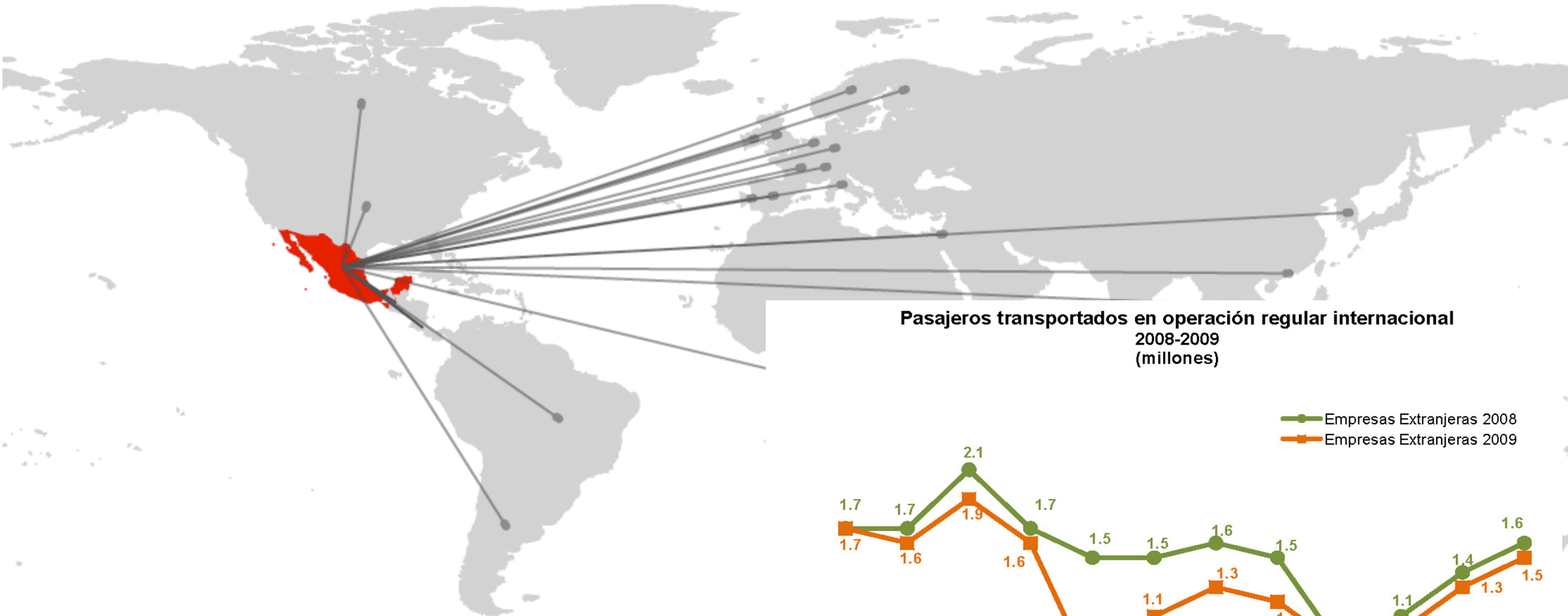
SIR metapopulation model: basic questions

- is there an epidemic threshold?
- what does it mean?

