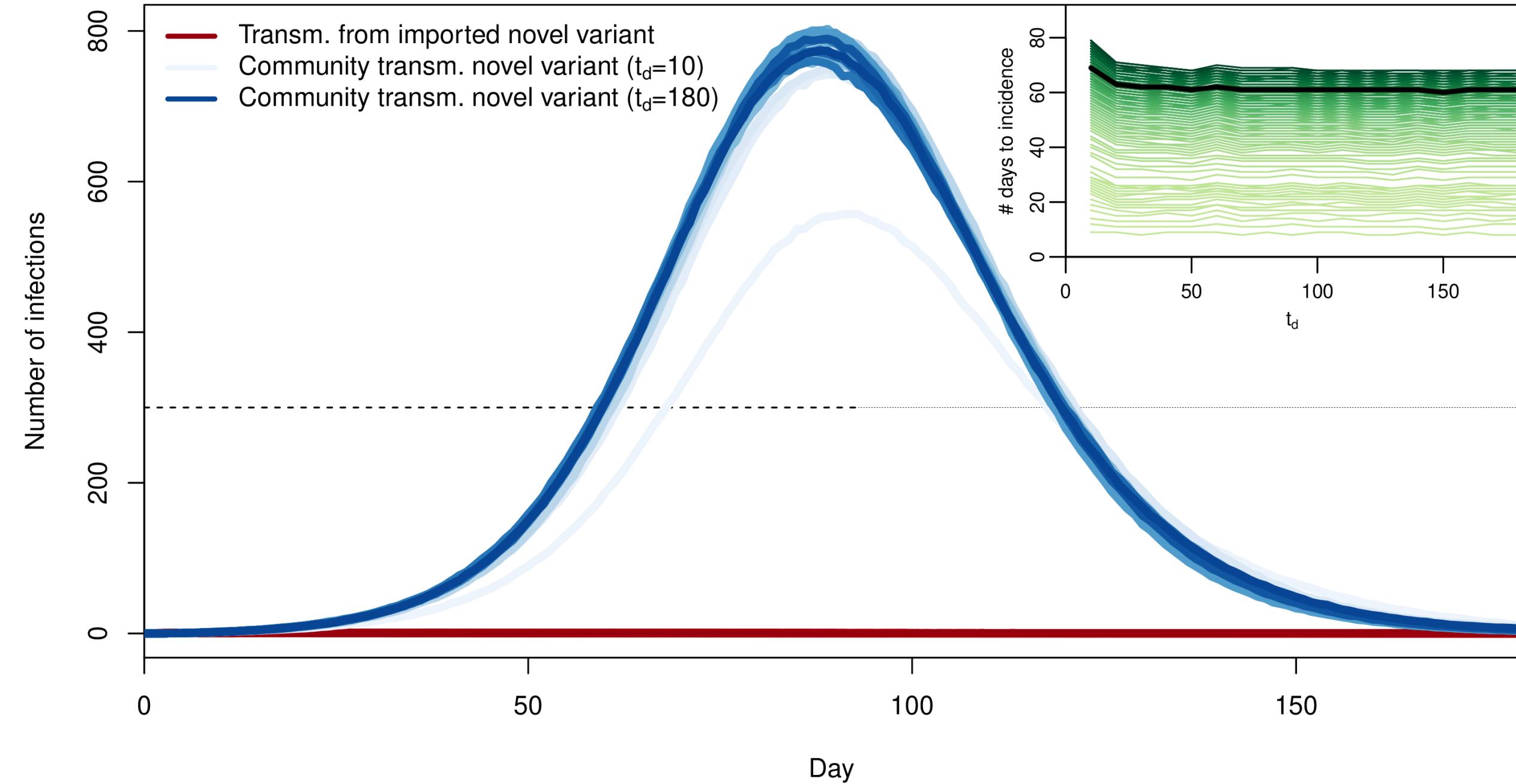
De 10 à 50 %

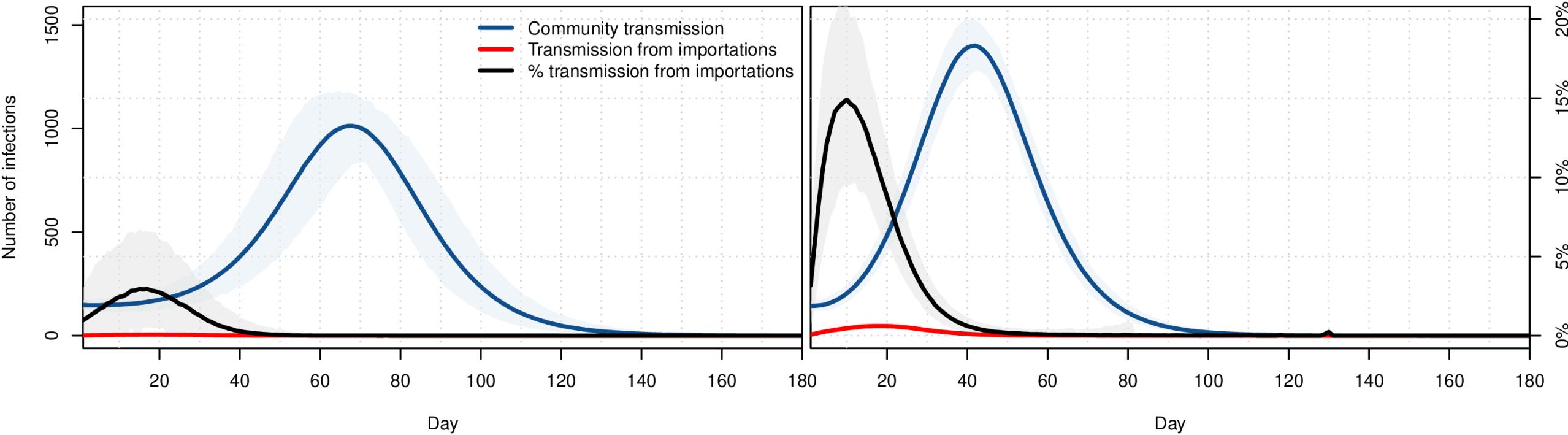
Moins de 10 %

D'après Jean-Noël Biraben,
Les Hommes et la peste,
Mouton, 1975

Légendes Cartographie

20 km





Interruption of travel during first wave

Country	Travel suspension	First_case
Seychelles	2020-03-03	2020-03-14
El Salvador	2020-03-17	2020-03-18
Cape Verde	2020-03-17	2020-03-20
Sudan	2020-03-17	2020-04-05
Marshall Islands	2020-04-22	2020-10-29
Vanuatu	2020-03-20	2020-11-11
North Korea	2020-01-21	Unreported
Turkmenistan	2020-03-20	Unreported
Tuvalu	2020-03-26	

Quarantine

(Quarantine)

