Mathematical models for disease propagation

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PROCC – FIOCRUZ

Colaboradores(as)

Links do Grupo de Métodos Analíticos em Vigilância Epidemiológica (MAVE):

Repositório: http://bit.ly/mave-repo
Site do MAVE: https://covid-19.procc.fiocruz.br/
Relatórios COVID-19: https://bit.ly/mave-covid19-relatorios
Dados processados: http://bit.ly/mave-covid19-dados

InfoGripe:

Site: http://info.gripe.fiocruz.br
Boletins do InfoGripe: http://bit.ly/mave-infogripe
Dados processados: https://bit.ly/mave-infogripe-dados

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Immediate questions from epidemics

- How many cases should I expect?
- What’s the mortality rate?

...not so much, but as fundamental

- What makes a disease “worst” than others?
- What is the role of agents’ interactions?
- Does it confers permanent, partial or no immunity at all?
- Does sociodemographics matter?
- What about mobility?
- Climate?
- ...

Case example: SARS x Influenza

- Both are respiratory diseases
- Both transmitted by shared environment (airborne and direct contact with surface deposition)

SARS

- Accumelated number of probable cases, from 2002-09-01 to 2003-07-31: 8096 worldwide

WHO, Global Alert and Response (GAR) - http://www.who.int/csr/sars/country/table2004_04_21/en/index.html

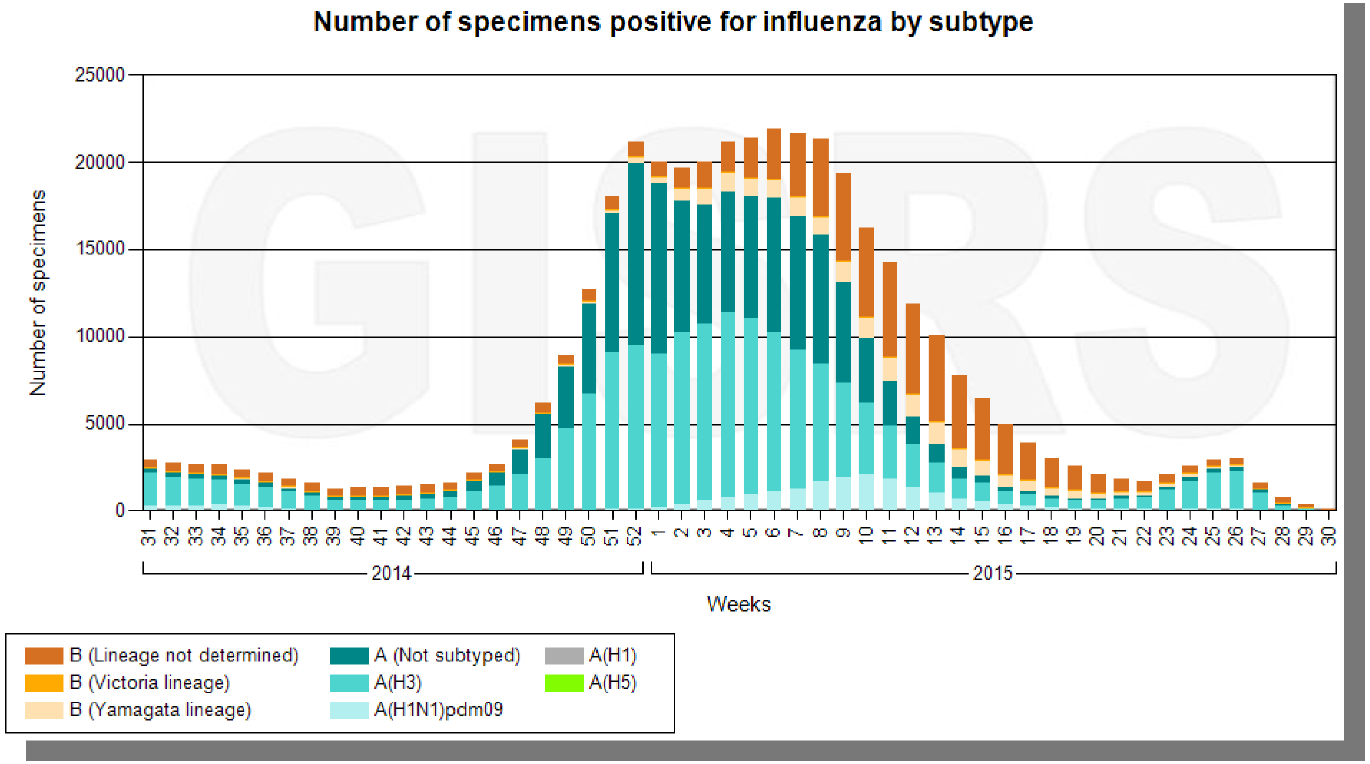
Influenza

- More than 20000 positive samples worldwide in the first week of 2015 alone

WHO, FluNet, GISRS. www.who.int/flunet

- More than 9500 positive samples during the year of 2016 in Brazil from SARI data alone.

SINAN, InfluenzaWeb, InfoGripe. info.gripe.fiocruz.br



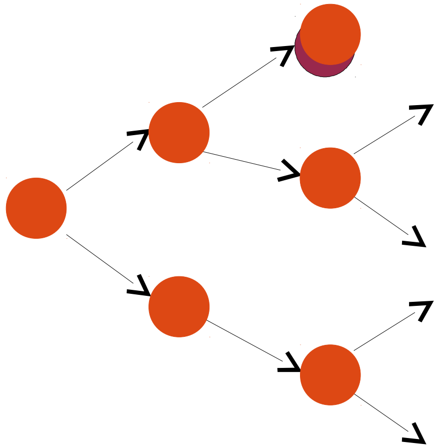
Outbreaks and the *basic reproductive number*, R_0

R_0: average number of secundary cases from a single infective in a fully susceptible population.

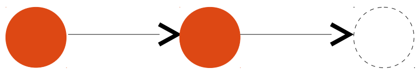
Outbreaks and the *basic reproductive number, R_0*

R_0: average number of secundary cases from a single infective in a fully susceptible population.

$R_0 > 1$

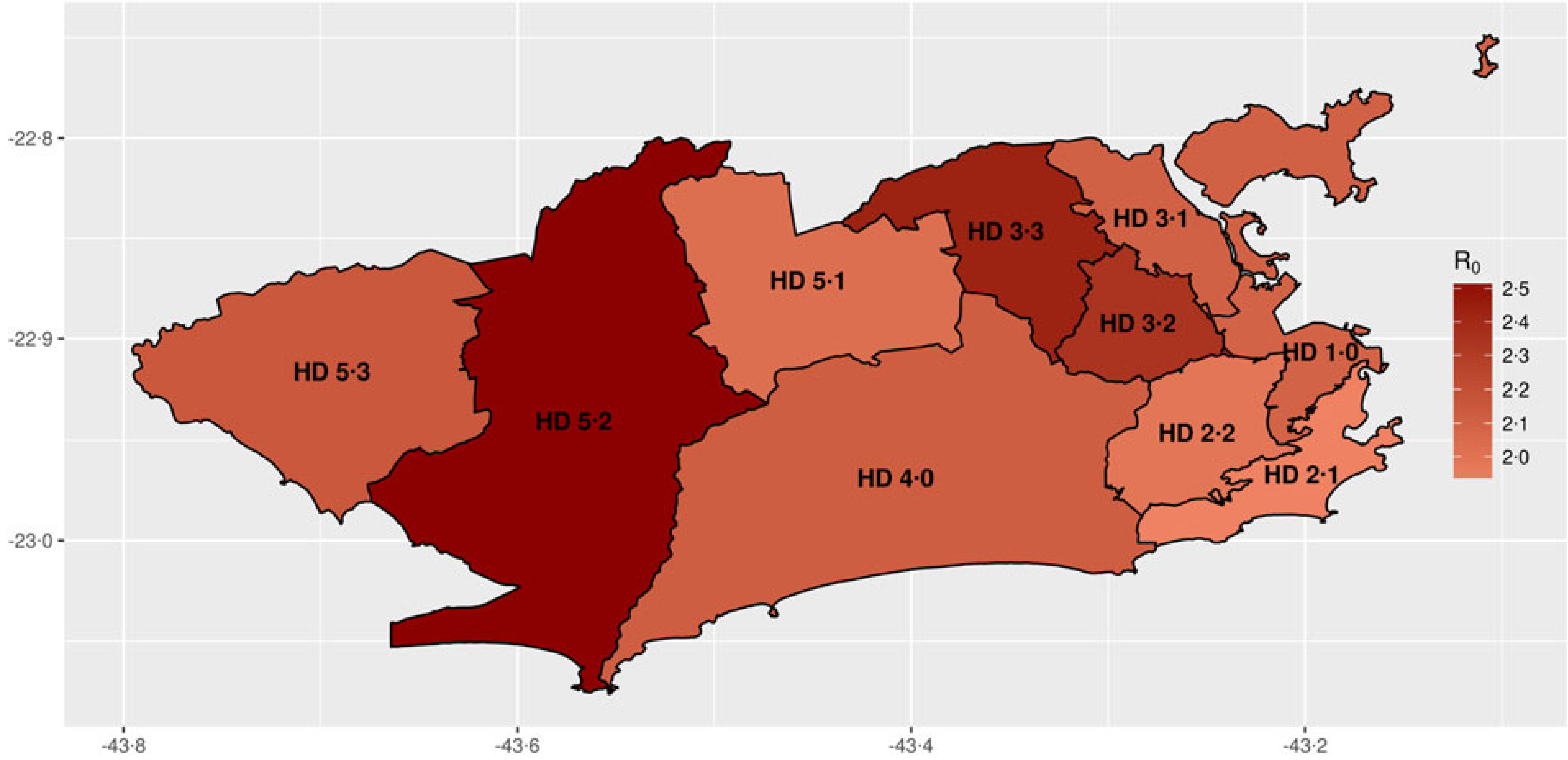


$R_0 < 1$



Example: Zika and Dengue outbreaks in Rio de Janeiro

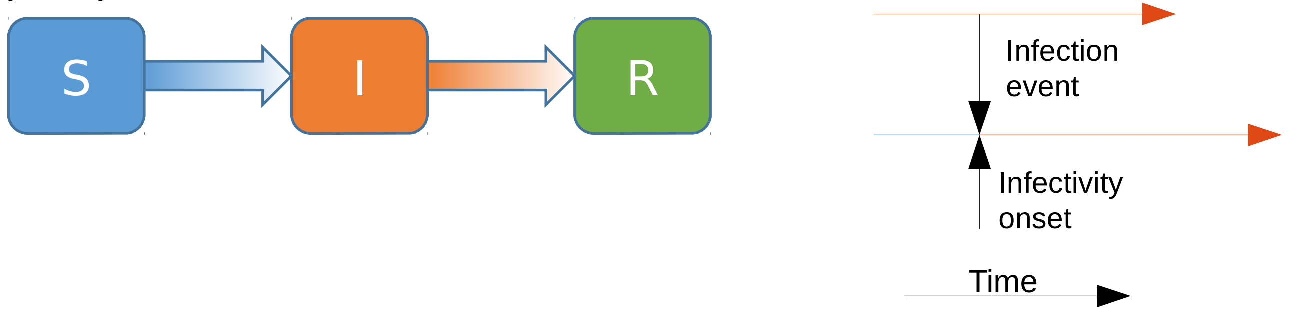
Zika in Rio de Janeiro: Assessment of basic reproduction number and comparison with dengue outbreaks. *Epidemiol. Infect.*, doi:10.1017/S0950268817000358



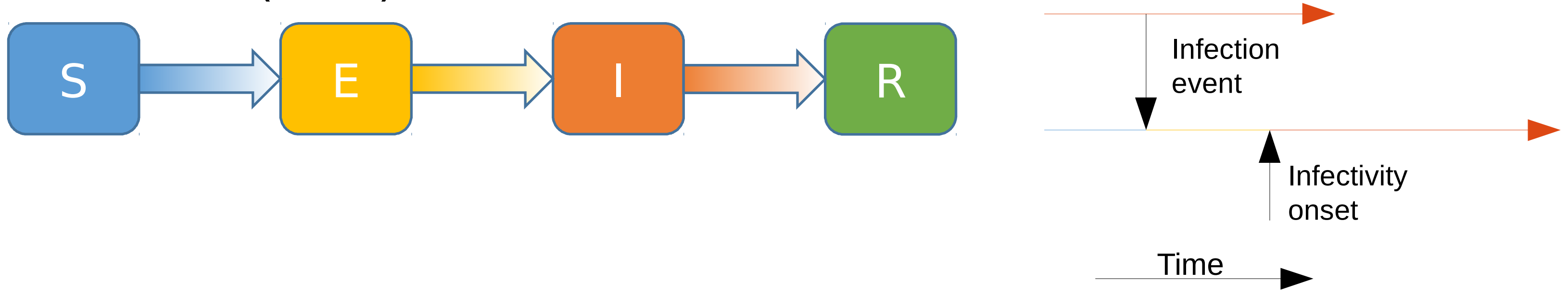
	R_0 [95% CI]
Zika	2.33[1.97-2.97]
Dengue 2002	1.70 [1.50-2.02]
Dengue 2012	1.25[1.18-1.36]
Zika u/ DEN2002	2.45[1.57-3.65]
Zika u/ DEN2012	1.82[1.19-2.68]

Compartimental models

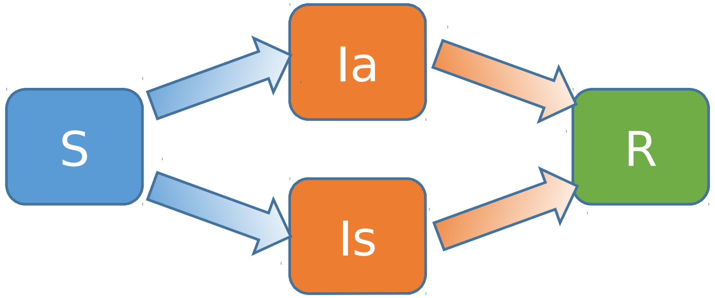
Susceptible – Infective – Recovered (SIR)

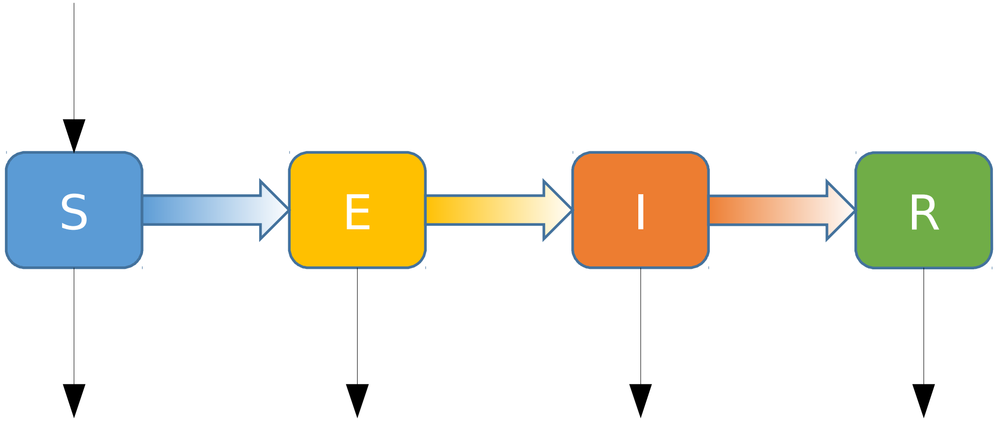


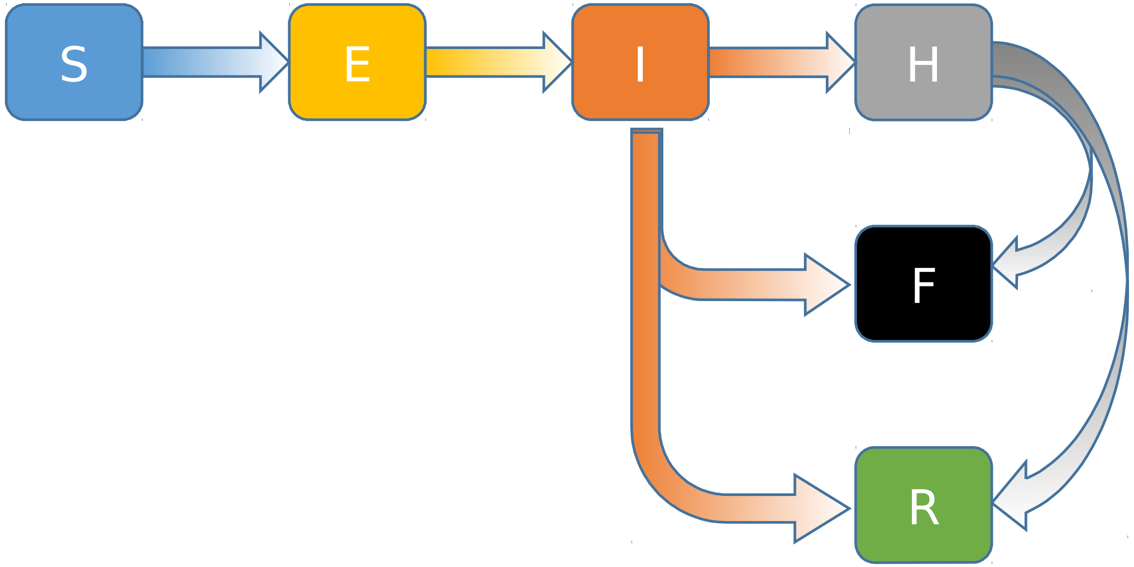
Susceptible – Infected ("Exposed") – Infective – Recovered (SEIR)



Compartimental models







Mathematical representation

- Deterministic:
System of differential equations

$$\frac{dS}{dt} = -\beta \frac{SI}{N}$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - \alpha I$$

$$\frac{dR}{dt} = \alpha I$$

$$R_0 = {}^{\beta}/_{\alpha} = \beta\tau$$

(Kermack & McKendrick, 1927)