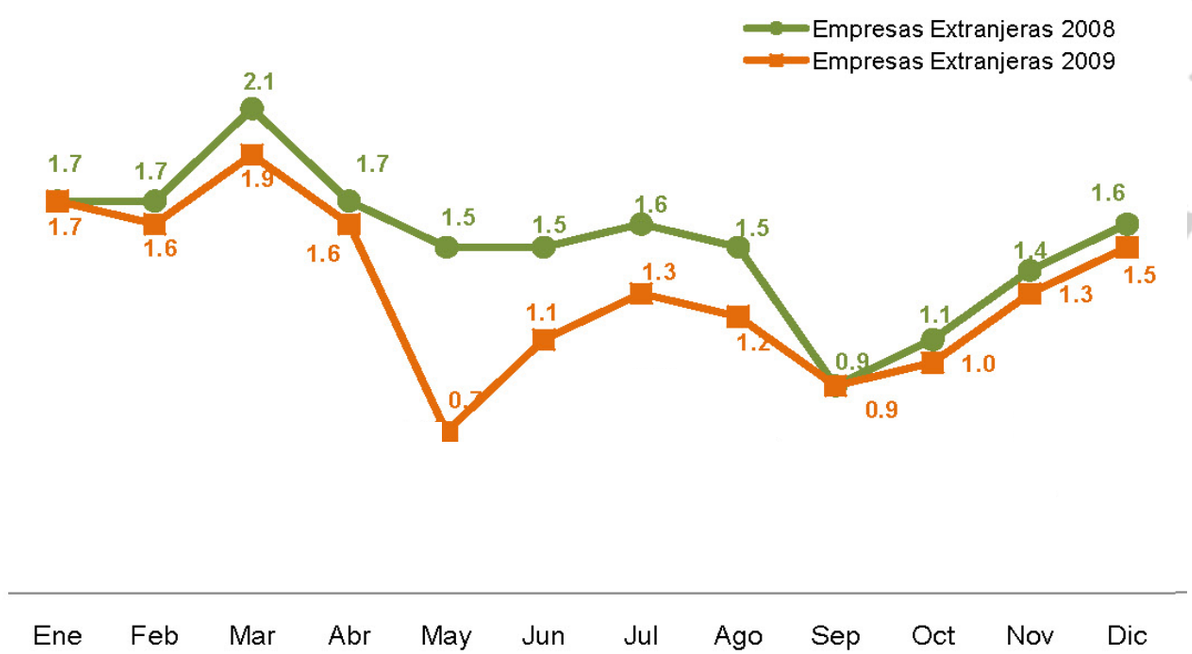
travel restrictions: control?

travel restrictions: control?

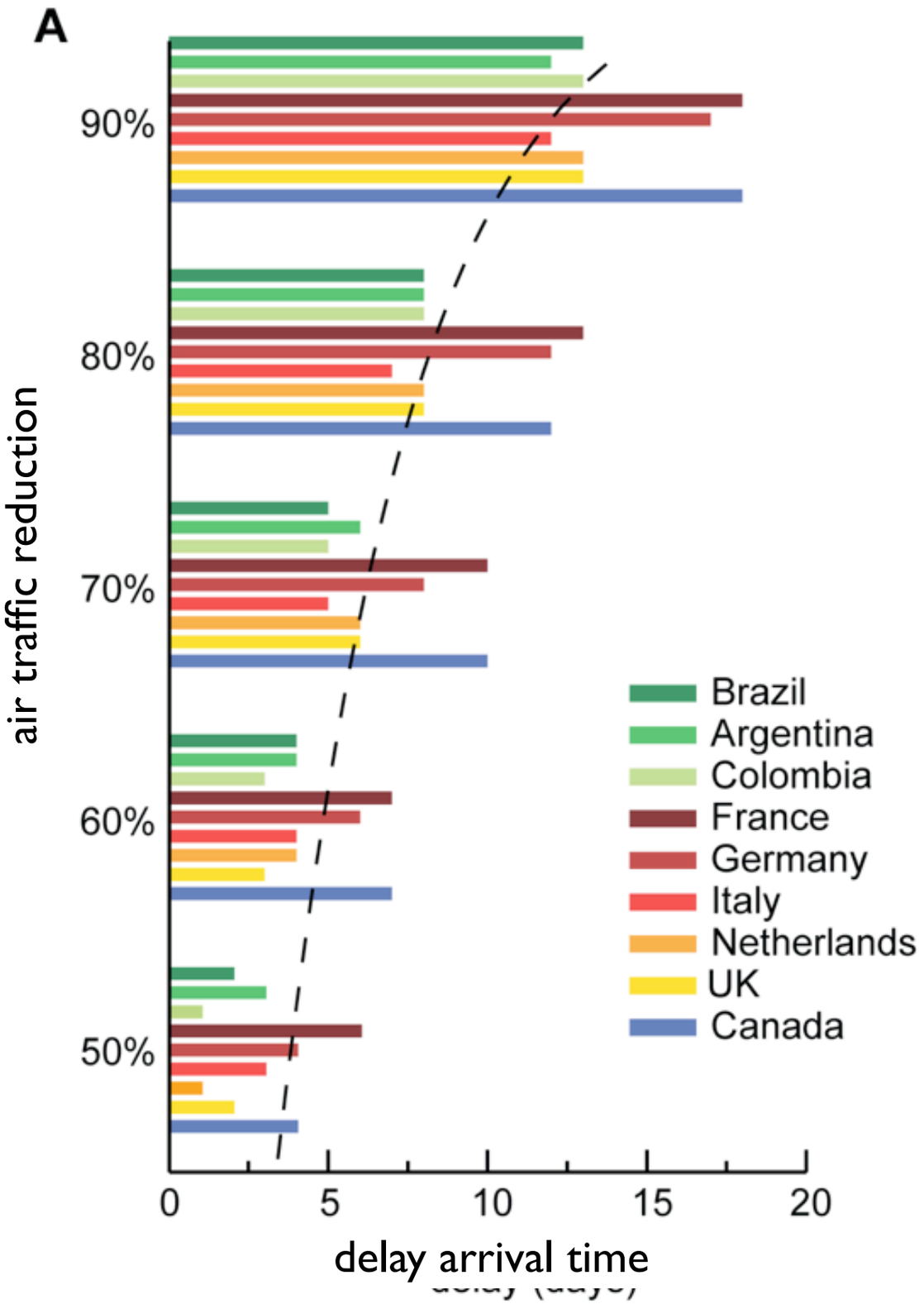
travel restrictions: control?