Quarantine ≠ Isolation

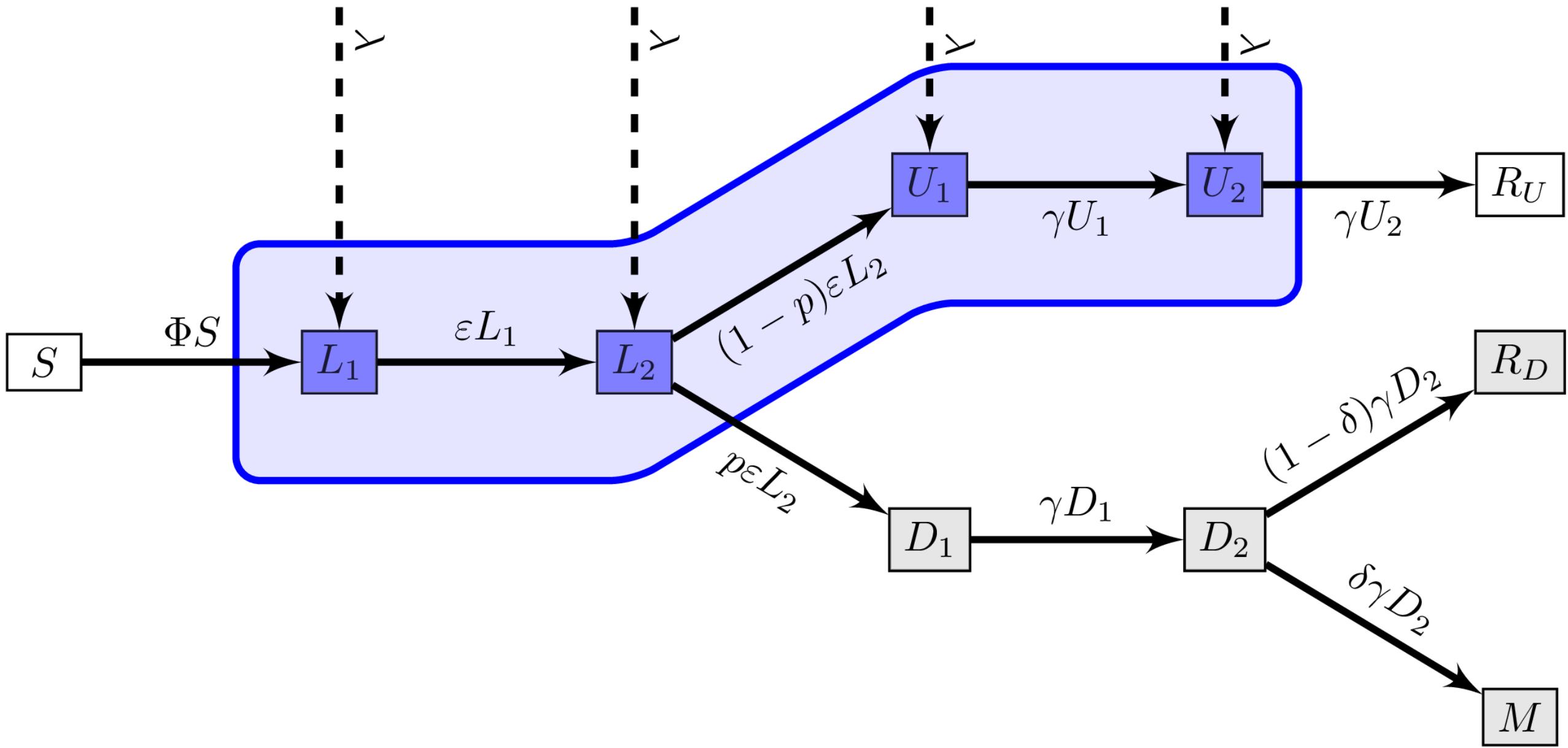
- *Quarantine* is indiscriminate and applies to all incoming flux
- *Isolation* is imposed to known or suspected cases and known contacts
- First used in (the lazarettos of) Dubrovnik in 1377
- Name comes from Venitian *quarantena*