- Stochastic:
Transition rates

Transition	Transition rate
(S,E) $\rightarrow$ (S-1, E+1)	$(\beta_I \mathrm{SI} + \beta_H \mathrm{SH} + \beta_F \mathrm{SF})/\mathrm{N}$
(E,I) $\rightarrow$ (E-1, I+1)	$\alpha \mathrm{E}$
(I,H) $\rightarrow$ (I-1, H+1)	$\gamma_h \theta_1 \mathrm{I}$
(H,F) $\rightarrow$ (H-1, F+1)	$\gamma_{dh} \delta_2 \mathrm{H}$
(F,R) $\rightarrow$ (F-1, R+1)	$\gamma_f \mathrm{F}$
(I,R) $\rightarrow$ (I-1, R+1)	$\gamma_i (1-\theta_1)(1-\delta_1)\mathrm{I}$
(I,F) $\rightarrow$ (I-1, F+1)	$\delta_1 (1-\theta_1)\gamma_d \mathrm{I}$
(H,R) $\rightarrow$ (H-1, R+1)	$\gamma_{ih}(1-\delta_2)\mathrm{H}$

$$R_0 = R_I + R_H + R_F$$

$$R_I = \frac{\beta_I}{\Delta_I}$$

$$R_H = \frac{\theta \beta_H}{\Delta_H}$$

$$R_F = \frac{\delta \beta_F}{\Delta_F}$$

(Legrand, 2004)

Mathematical representation

Characteristic times following an exponential distribution → homogeneous transition rate

$$\frac{dS}{dt} = -\beta\frac{SI}{N}$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - \alpha I$$

$$\frac{dR}{dt} = \alpha I$$

$$R_0 = {}^{\beta}/_{\alpha} = \beta\tau$$

(Kermack & McKendrick, 1927)

Characteristic times with explicit distributions → integro-differential system

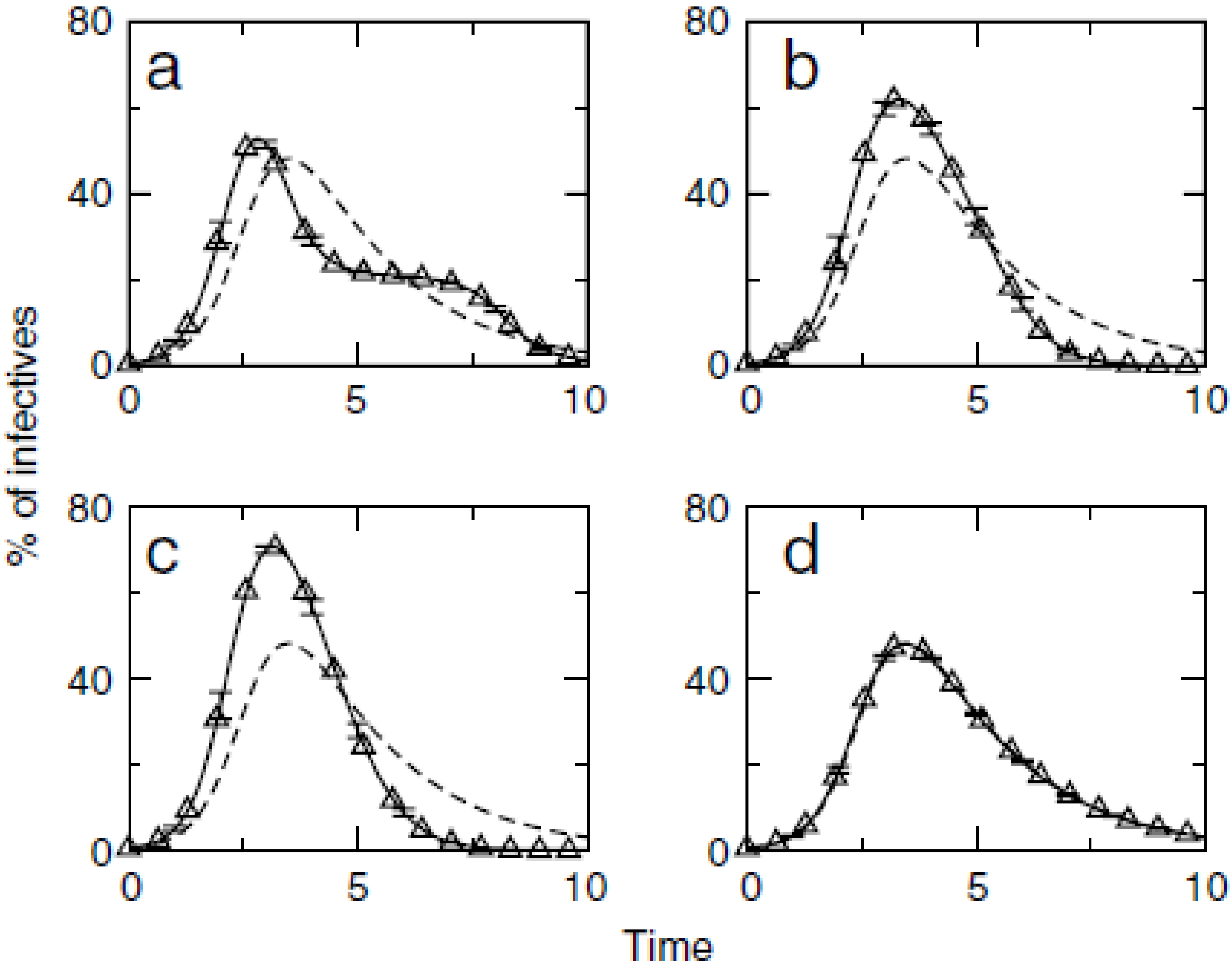
$$\frac{dS}{dt} = -\beta\frac{SI}{N}$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - \frac{\beta}{N}\int S(t-\tau)I(t-\tau)p(\tau)d\tau$$

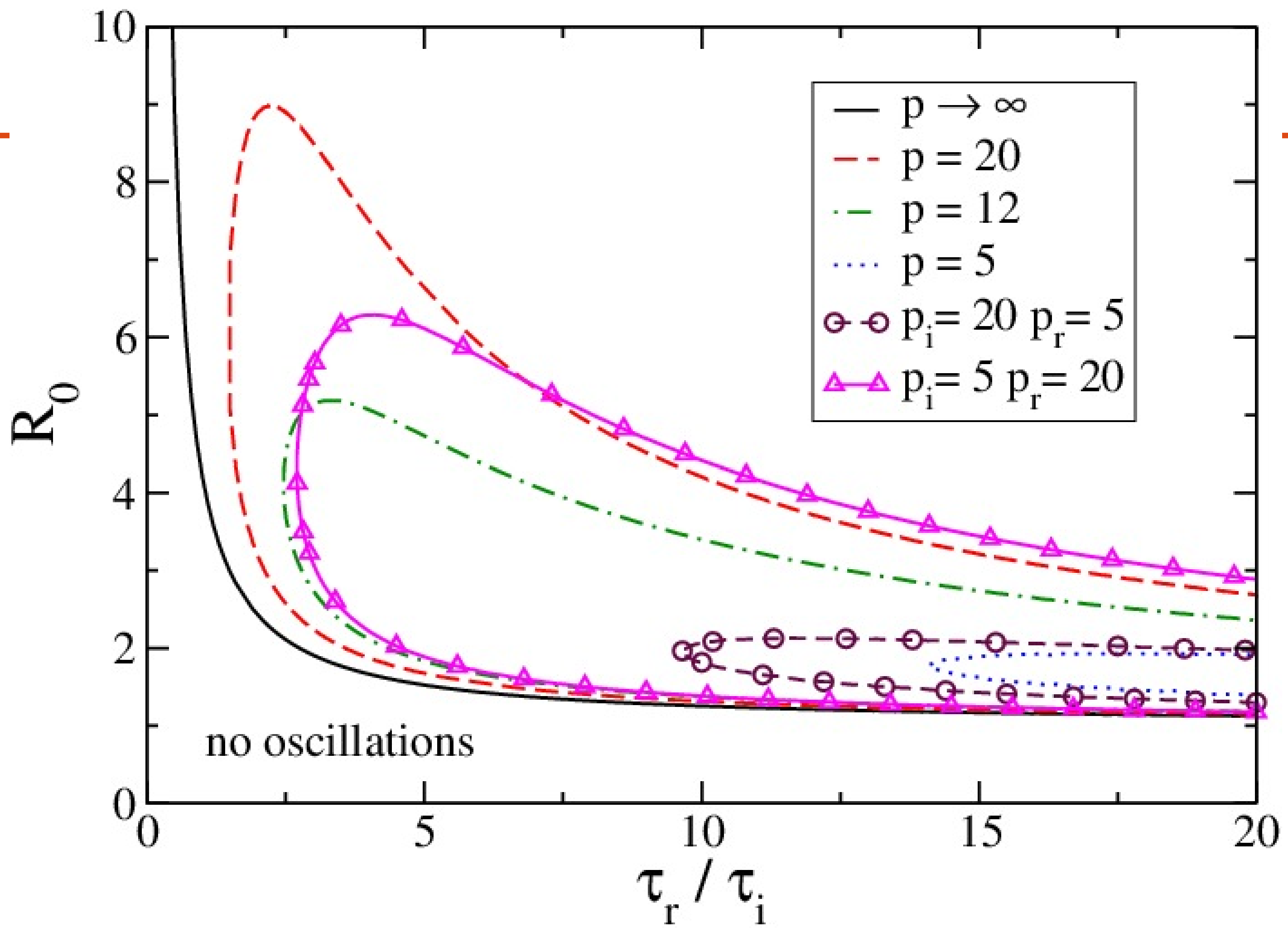
$$\frac{dR}{dt} = \frac{\beta}{N}\int S(t-\tau)I(t-\tau)p(\tau)d\tau$$

$$\boxed{R_0 = {}^{\beta}/_{\alpha} = \beta\tau}$$

For an SIR model without “vital dynamics”, the epidemic threshold does not depend on the distribution, only on its mean



(Gomes & Gonçalves, 2009)



Modelo SIRS com distribuições explícitas para o período de infecção e período de imunidade

(Gonçalves, Abramson, Gomes, 2011)

$$\frac{ds}{dt} = -\beta si + \beta \int_0^t H(v) \int_0^{t-v} G(u)s(t-u-v)i(t-u-v)du\,dv$$

$$\frac{di}{dt} = \beta si - \beta \int_0^t G(u)s(t-u)i(t-u)du$$

Sociodemographic aspects

Sociodemographics

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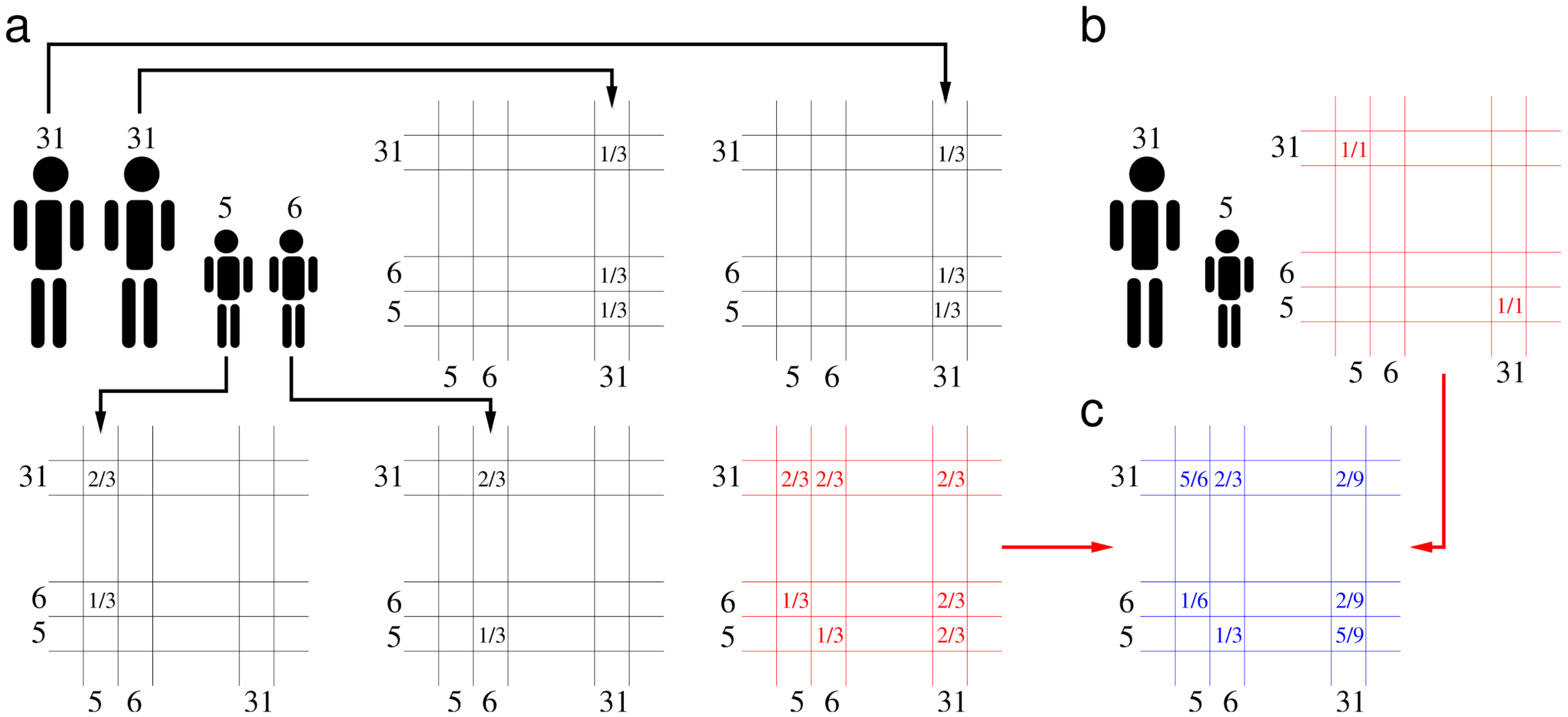
- Age distribution
- Household composition ("family" structure)
- Educational structure (age-dependent levels, frequency)
- Workplace structure (number and age of workers distribution)

Agent interactions



Fumanelli et al,
PLoS Comput. Biol., 2012

Mistry et al.,
Nature Communications,
2021.

$$S_i\lambda_i = \sum_j S_i\beta_{ij}M_{ij}I_j/N_j$$

$$M_{ij} = \sum_{K\in\{H,S,W,C\}} \alpha_K M_{ij}^K$$

Interactions at workplaces, educational centers, leisure areas, household, ..., can define transmission settings.

Each of those settings can have especific characteristics that confers particular interaction rates that can enhance or hinder transmission.

All of that can be modelled mathematically.

Sinthetic populations

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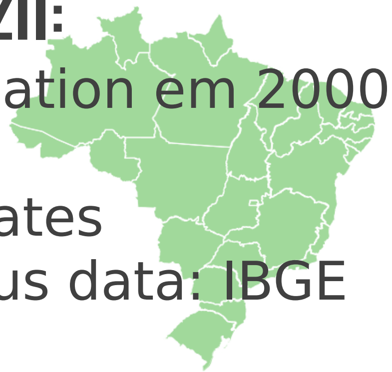
Argentina:

- Population in 2000 ~ 35mi.
- 23 provinces
- Census data: INDEC

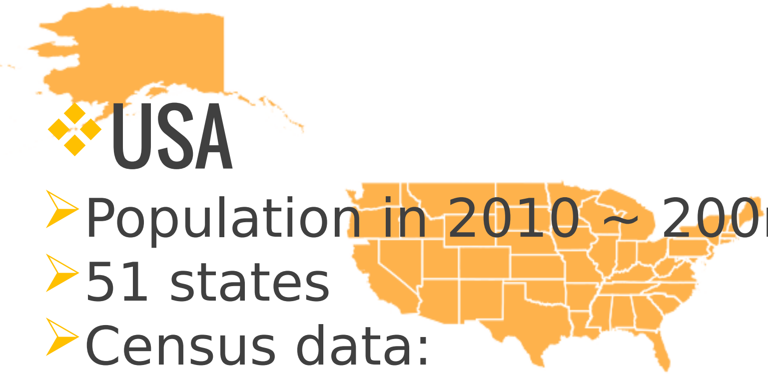


Brazil:

- Population em 2000 ~ 168mi.
- 27 states
- Census data: IBGE

Mexico:

- Population in 2005 ~ 100mi.
- 33 states
- Census data: INEGI



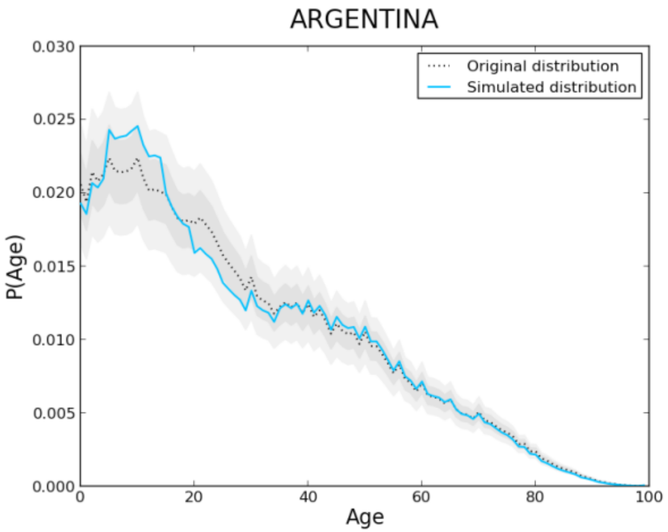
USA

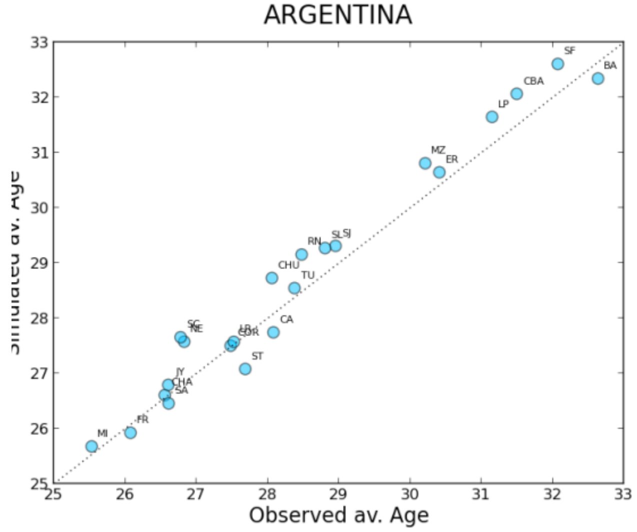
- Population in 2010 ~ 200mi.
- 51 states
- Census data: AmericanFactFinder