Pasajeros transportados en operación regular internacional
2008-2009
(millones)



simulation results

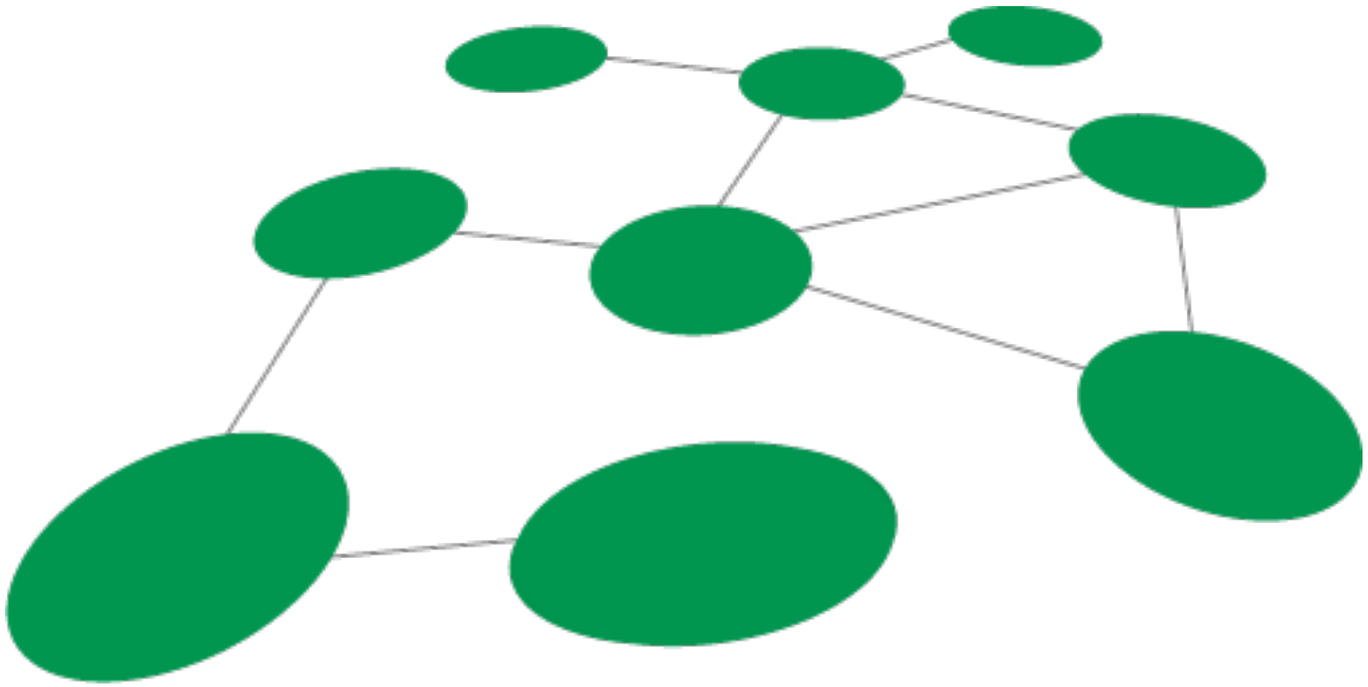


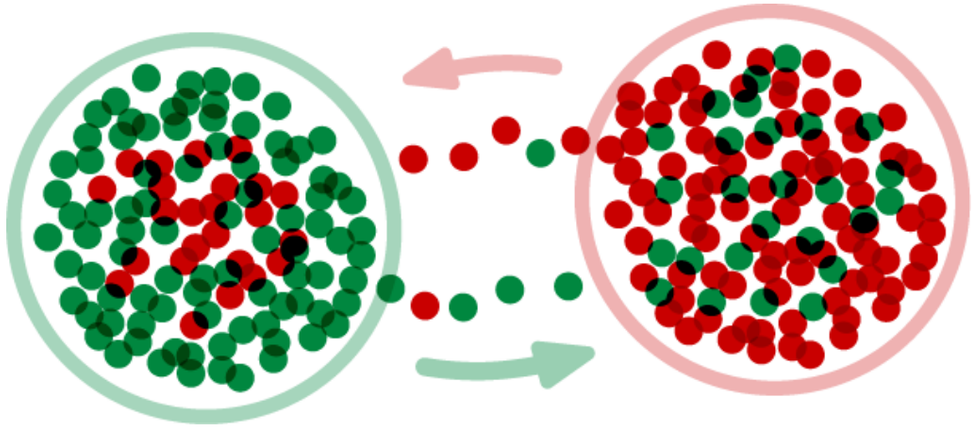
Bajardi et al. PLoS ONE (2011),