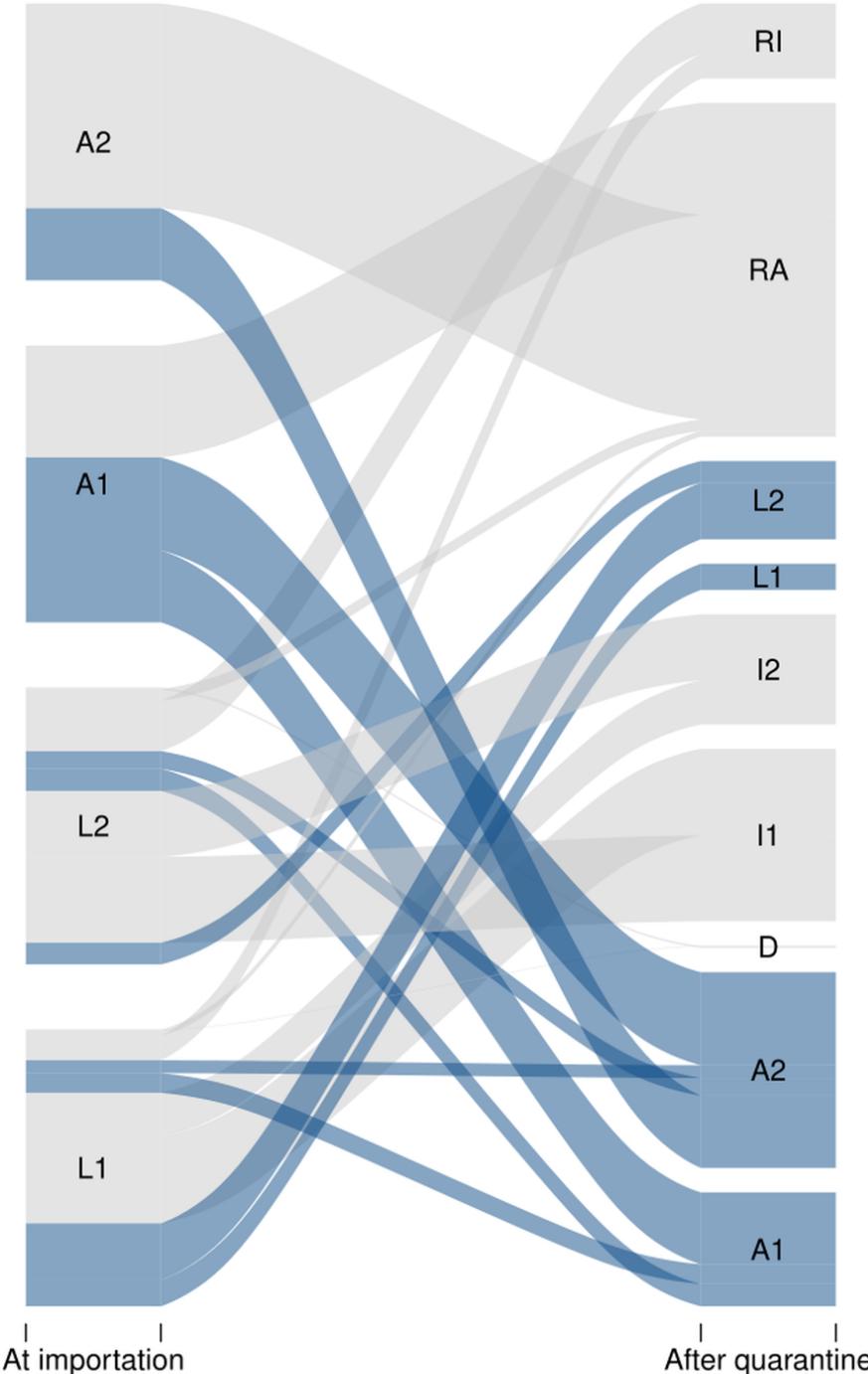


Lazzaretto vecchio

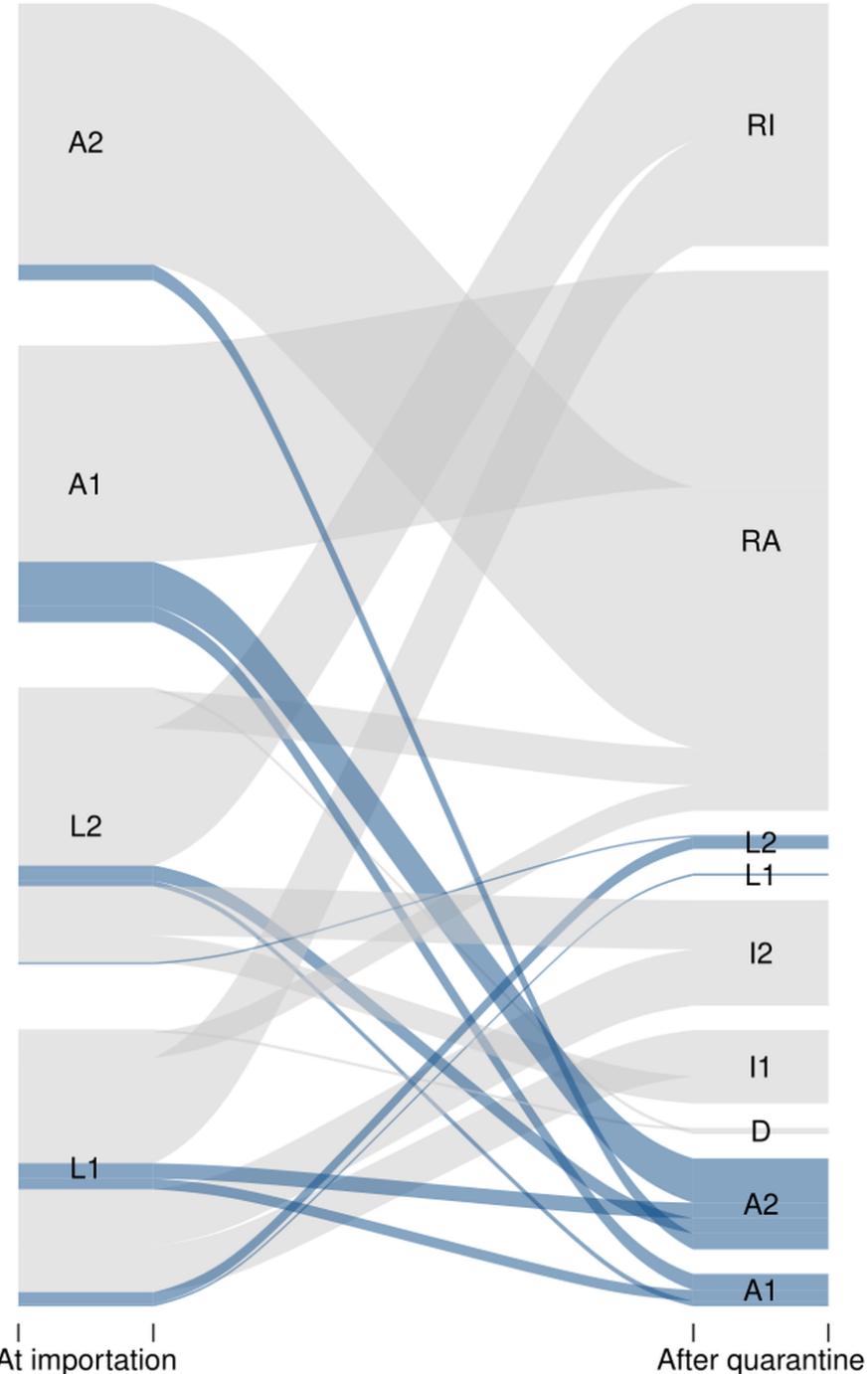
Lazzaretto nuovo







(a) $t_q = 7$ days



(b) $t_q = 14$ days

Effect of quarantine on importation rates

$1/\lambda$ the mean time between case importations, $1/\lambda_q$ the mean quarantine-regulated time between case importations, c the efficacy of quarantine (in %). Then

$$\lambda_q = (100 - c) \times \lambda$$

Suppose $1/\lambda = 5$ days and efficacy of quarantine is 90% at 7 days and 98% at 14 days, respectively

Then $1/\lambda_q = 50$ and 250 days, respectively

Conclusion

- Case importations **will** occur no matter what
- Success of an importation depends on transmissibility of novel vs resident variant
- Travel interruptions are not efficacious at all on average
 - Need to be put in place very early on
- Quarantine is an efficacious tool to control case importations
 - It does not stop spread, but helps slow it down
 - Less stigmatising than travel interruptions
- Problem very quickly switches from input to local control

Emergency response during public health crises

- Get in there to help .. and for the adrenalin
- Get out of there burned out (19-20 hours a day 7 days a week the first two months, down to 80-100 hours/week now)
- Interesting and frustrating at the same time
- You are one of many being consulted. Don't expect anything you say to be used
- Expect wild goose chases, many aborted publications (*it's not relevant anymore!*)
- You sometimes get *insider* information and data but are often sworn to secrecy

Merci / Miigwech / Thank you / Xièxie