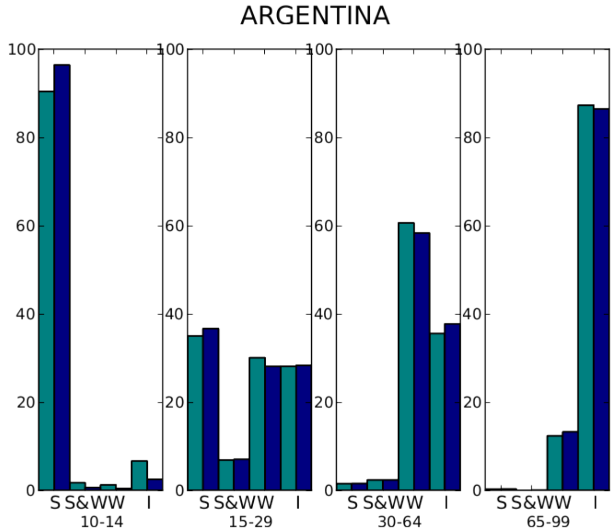
Age distribution

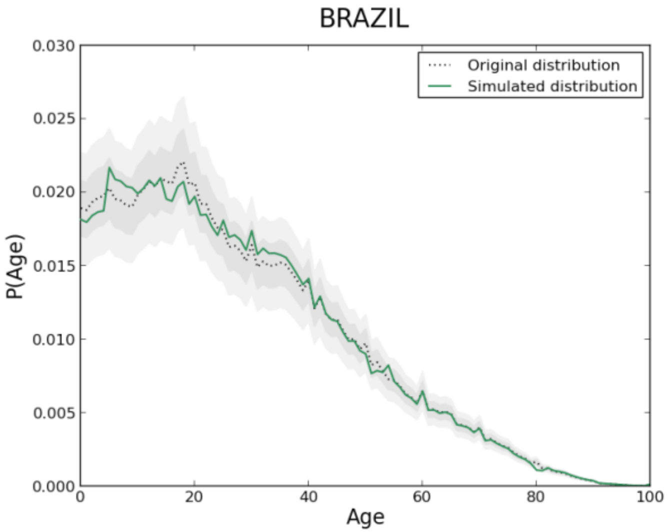
Average

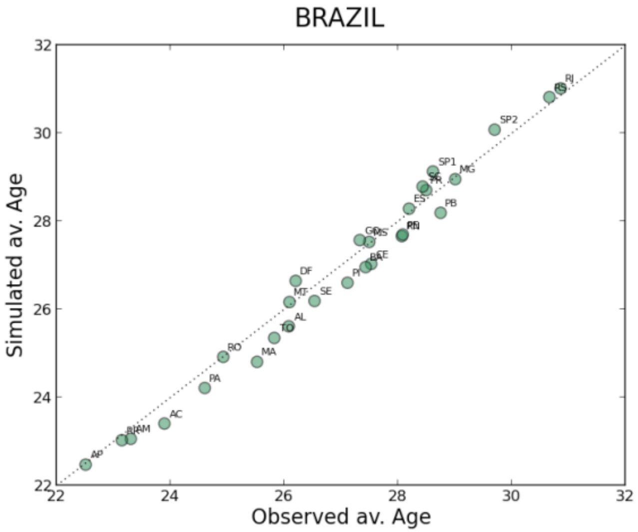
Occupation

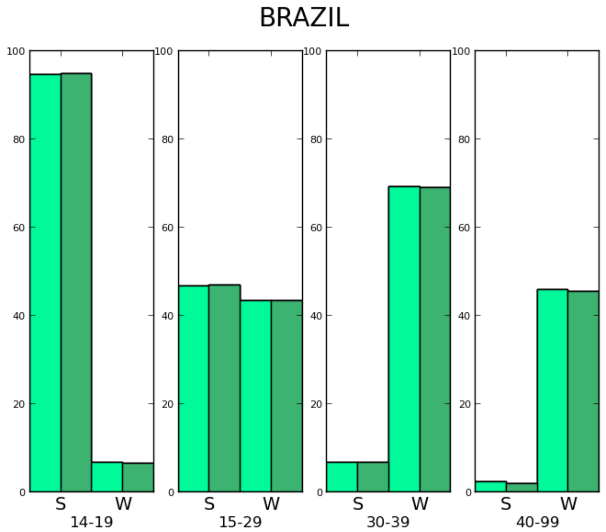




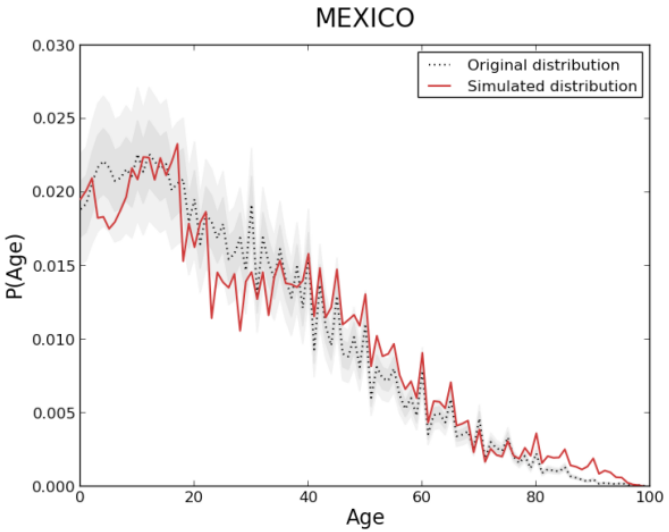


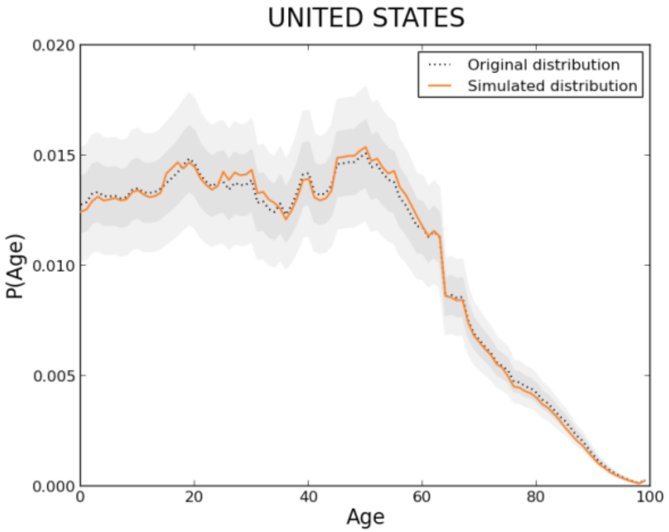




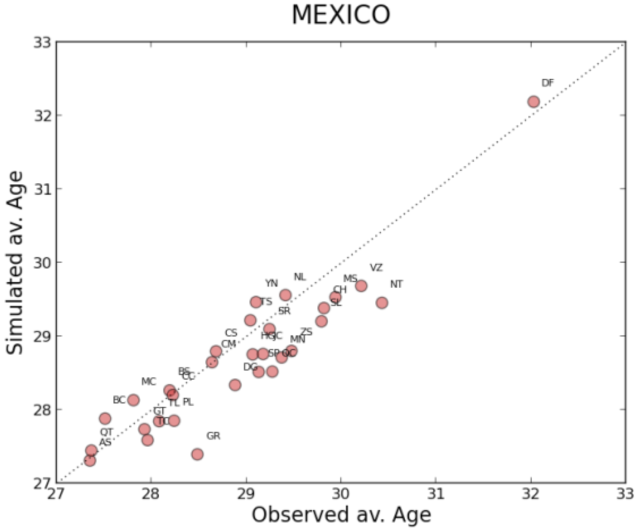


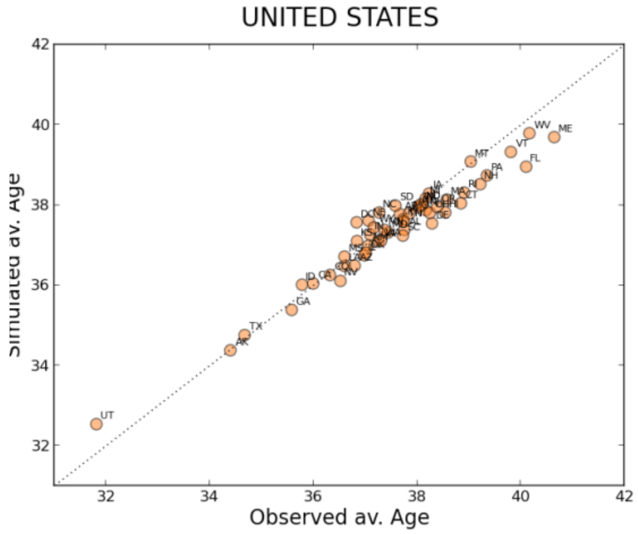
Age distribution



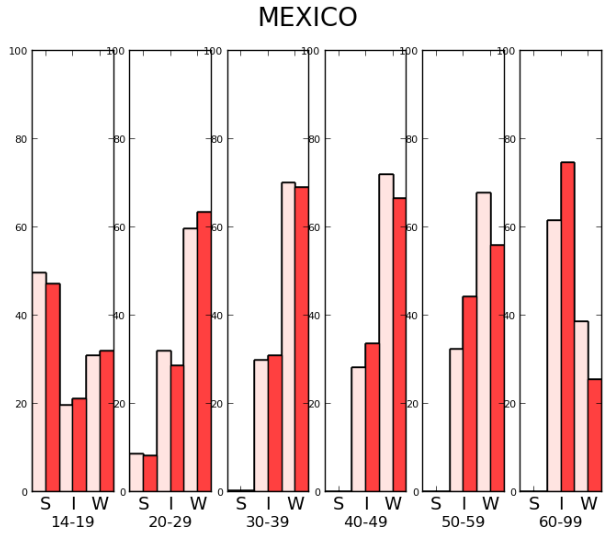


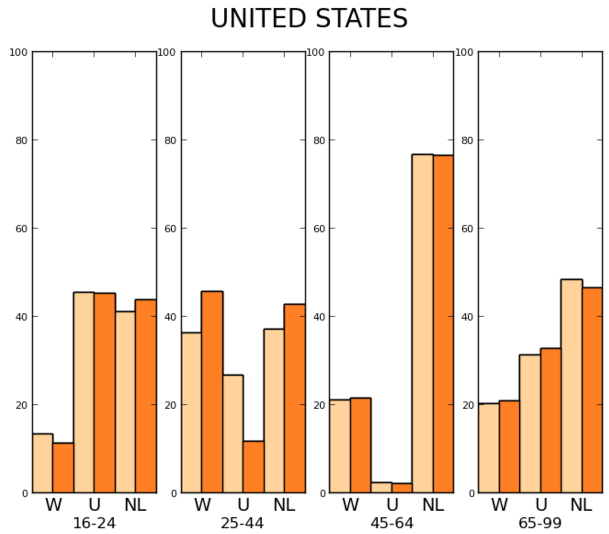
Average

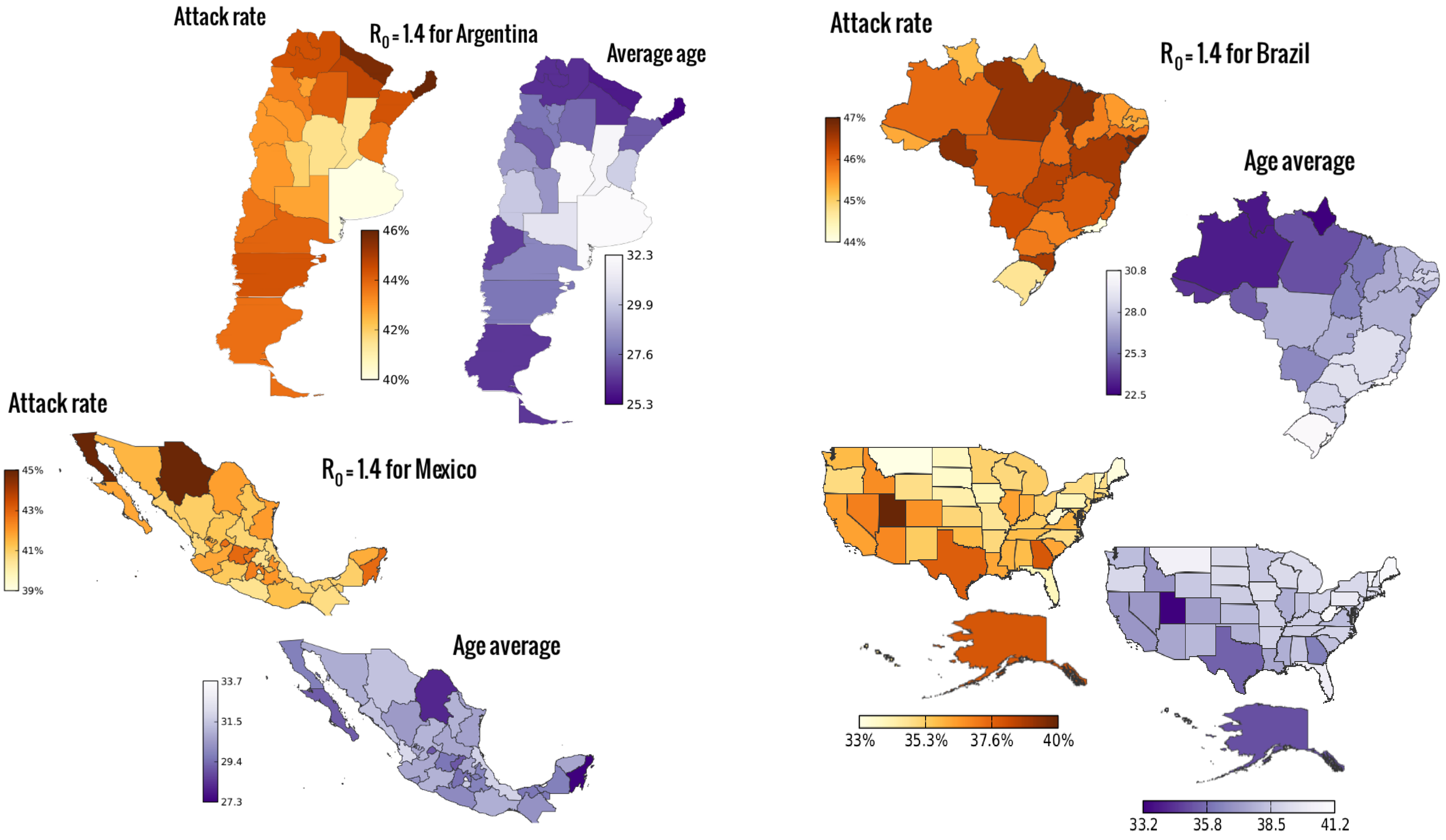




Occupation

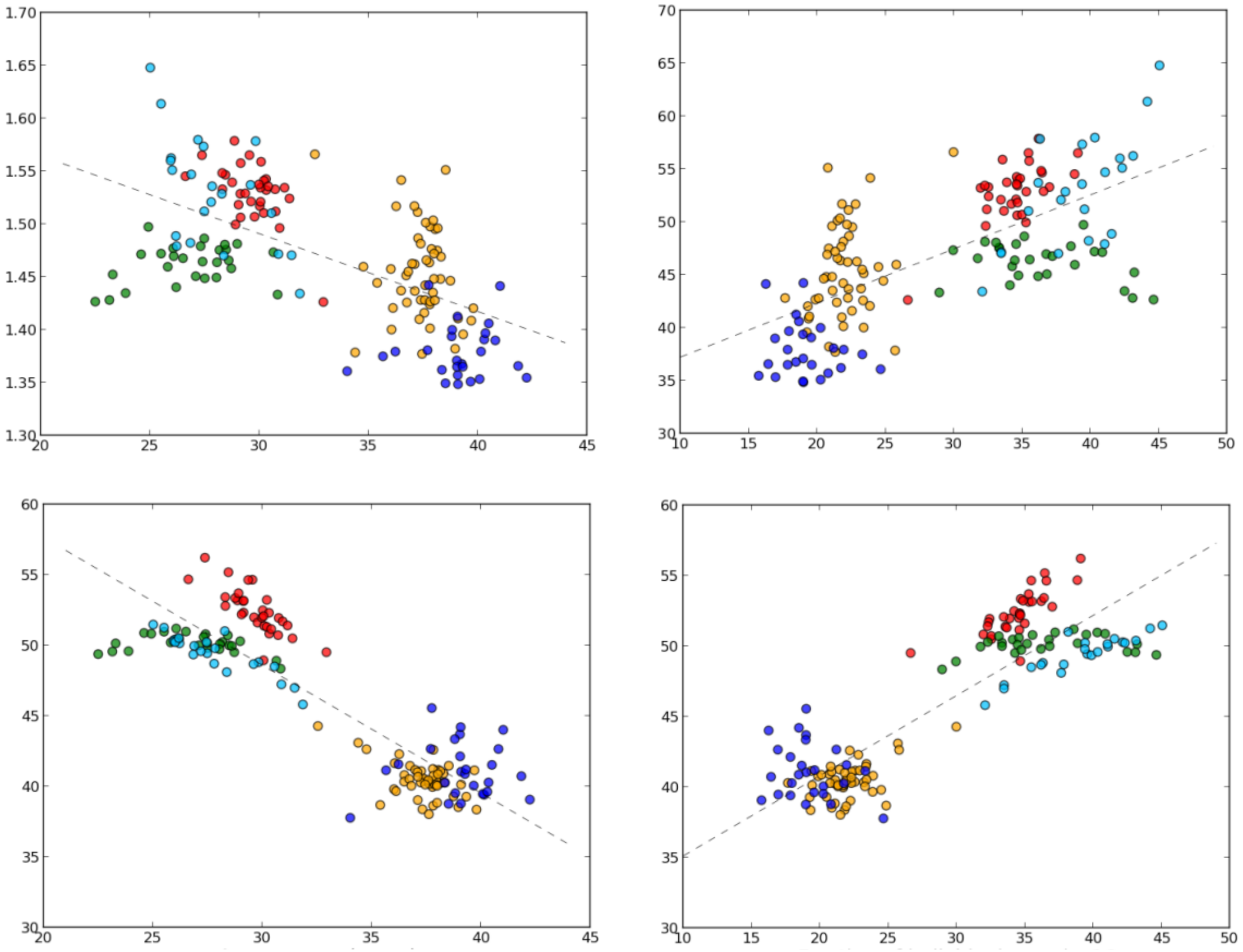





Attack rate
R_0 = 1.4 for Argentina
Average age
46%
44%
42%
40%
32.3
29.9
27.6
25.3
Attack rate
R_0 = 1.4 for Brazil
47%
46%
45%
44%
Age average
30.8
28.0
25.3
22.5
Attack rate
R_0 = 1.4 for Mexico
45%
43%
41%
39%
Age average
33.7
31.5
29.4
27.3
33%
35.3%
37.6%
40%
33.2
35.8
38.5
41.2