Colizza et al PLoS Medicine (2007)

Cooper et al, 2006;
Hollingsworth et al, 2006;
Epstein et al, 2007.

www.gleamviz.org
Bajardi et al. PLoS ONE 2011

metapopulation approach





ingredients

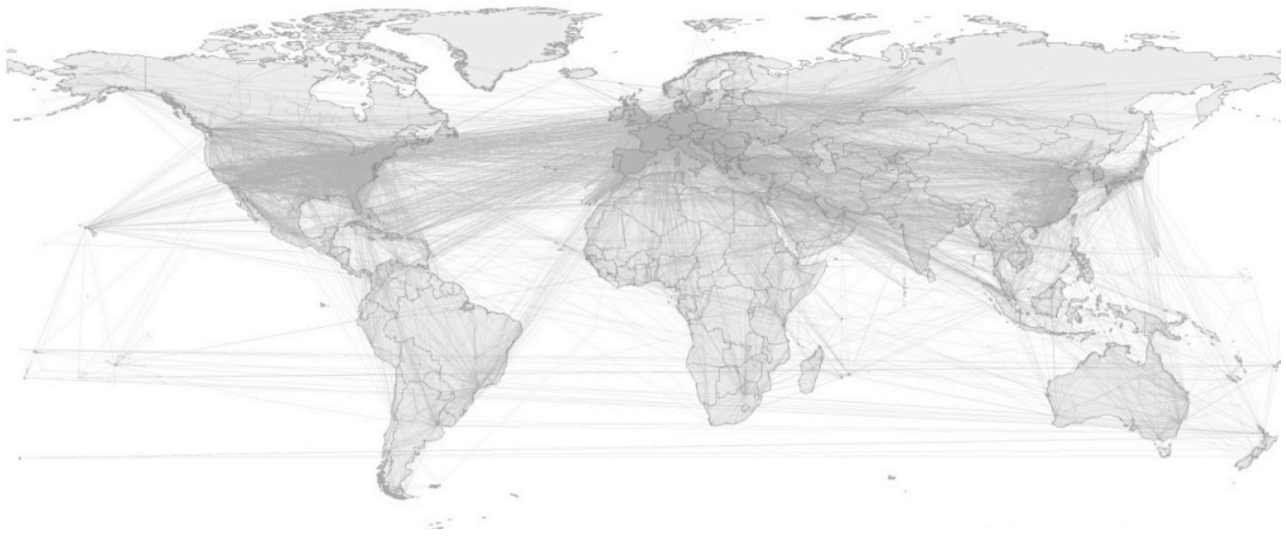
diffusion:

1. mobility networks structure
2. traffic pattern

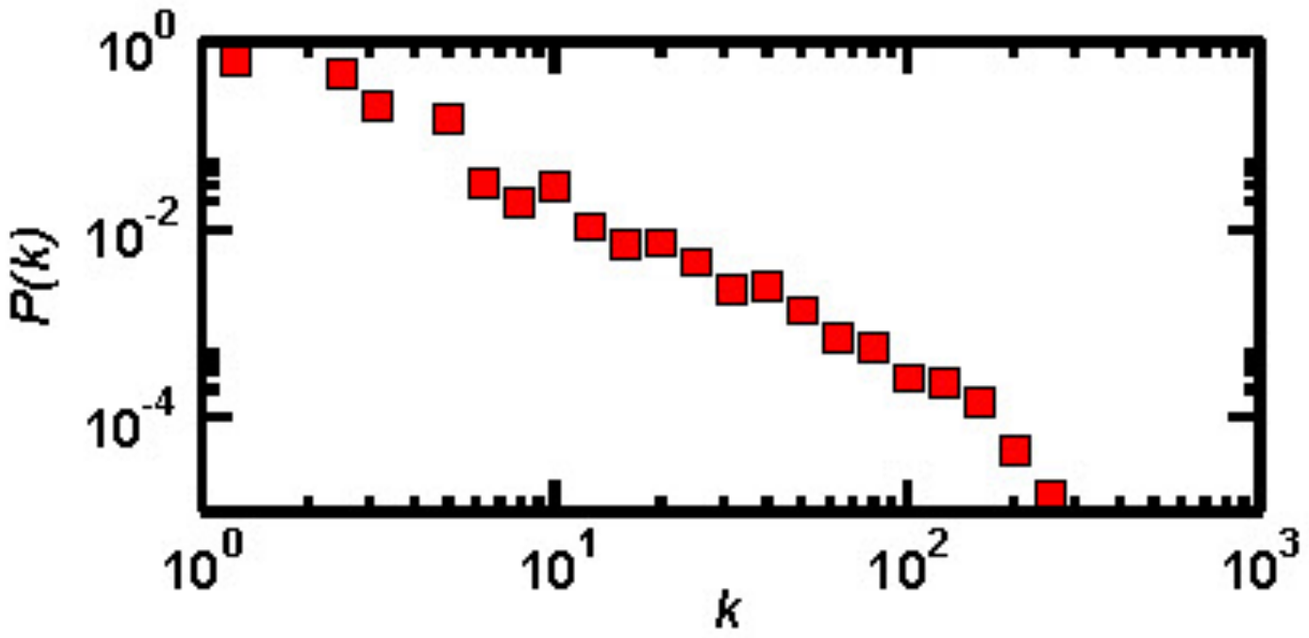
reaction:

3. infection dynamics

mobility pattern



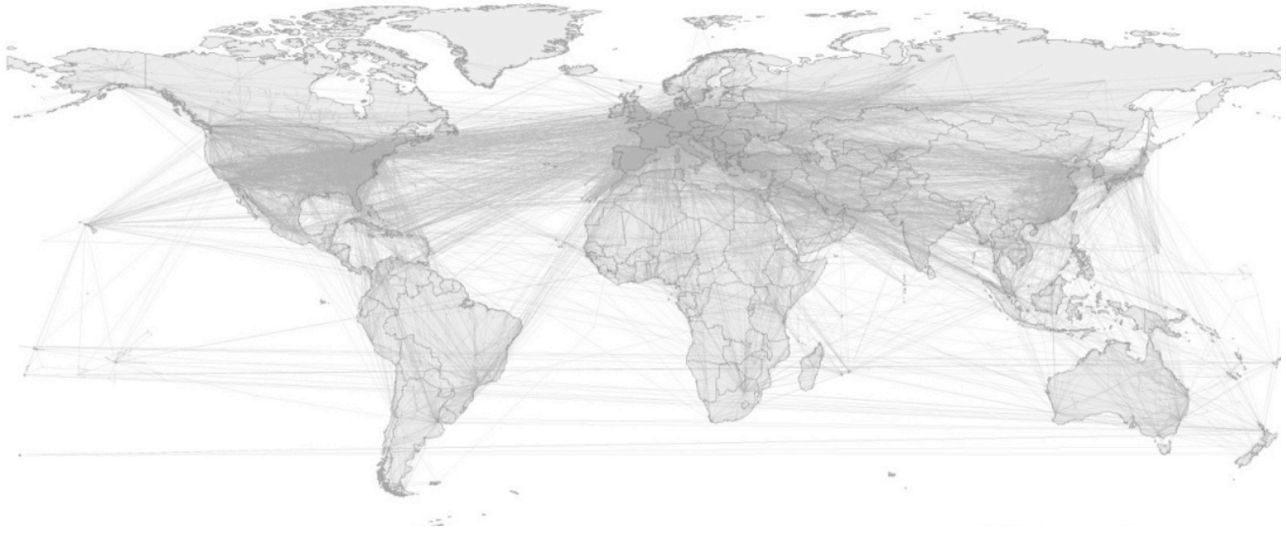
worldwide airport network
>3000 airports
about 20,000 connections