R_0

Attack rate (%)

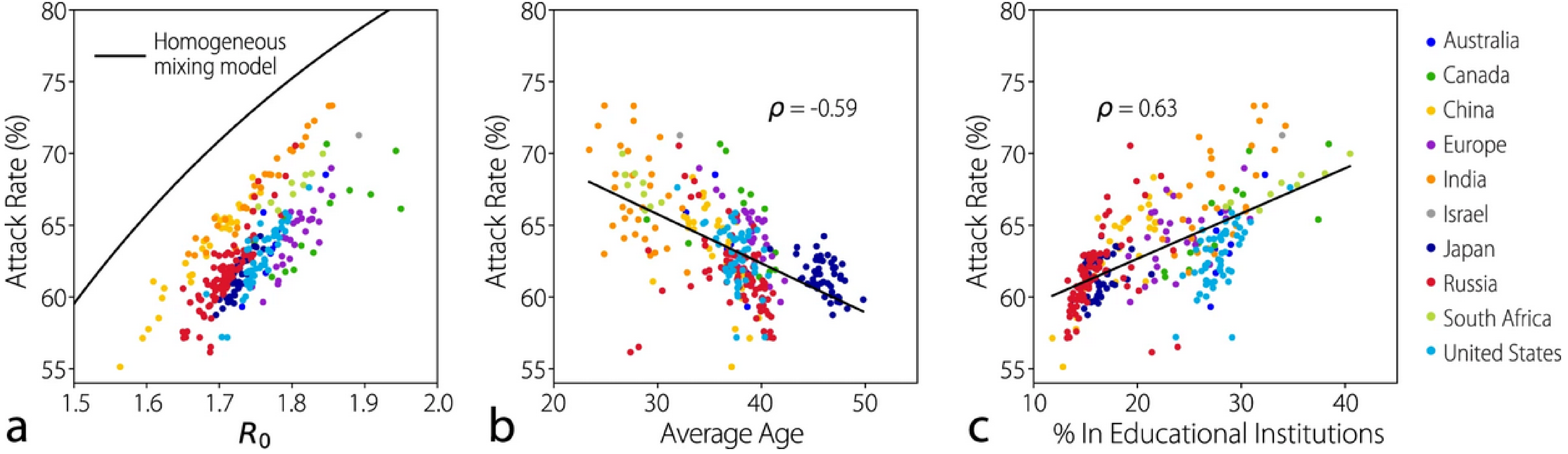


Age average

<16yo (%)

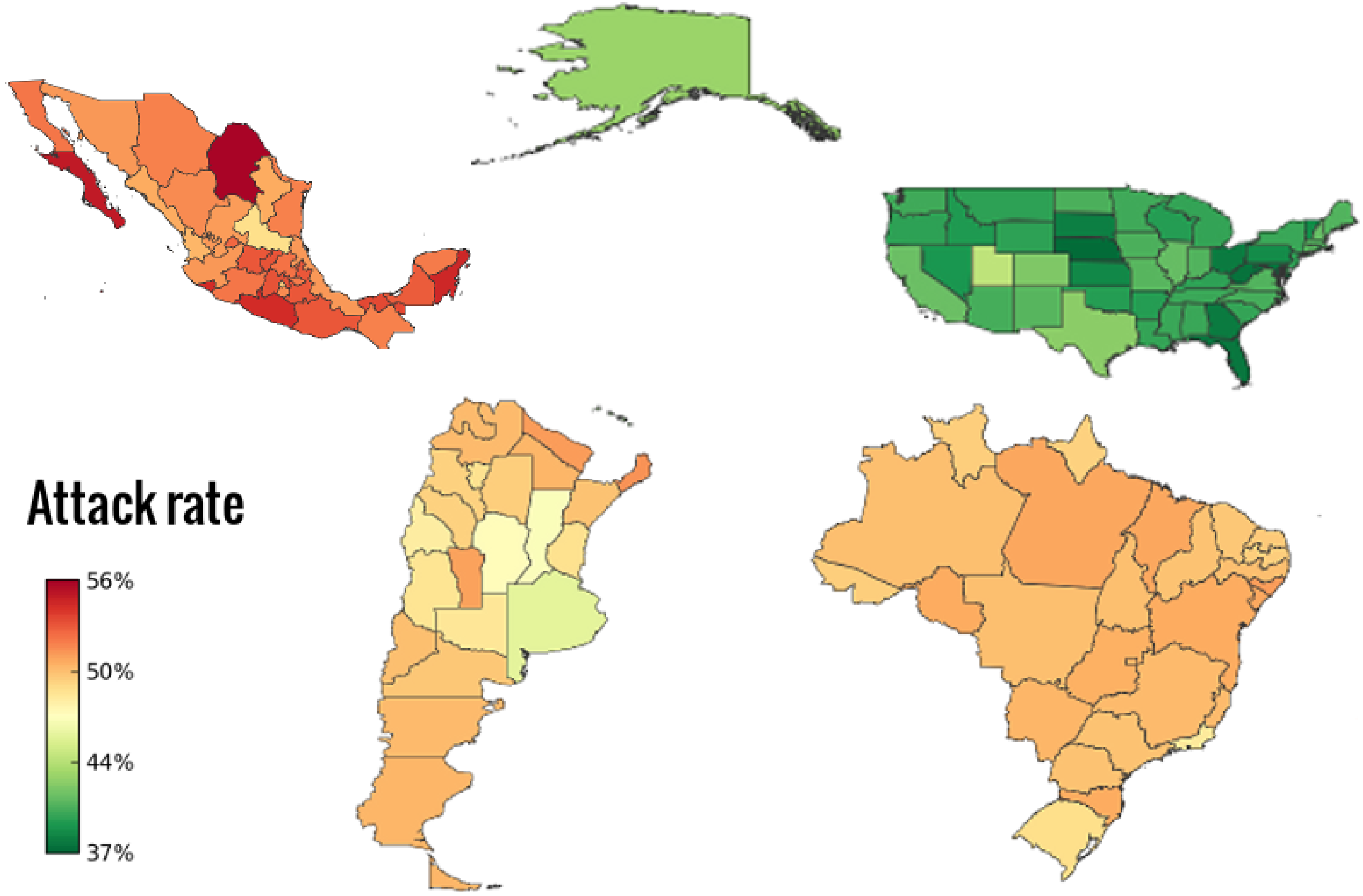
Fig. 6: Epidemic impact.

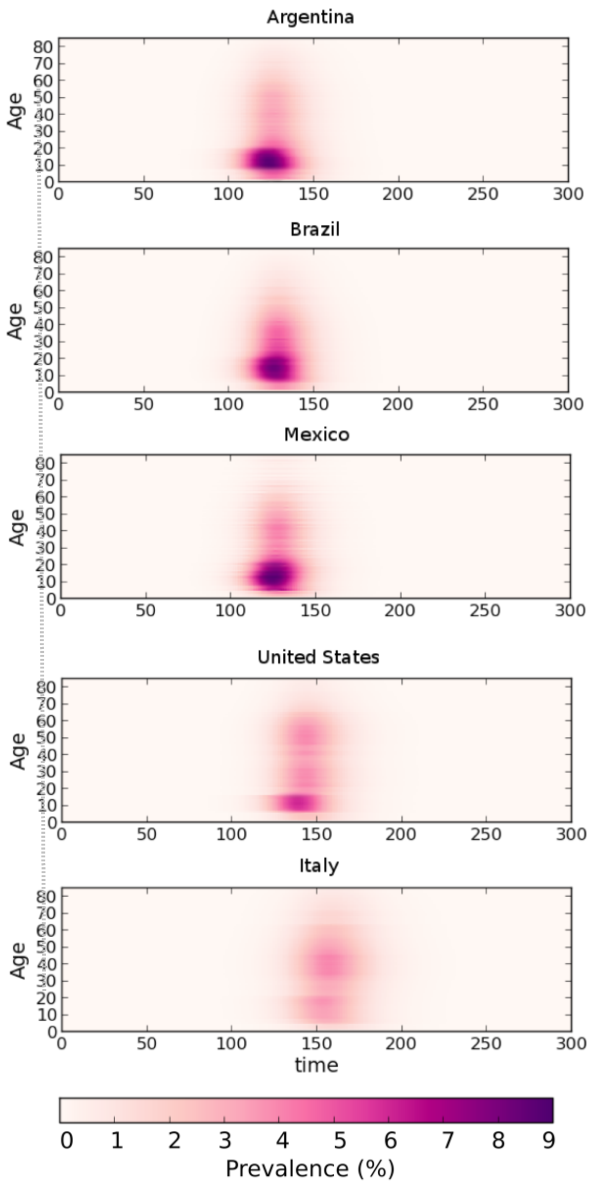
From: Inferring high-resolution human mixing patterns for disease modeling



a Scatter plot of the attack rate and the reproduction number R_0 from an age-structured SIR model using the contact matrix for each subnational location. European countries are included. The black line shows the results of the classic homogeneous mixing SIR model (no age groups). **b** Scatter plot of attack rates and the average age in each location. The black line represents the best-fitting linear model demonstrating a negative linear correlation between attack rates and the average age of the population. **c** Scatter plot of attack rates and percentage of the population attending educational institutions in each location. The black line represents the best-fitting linear model.

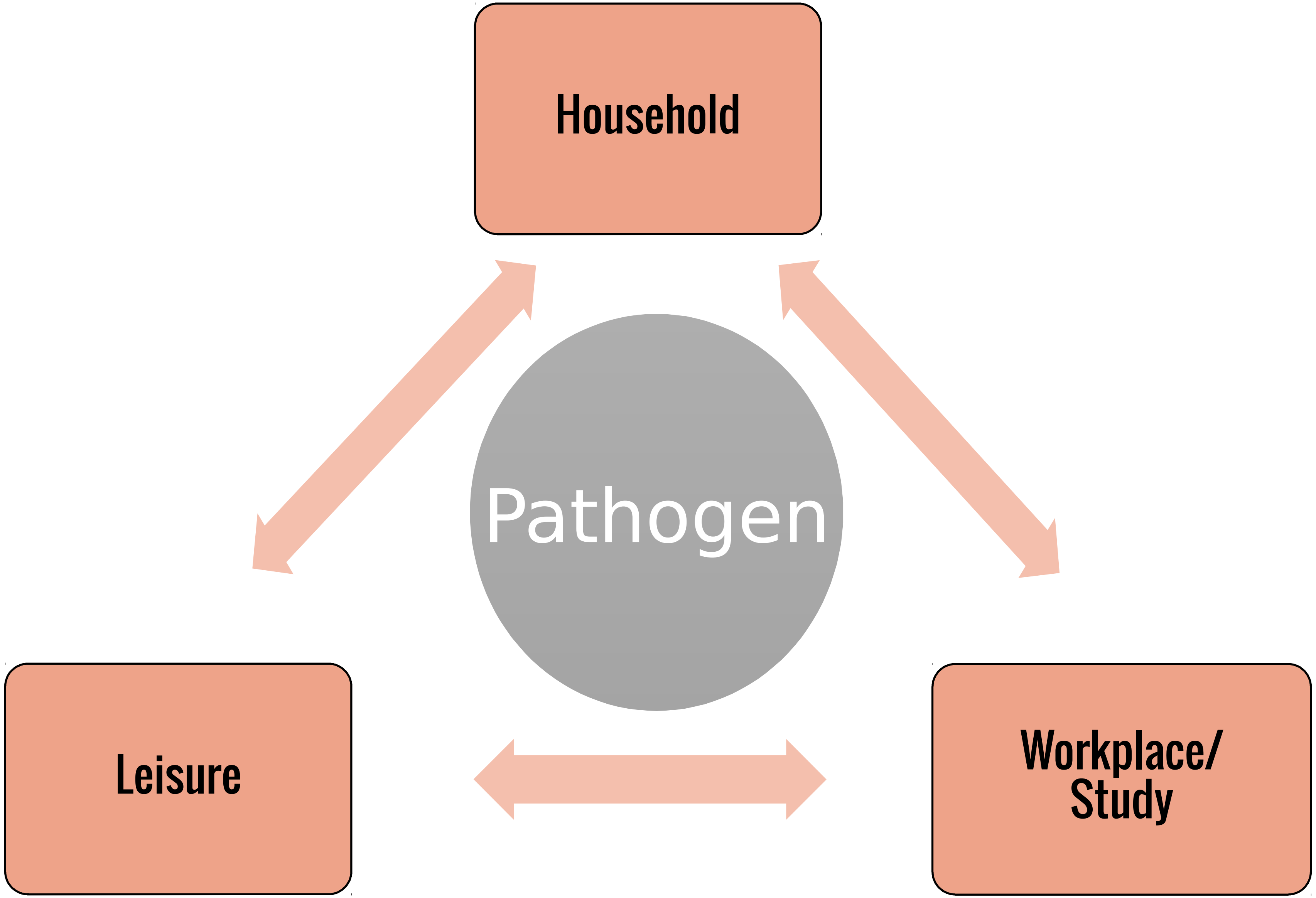
R_0 = 1.4 for Europe



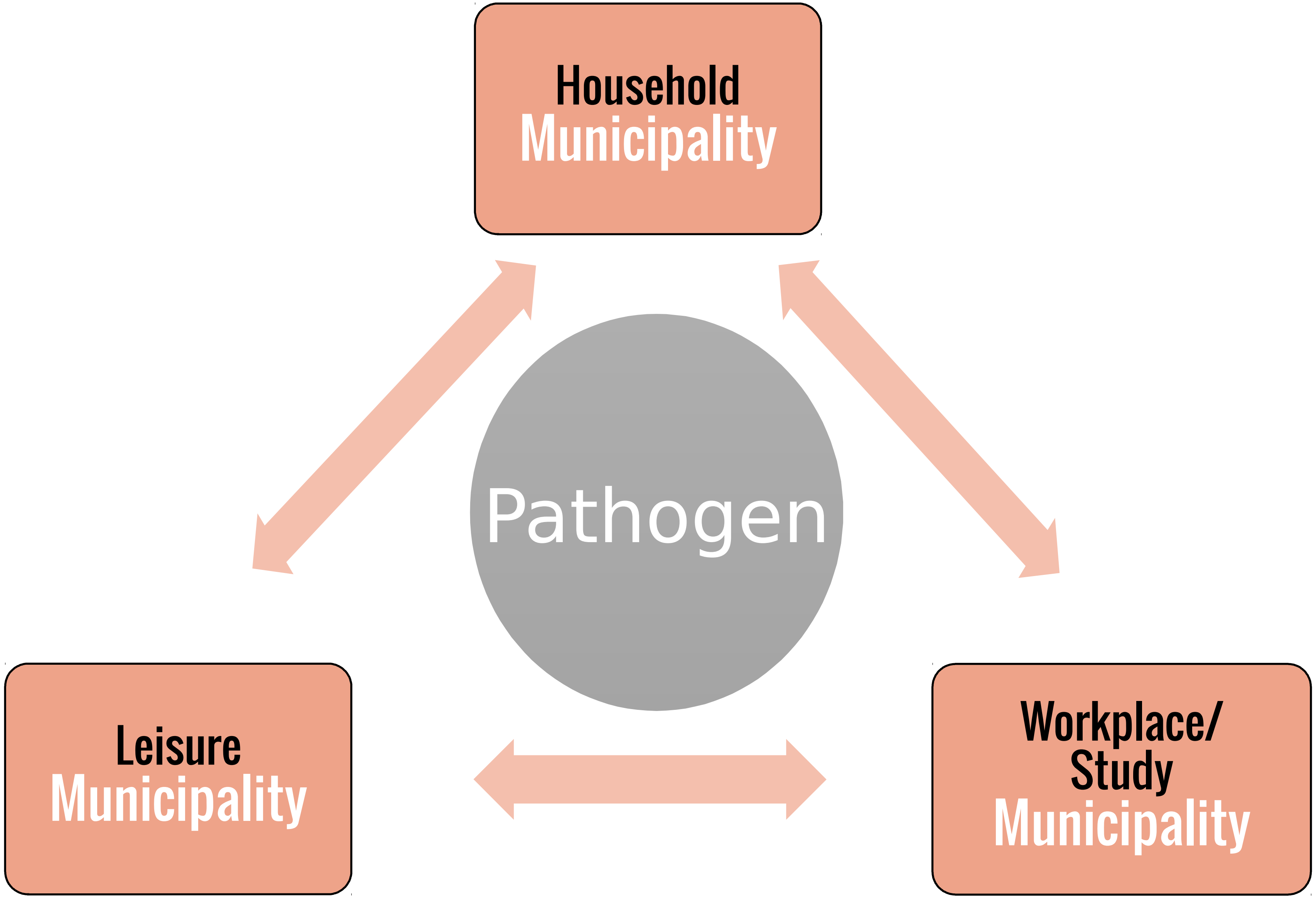


Mobility

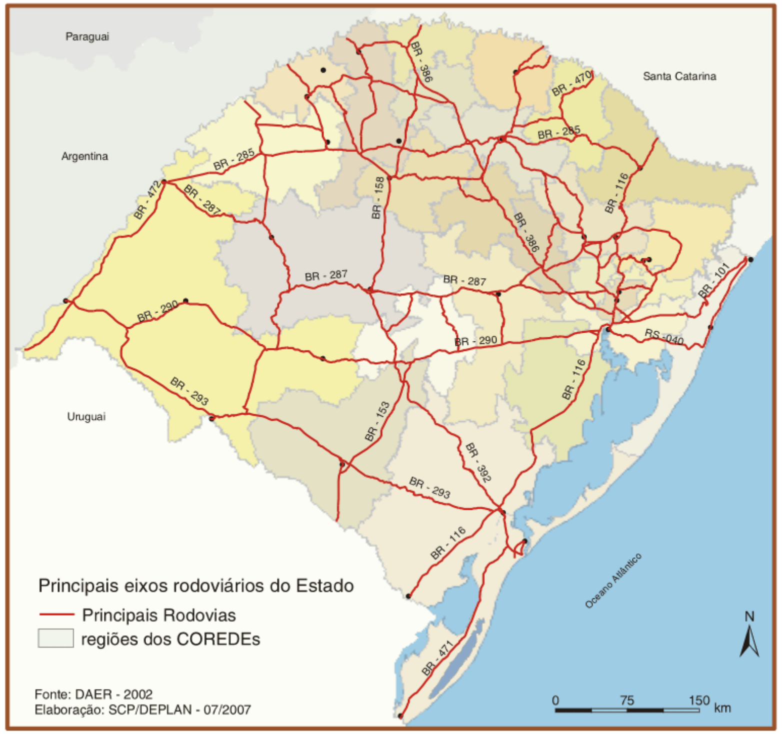
Mobility



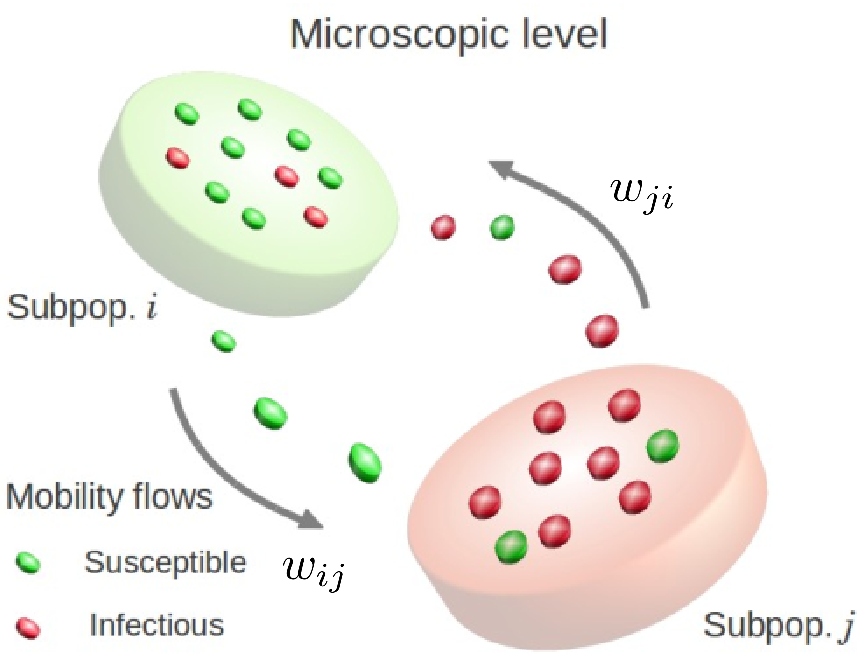
Mobility

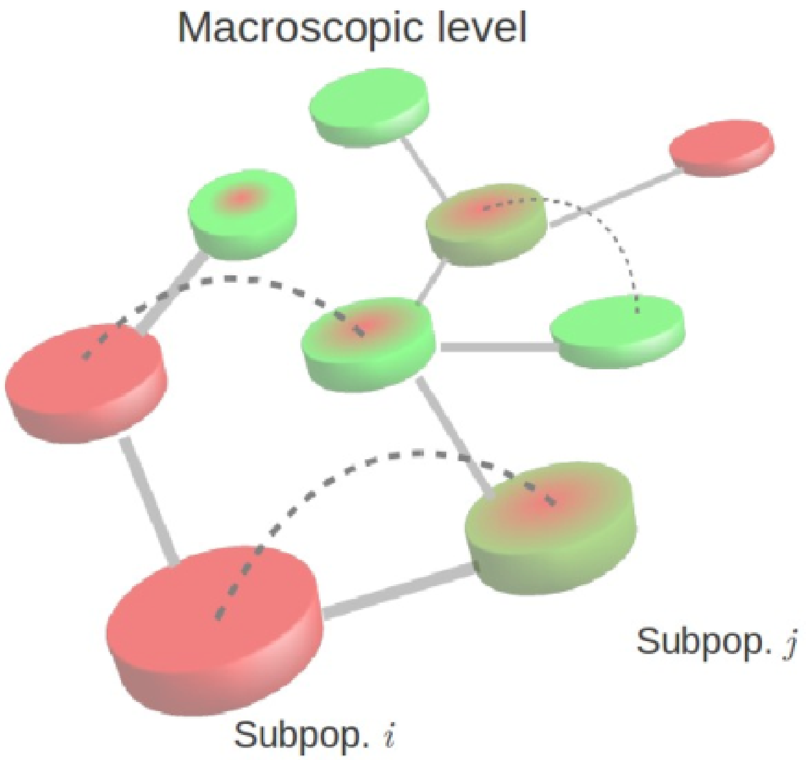

Household
Municipality
Pathogen
Leisure
Municipality
Workplace/
Study
Municipality

Mobility

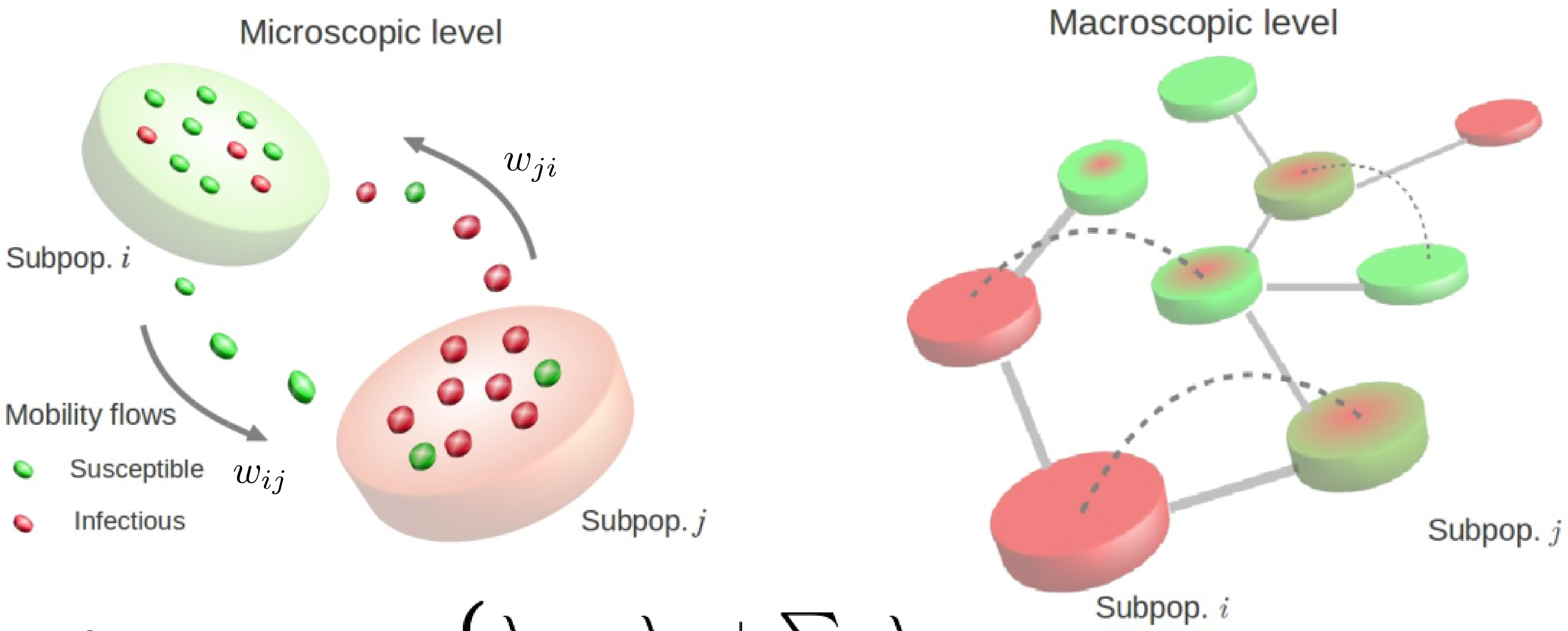

Paraguai
Argentina
Santa Catarina
Uruguai
Oceano Atlântico
BR - 287
BR - 290
BR - 293
BR - 116
BR - 153
BR - 392
BR - 471
BR - 472
BR - 285
BR - 158
BR - 386
BR - 470
BR - 101
RS - 040
Principais eixos rodoviários do Estado
Principais Rodovias
regiões dos COREDEs
N
0
75
150
km
Fonte: DAER - 2002
Elaboração: SCP/DEPLAN - 07/2007

Metapopulation network





Metapopulation network

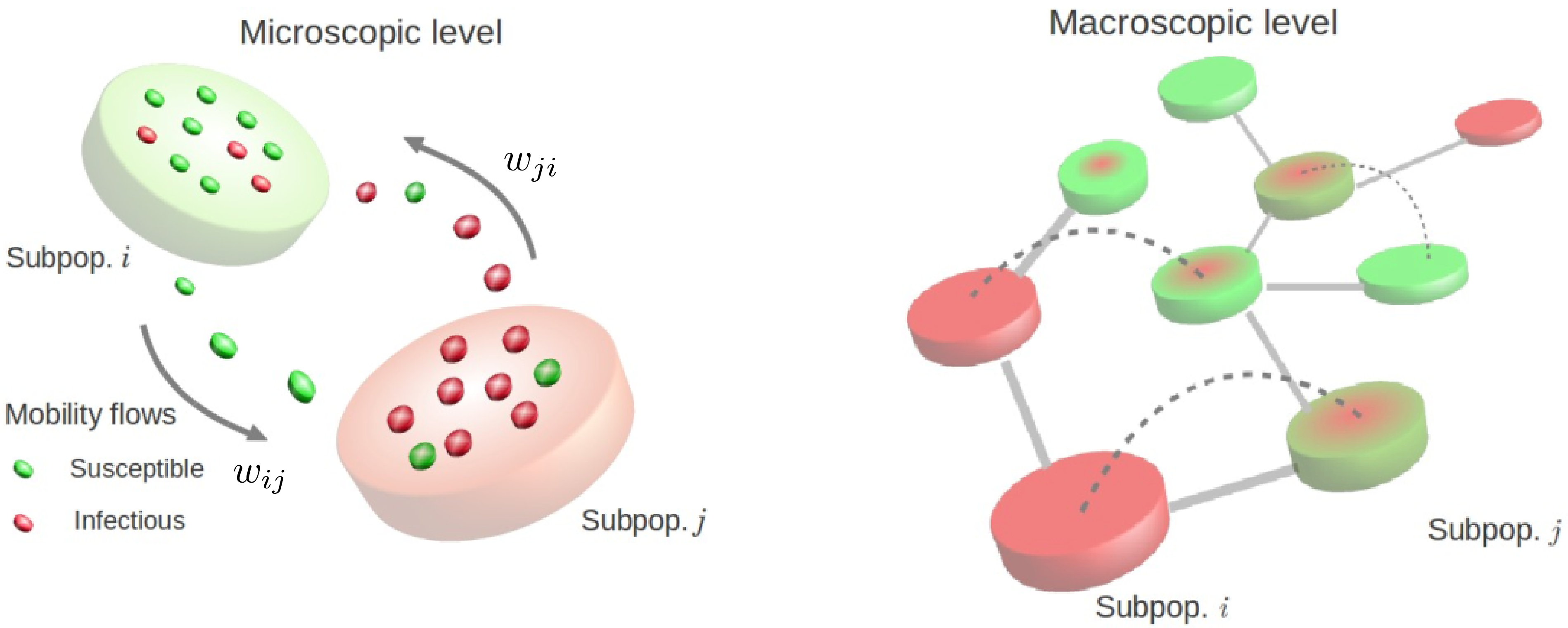


With memory for short distance, no actual transfer.
E.g. GLEAM

$$S_i \lambda_i : \begin{cases} \lambda_i \sim \lambda_{ii} + \sum_j \lambda_{ij} \\ \lambda_{ii} \sim \frac{\beta}{N_i^*} \left(I_{ii} + \sum_j I_{ji} \right) \\ \lambda_{ij} \sim \sigma_{ij} \frac{\beta}{N_j^*} \left(I_{jj} + \sum_k I_{kj} \right) \end{cases}$$

www.gleamviz.org
www.pnas.org/cgi/doi/10.1073/pnas.0906910106

Metapopulation network



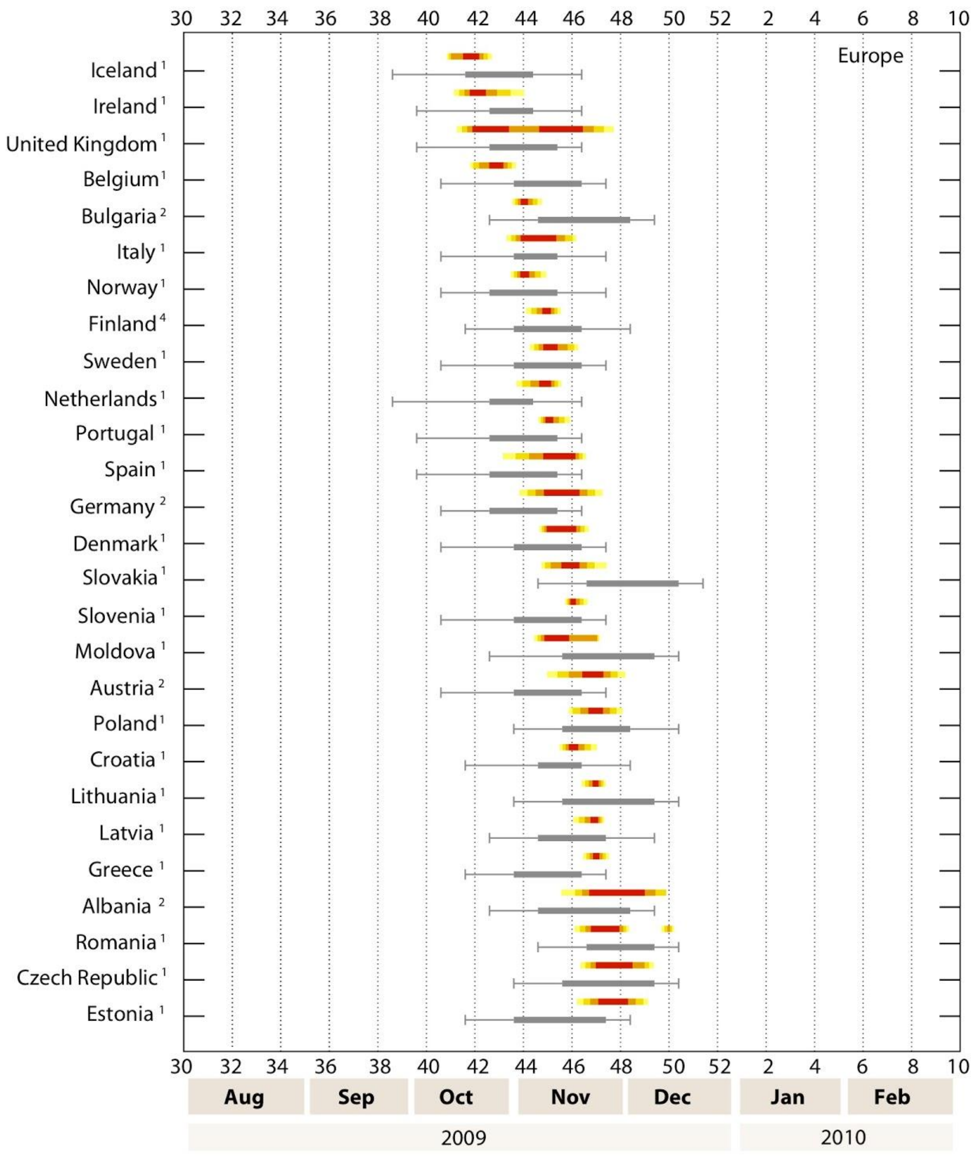
With transfer.
E.g. Rvachev-Longini model

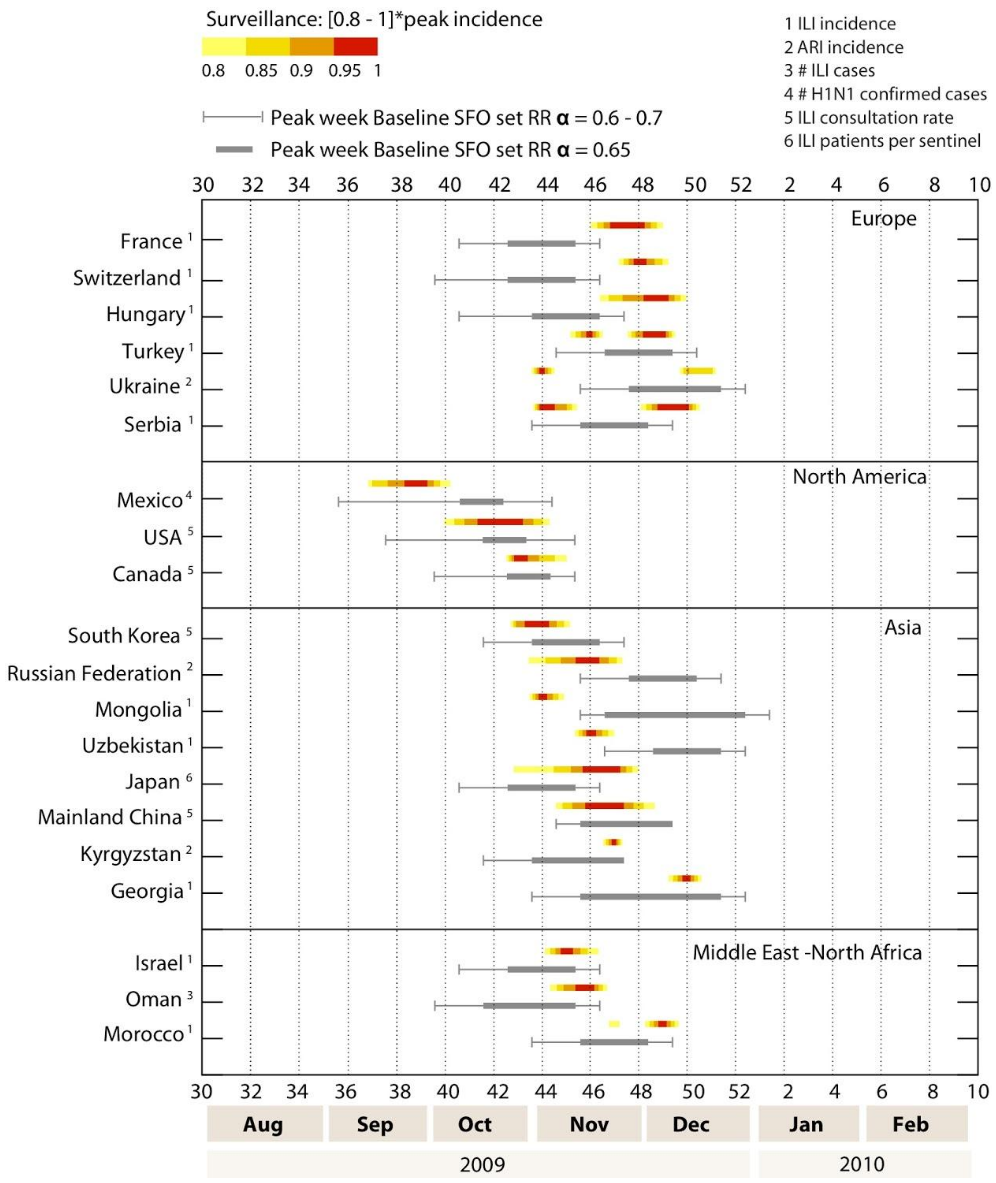
$$\frac{dI_i}{dt} = \Lambda(t) + \sum_j \sigma_{ji} I_j - \sum_j \sigma_{ij} I_i$$

Rvachev L A and Longini I M, 1985 Math. Biosci. 75 3

Propagation routes

Propagation routes



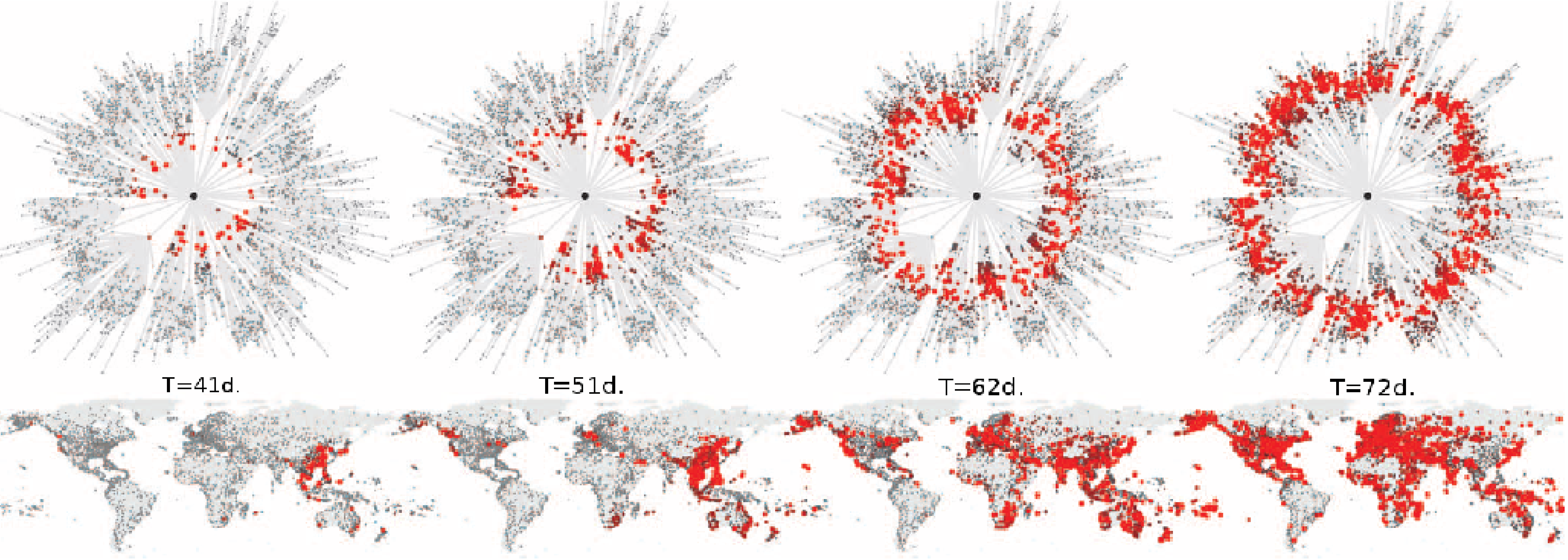


Estimation of the infection peak occurence in idfferent countries

Tizzoni, 2012, *BMC Med.*

Propagation routes

Geographic distance x Network distance



Brockmann & Helbing, 2013, *Science*

Propagation routes

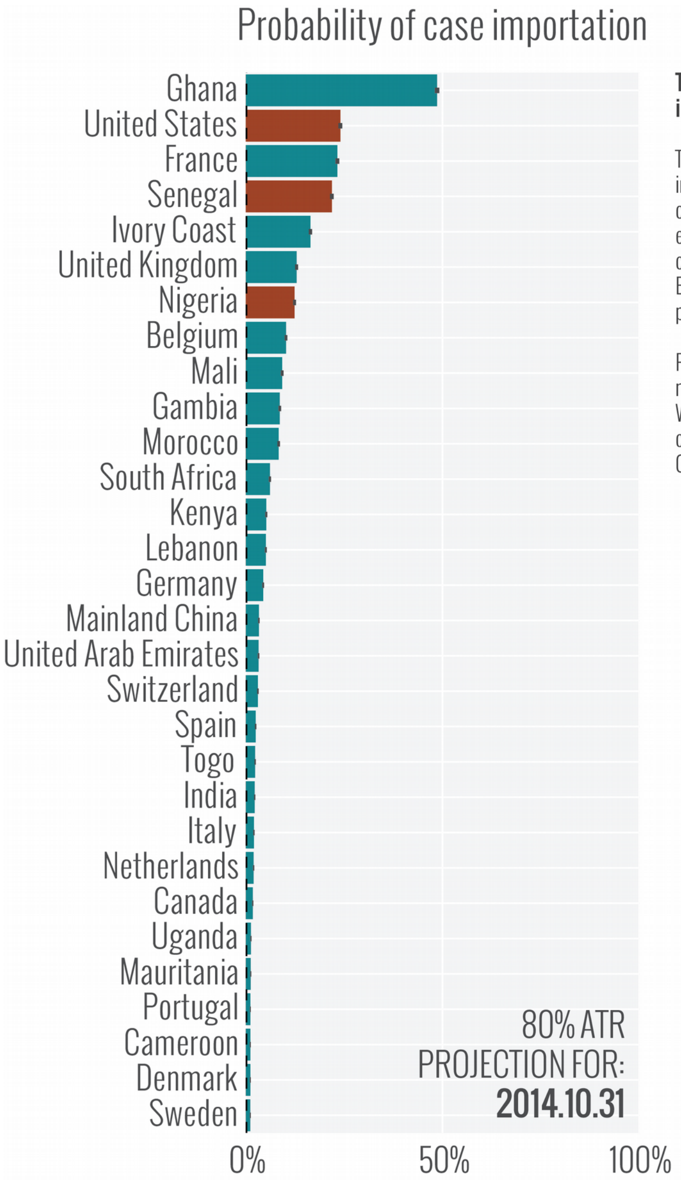
Geographic distance x Network distance: arrival time

- Gautreau, A., Barrat, A., & Barthélemy, M. (2008). Global disease spread: Statistics and estimation of arrival times. Journal of Theoretical Biology, 251(3), 509–522. doi:10.1016/j.jtbi.2007.12.001

- Iannelli, F., Koher, A., Brockmann, D., Hövel, P., & Sokolov, I. M. (2017). Effective distances for epidemics spreading on complex networks. Physical Review E, 95(1). doi:10.1103/physreve.95.012313

Key facts:
- mobility based on Rvachev-Longini model;
- SI or SIR epidemiological models.
- assumes that seeding events take place during exponential growth at seeder. That is: $I(t) \sim I_0 e^{\lambda t}$

Ebola - real time projections/2014

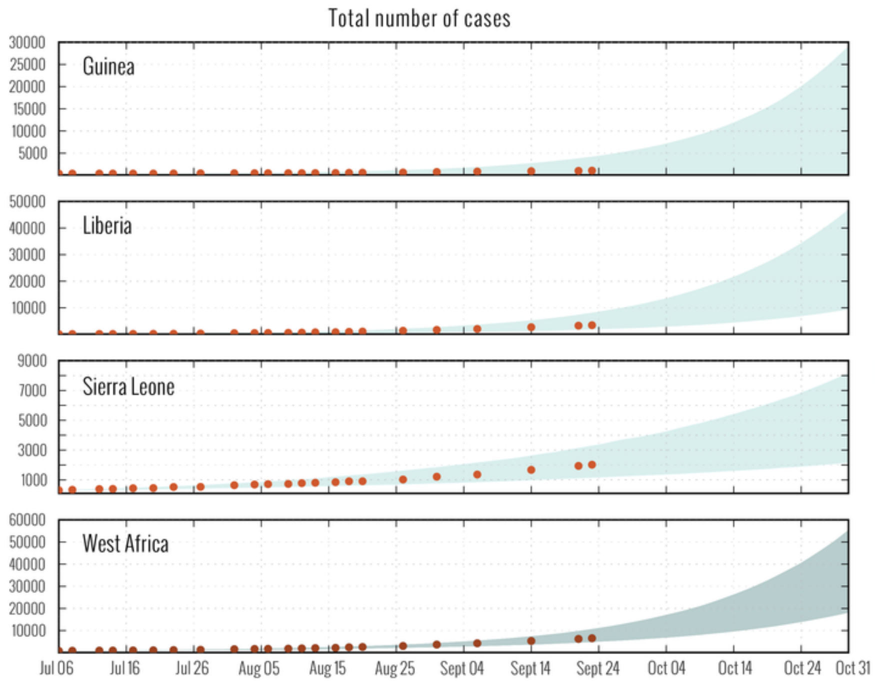


Top 30 countries ranked according to EVD importation risk.

The plot shows the top 30 countries ranked according to the relative probability of importation of EVD cases. Nigeria, Senegal, and the US have already experienced case importation. The projection considers an 80% traffic reduction to and from the EVD affected countries. The maximum probability projected for 31 October is about 49%.

Probabilities obtained from calibrating the model using total number of cases reported by WHO from 09 Aug. 2014 to 23 Sept. 2014, and considers the probability of invasion from 01 Oct. 2014 to 31 Oct. 2014

Gomes et al. 2014, *Plos Currents Outbreaks*
www.mobs-lab.org/ebola



Guinea	Cases
Oct 04 2014	[400 - 7200]
Oct 14 2014	[400 - 11900]
Oct 24 2014	[400 - 20100]
Oct 31 2014	[400 - 29200]

Liberia	Cases
Oct 04 2014	[2900 - 13600]
Oct 14 2014	[4500 - 21700]
Oct 24 2014	[6900 - 34400]
Oct 31 2014	[9400 - 47000]

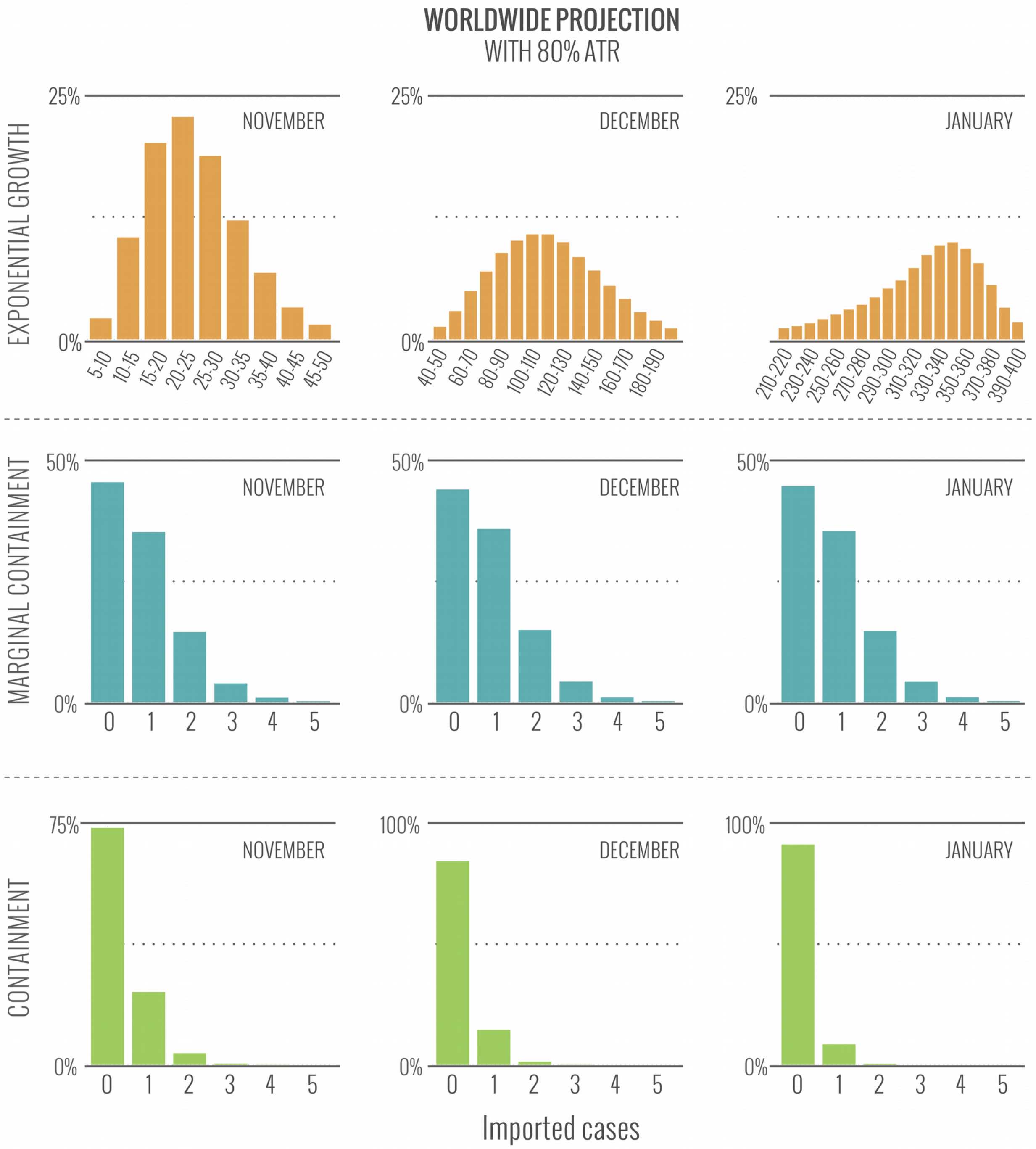
Sierra Leone	Cases
Oct 04 2014	[1400 - 4200]
Oct 14 2014	[1600 - 5400]
Oct 24 2014	[1900 - 6800]
Oct 31 2014	[2200 - 8200]

West Africa	Cases
Oct 04 2014	[6800 - 17100]
Oct 14 2014	[9600 - 26300]
Oct 24 2014	[13900 - 40600]
Oct 31 2014	[18100 - 55400]

Projections for the number of cases in West Africa

The shaded areas correspond to the fluctuations cone provided by the stochastic microsimulations of the models selected by the calibration to data. WHO offical data are reported as red circles. The projected values consider that the epidemic continues to follow the current growth rate, thus assuming a worst-case scenario in which containment measures are not successful at curtailing the outbreak.

Projection published on
7 October 2014
MOBS LAB


WORLDWIDE PROJECTION
WITH 80% ATR
EXPONENTIAL GROWTH
MARGINAL CONTAINMENT
CONTAINMENT
NOVEMBER
DECEMBER
JANUARY
25%
0%
50%
75%
100%
5-10
10-15
15-20
20-25
25-30
30-35
35-40
40-45
45-50
40-50
60-70
80-90
100-110
120-130
140-150
160-170
180-190
210-220
230-240
250-260
270-280
290-300
310-320
330-340
350-360
370-380
390-400
0
1
2
3
4
5
Imported cases

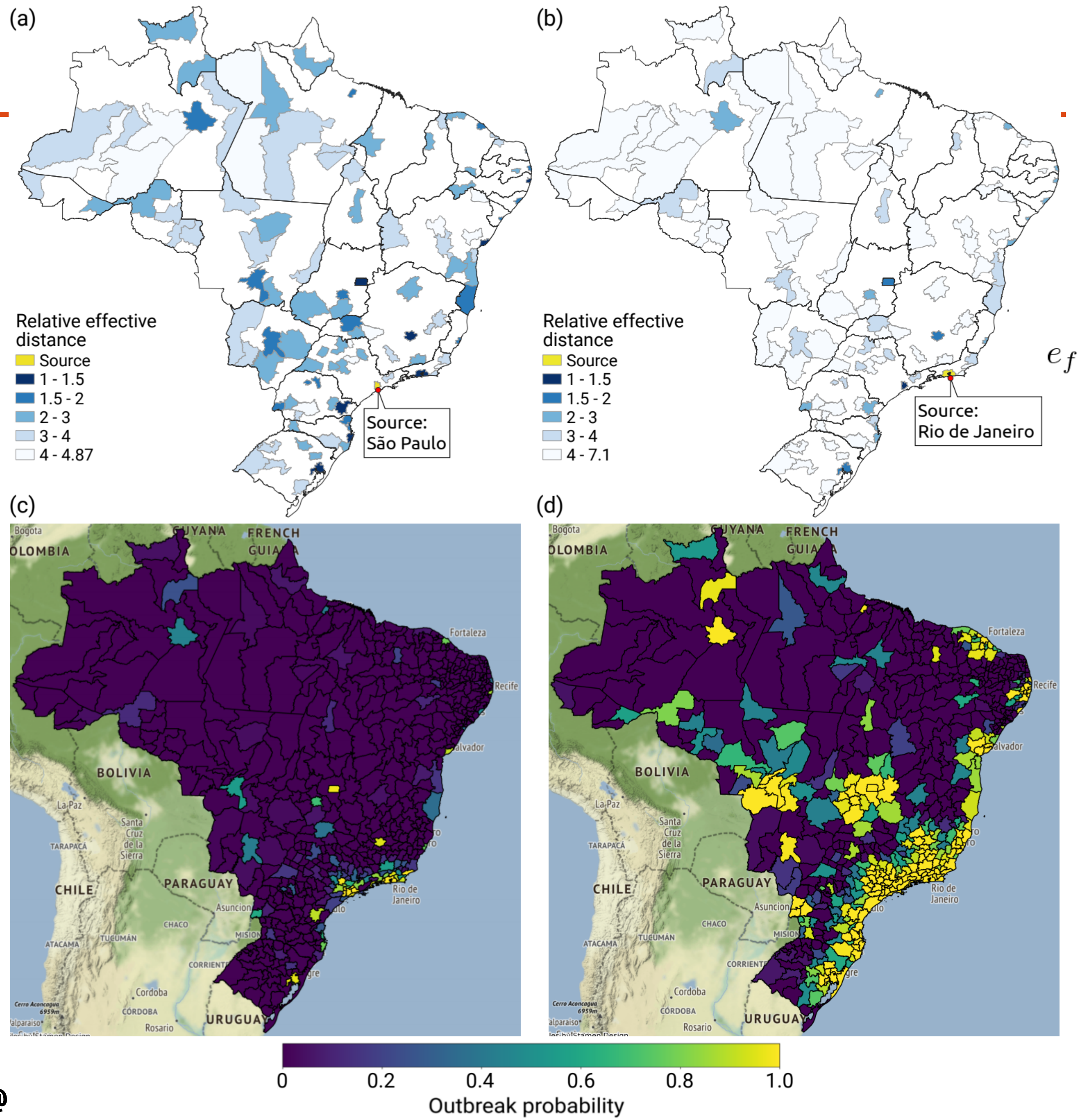
SARS-CoV-2 introduction in Brazil

Exposure

Estimates published on march 23 and 25, using just SP and RJ as local sources
http://bit.ly/mave-covid19-relatorio2

Medrxiv:
https://doi.org/10.1101/2020.03.19.20039131

Plos One:
Assessing the spread of COVID-19 in Brazil: Mobility, morbidity and social vulnerability
https://doi.org/10.1371/journal.pone.0238214



$$e_f(i,j) = \frac{E_f(i,j)}{\min_k E_f(i,k)}$$

$$p_j = 1 - \left(\frac{1}{R_0}\right)^{I_j}$$

$$I_j = k\tau \sum_i f_{i,j} \frac{I_i}{N_i}$$

Official data as of 2020-09-22

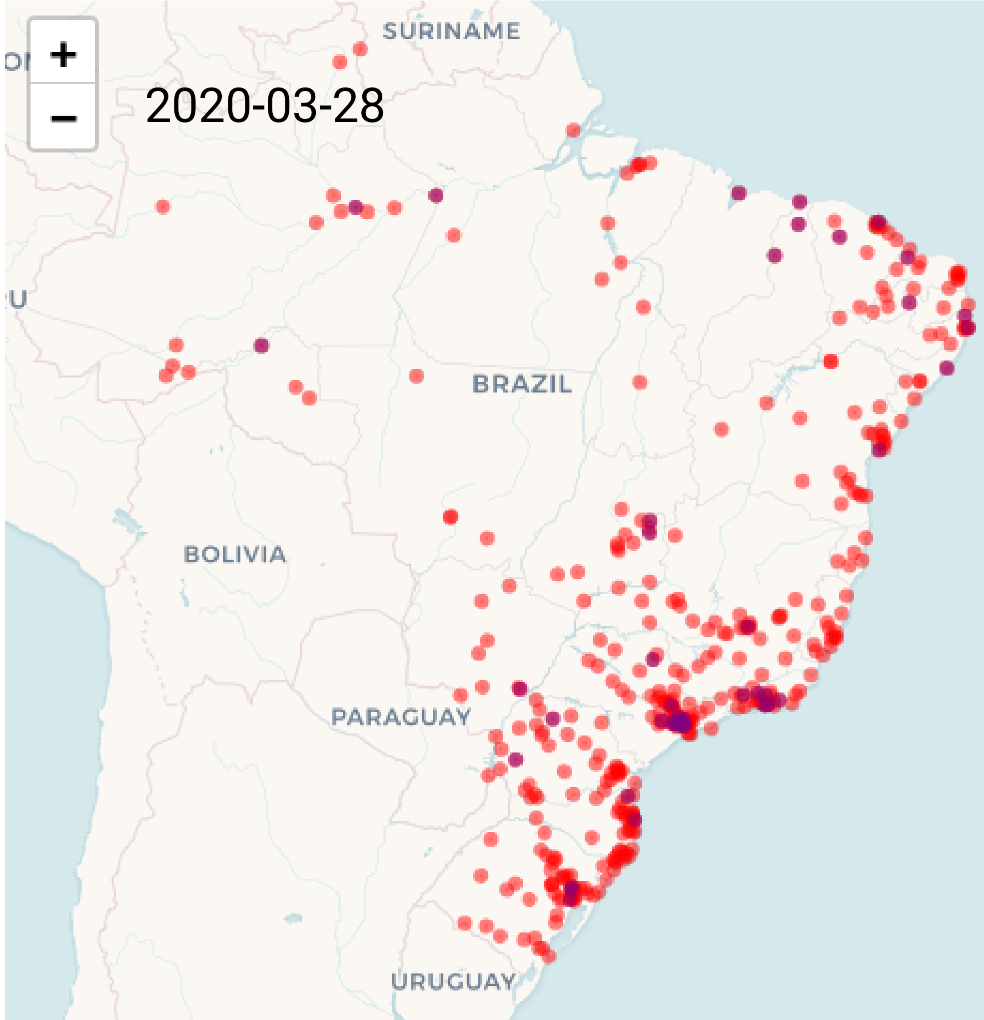
FIOCRUZ Fale com a Fiocruz

ICICT Instituto de Comunicação e Informação Científica e Tecnológica em Saúde

- Relatório municipal
- Duplicação de casos e óbitos
- Fator de crescimento
- Mapa Brasil
- Medidas de combate
- População em risco
- Notas técnicas
- Sobre o projeto

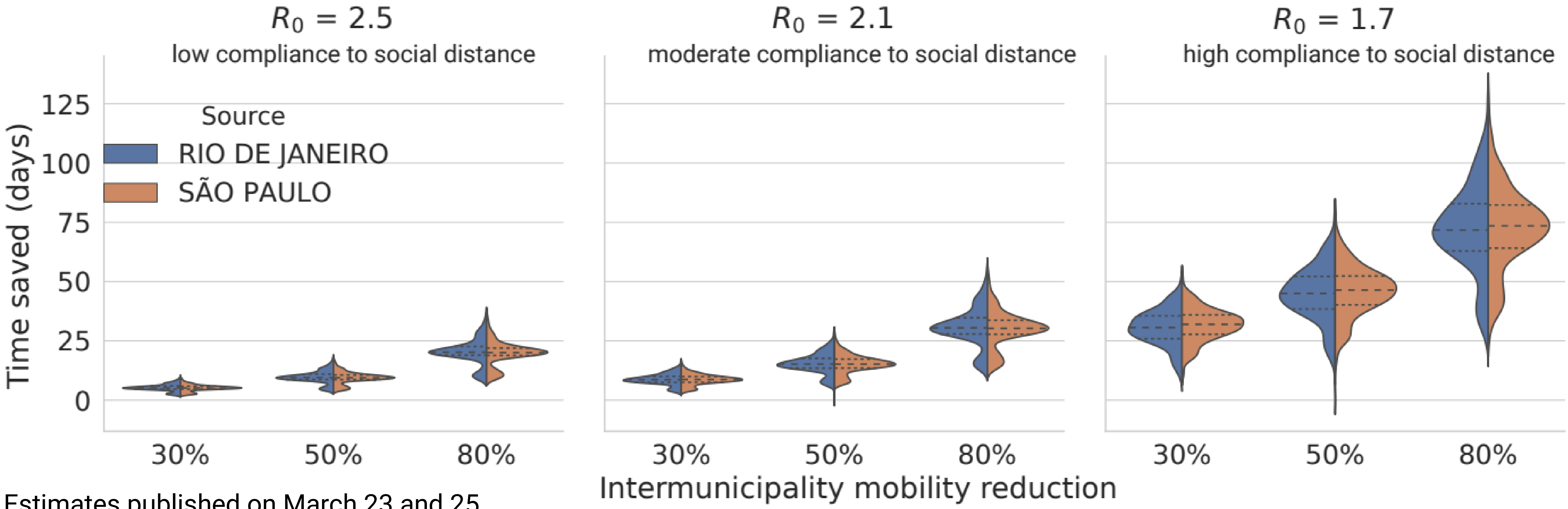
Atualização dos dados

22/09/2020 20:45:06



https://bigdata-covid19.icict.fiocruz.br/

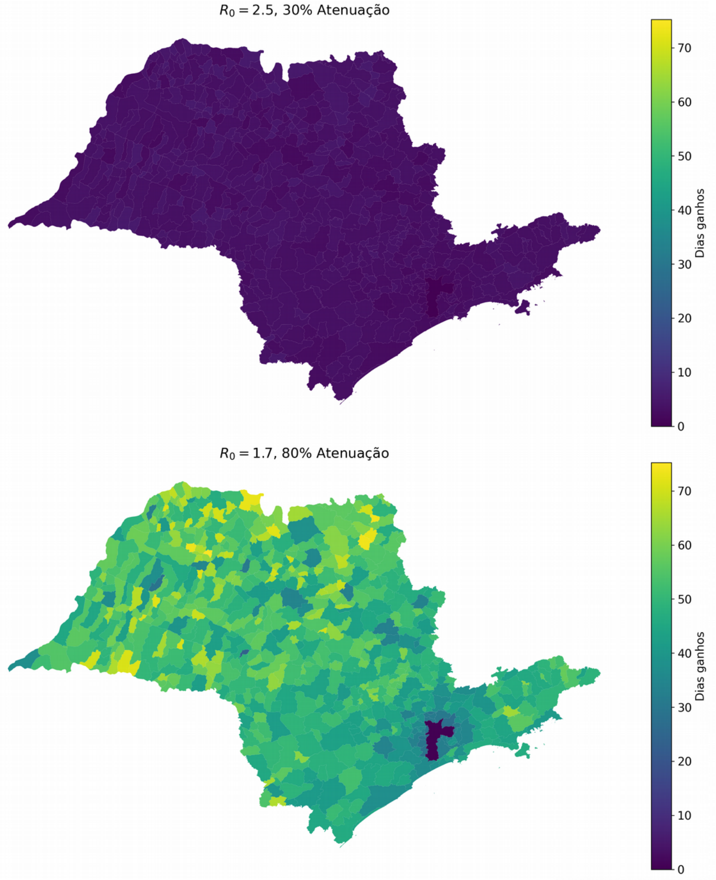
Time to invasion

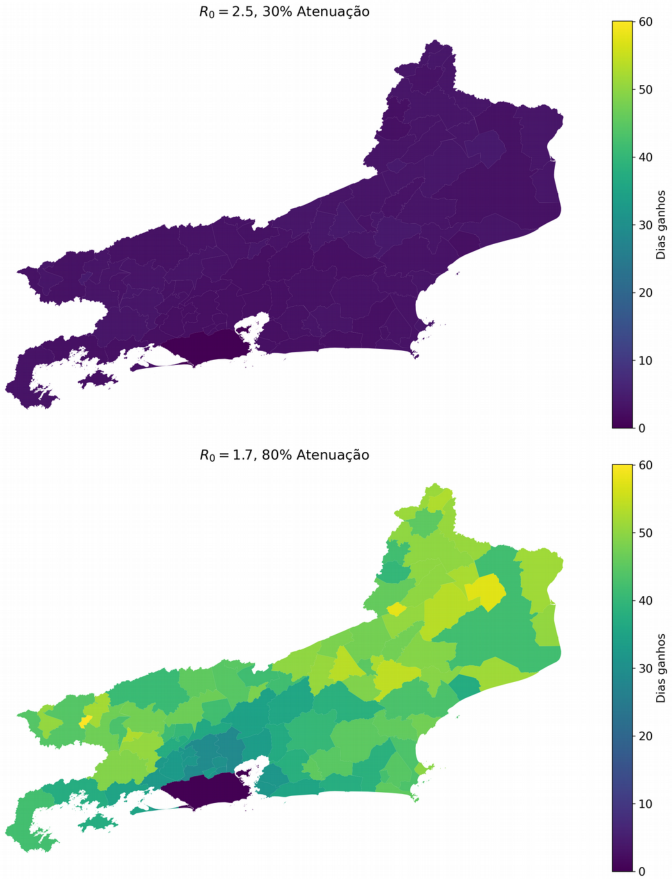


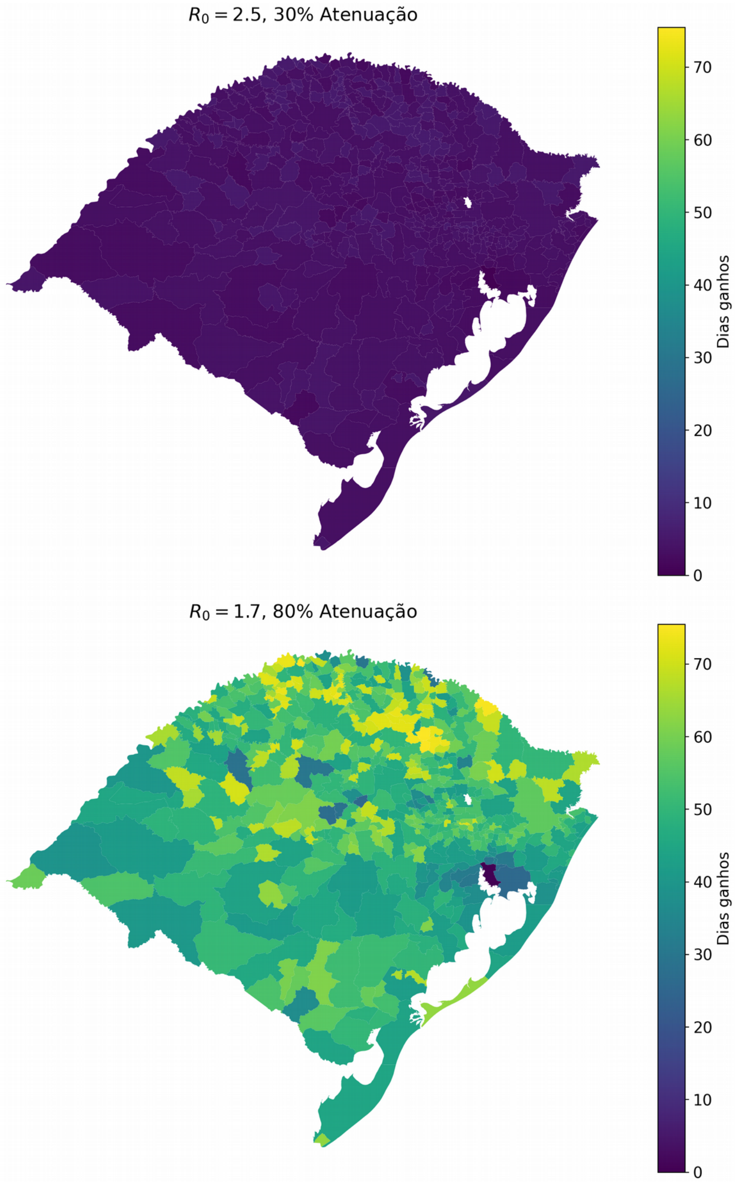
Estimates published on March 23 and 25.
http://bit.ly/mave-covid19-relatorio2
Medrxiv: https://doi.org/10.1101/2020.03.19.20039131
Plos One: Assessing the spread of COVID-19 in Brazil: Mobility, morbidity and social vulnerability
https://doi.org/10.1371/journal.pone.0238214
Por município: https://bit.ly/mave-covid19-estados2020-04-01

Interiorization

Estimates published on April 01, 2020.
Country: https://bit.ly/mave-covid19-relatorio3-20200401
States:https://bit.ly/mave-covid19-estados2020-04-01
”Estimativa de risco de espalhamento da COVID-19 nos estados brasileiros e avaliação da vulnerabilidade socioeconômica nos municípios.”

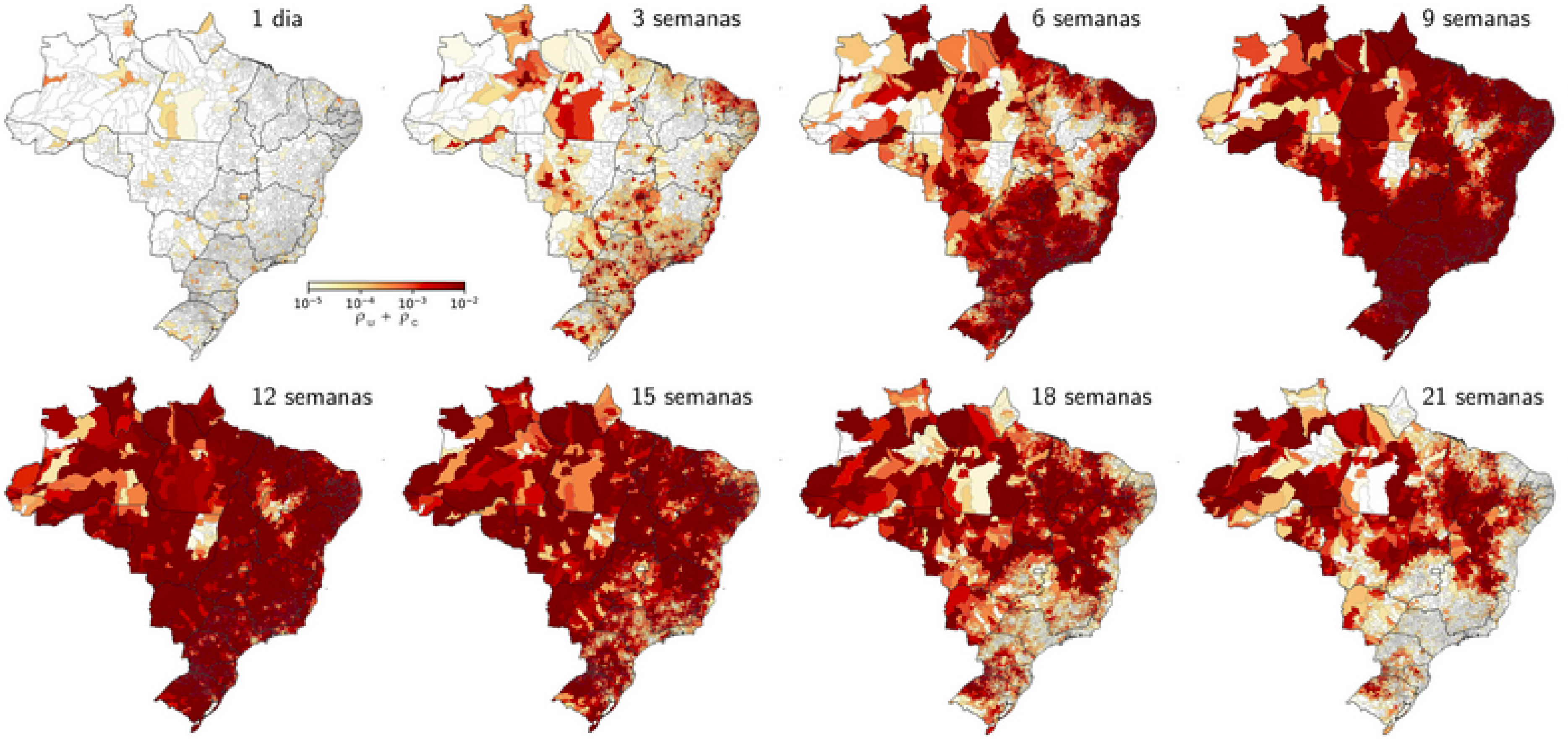






Interiorization

Metapopulation modeling of COVID-19 advancing into the countryside: an analysis of mitigation strategies for Brazil
medRxiv 2020.05.06.20093492; doi: https://doi.org/10.1101/2020.05.06.20093492



Metapopulation modeling of COVID-19 advancing into the countryside: an analysis of mitigation strategies for Brazil (2020)
Guilherme S. Costa, Wesley Cota, Silvio C. Ferreira

@ghscosta271, @wlcota, @silviojrufv

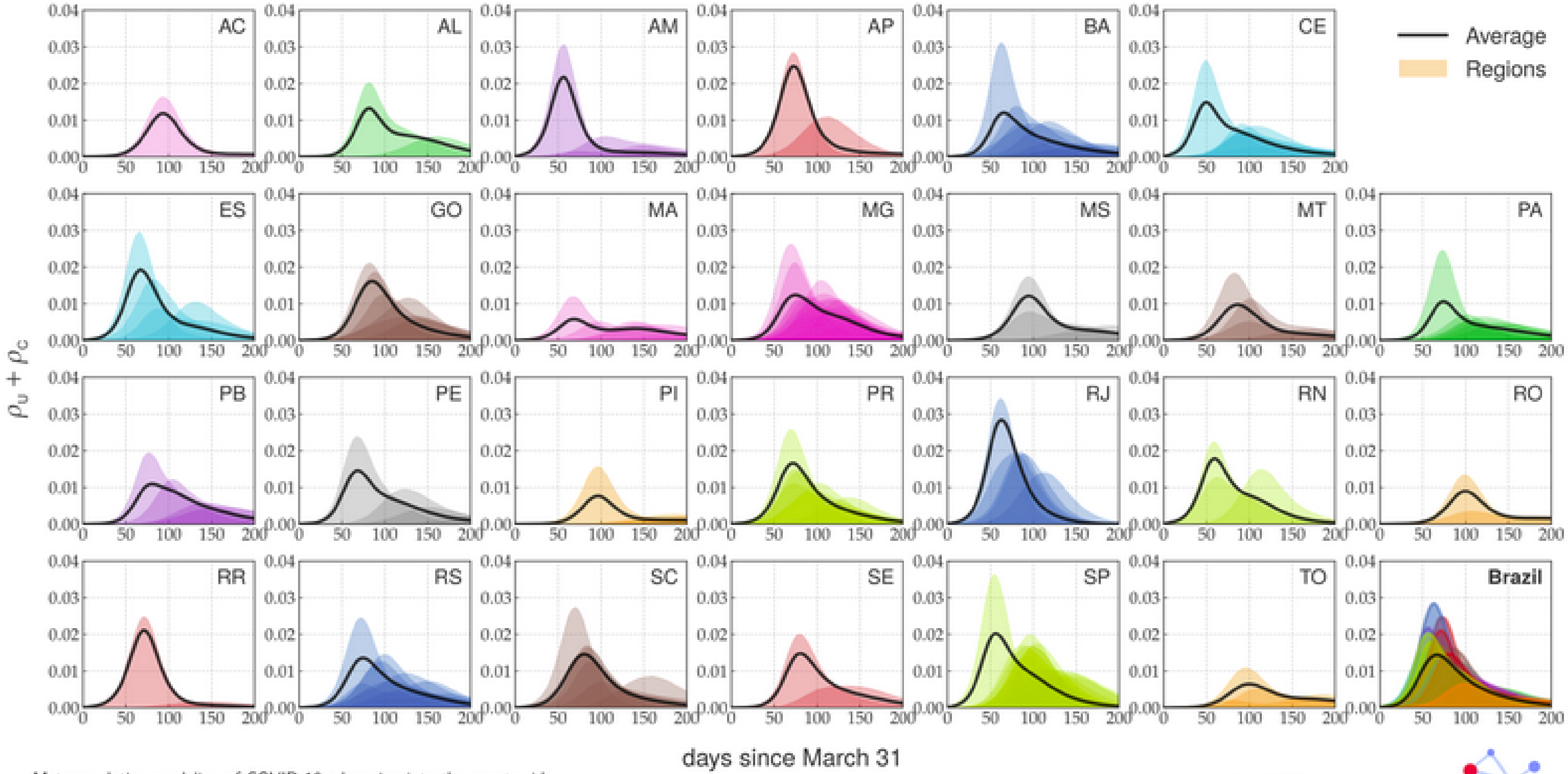
Cenário simulado sob a hipótese de confinamento moderado

UFV Pós-Graduação em Física

GISC Grupo de Investigação de Sistemas Complexos

Interiorization

Metapopulation modeling of COVID-19 advancing into the countryside: an analysis of mitigation strategies for Brazil
medRxiv 2020.05.06.20093492; doi: https://doi.org/10.1101/2020.05.06.20093492

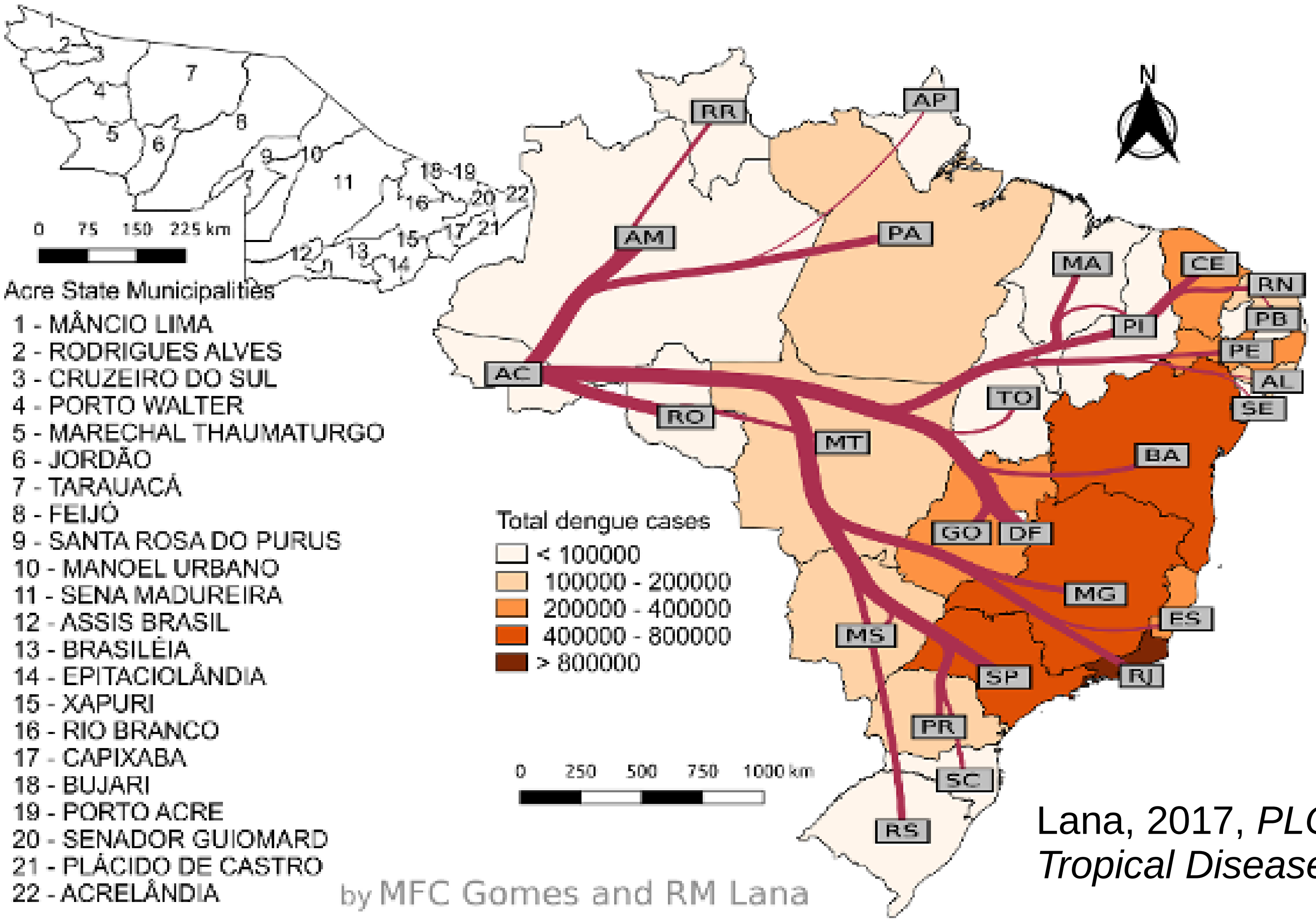


Metapopulation modeling of COVID-19 advancing into the countryside: an analysis of mitigation strategies for Brazil (2020)
Guilherme S. Costa, Wesley Cota, Silvio C. Ferreira
@ghscosta271, @wlcota, @silviojrufv

Cenário simulado sob a hipótese de confinamento forte

Dengue introduction and establishment in Acre, 2001-2012

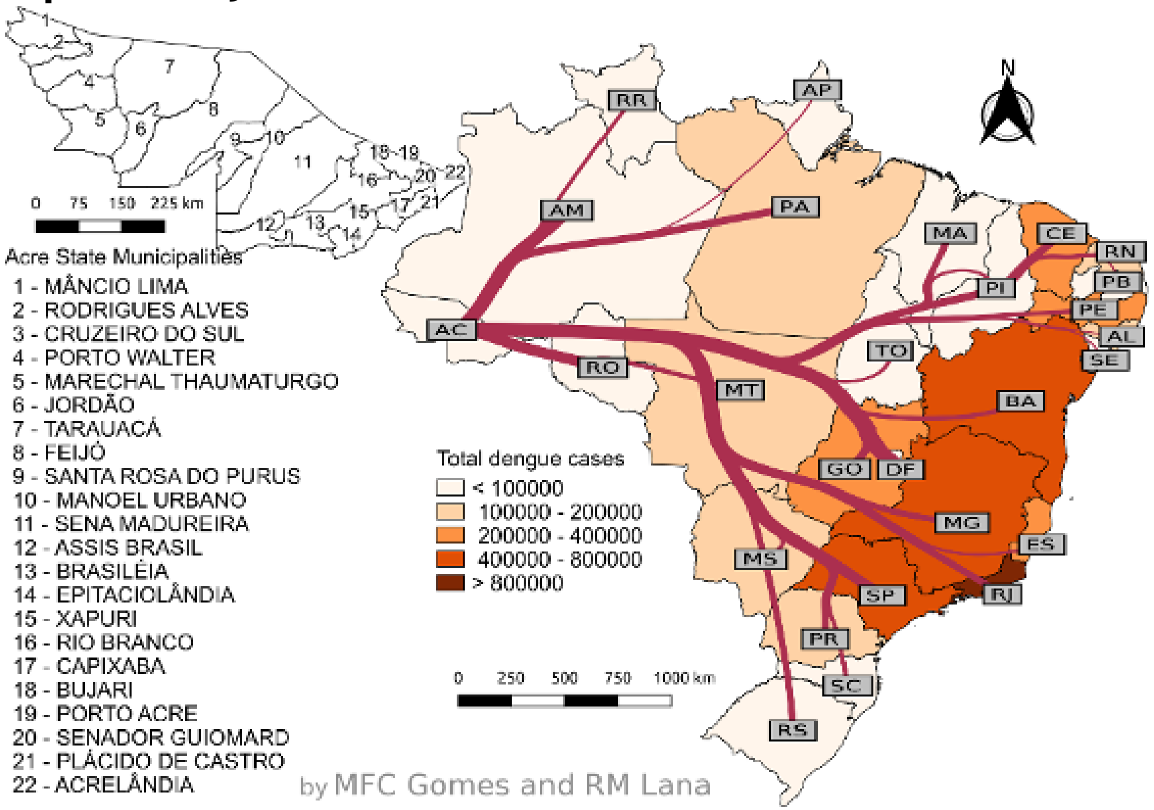
Interstate flow and case importation probability



Lana, 2017, *PLOS Neglected Tropical Diseases*

Dengue introduction and establishment in Acre, 2001-2012

Interstate flow and case importation probability



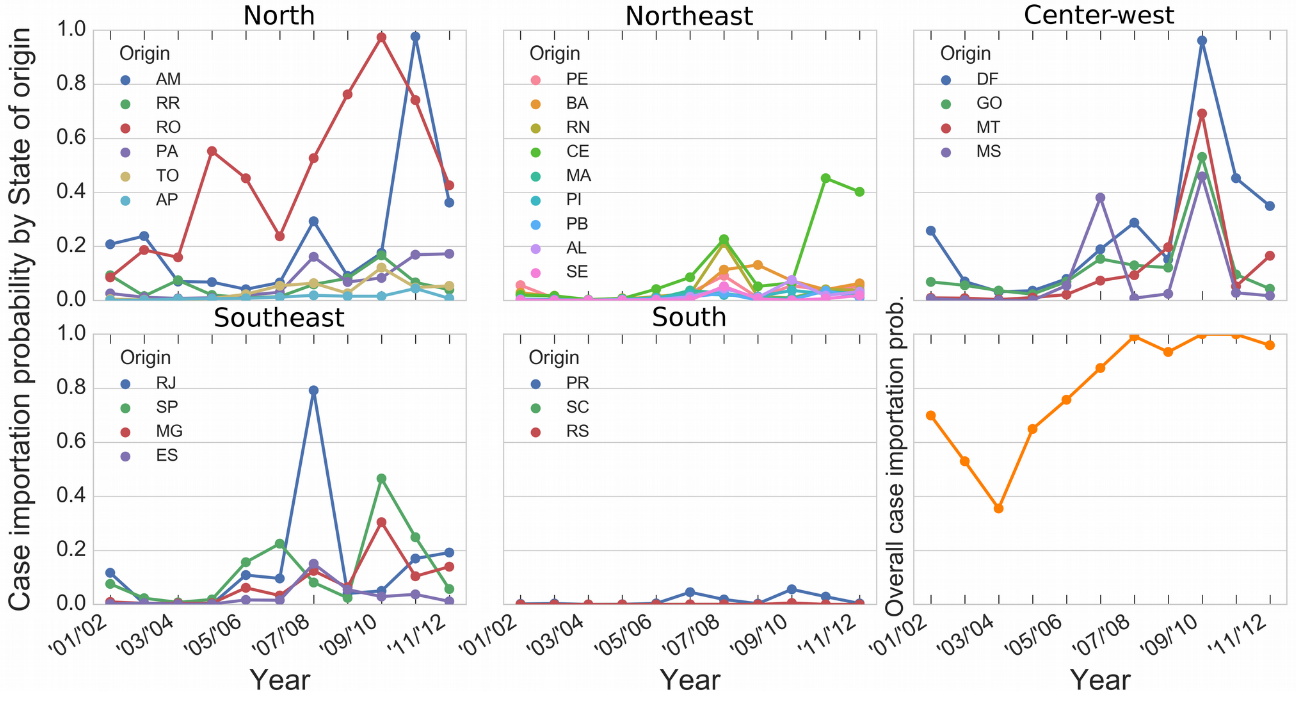
$\pi_{i,m}$: Average daily flow from state *i*, on month *m*

τ_k : Instrinsic infectious period

$k_{i,m}$: Number of dengue cases in state *i*, on month *m*

$$p_{i,m} = 1 - (1 - \pi_{i,m})^{\sum_{k=1}^{k_{i,m}} \tau_k}$$: Case importation prob. on month *m*

$$P_{i,Y} = 1 - \prod_m (1 - p_{i,m})$$: Case importation prob. at year *Y*.



Obrigado!

PROCC PROGRAMA DE COMPUTAÇÃO CIENTÍFICA

Links do Grupo de Métodos Analíticos em Vigilância Epidemiológica (MAVE):

Repositório: http://bit.ly/mave-repo
Site do MAVE: https://covid-19.procc.fiocruz.br/
Relatórios COVID-19: https://bit.ly/mave-covid19-relatorios
Dados processados: http://bit.ly/mave-covid19-dados

InfoGripe:
Site: http://info.gripe.fiocruz.br
Tendências: http://157.86.198.43/
Boletins do InfoGripe: http://bit.ly/mave-infogripe
Dados processados: https://bit.ly/mave-infogripe-dados

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Raquel M. Lana - PROCC – Fiocruz
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