$$P(k) \propto k^{-\gamma}$$

Barrat et al. PNAS (2004)
Colizza et al. PNAS (2006)

mobility flows



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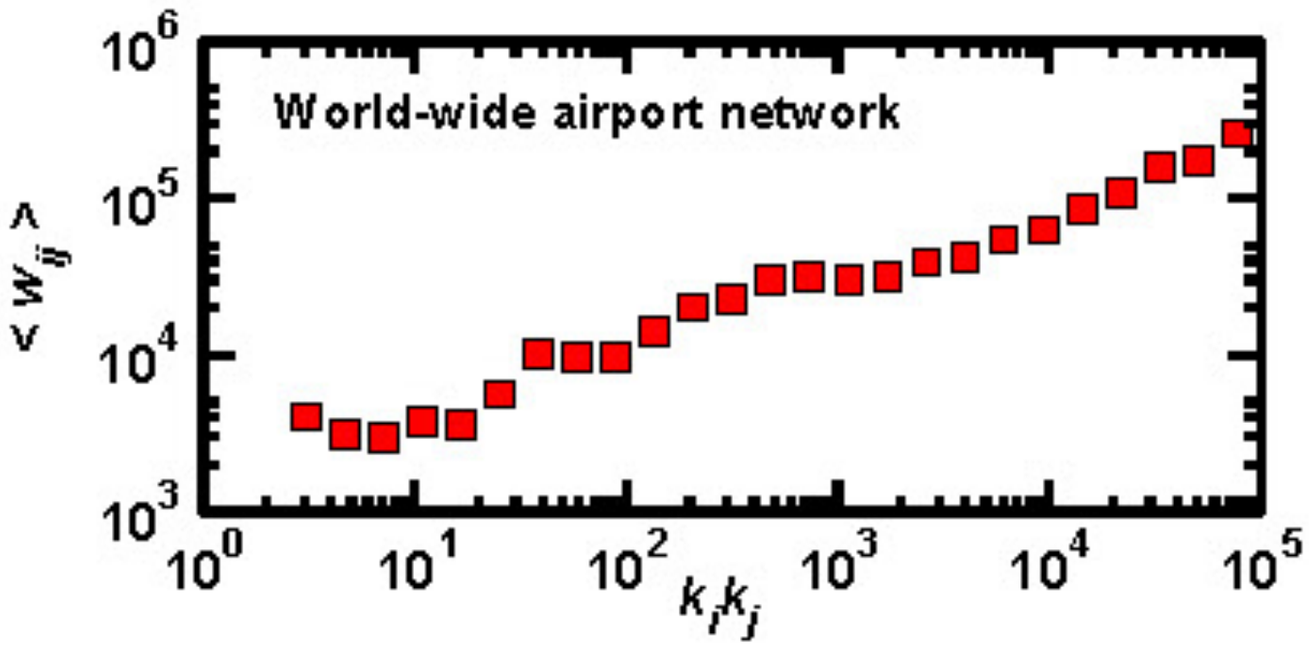


$$w_{ij} \propto (k_i k_j)^{\theta}$$

$$d_{ij} = w_{ij} / N_i$$

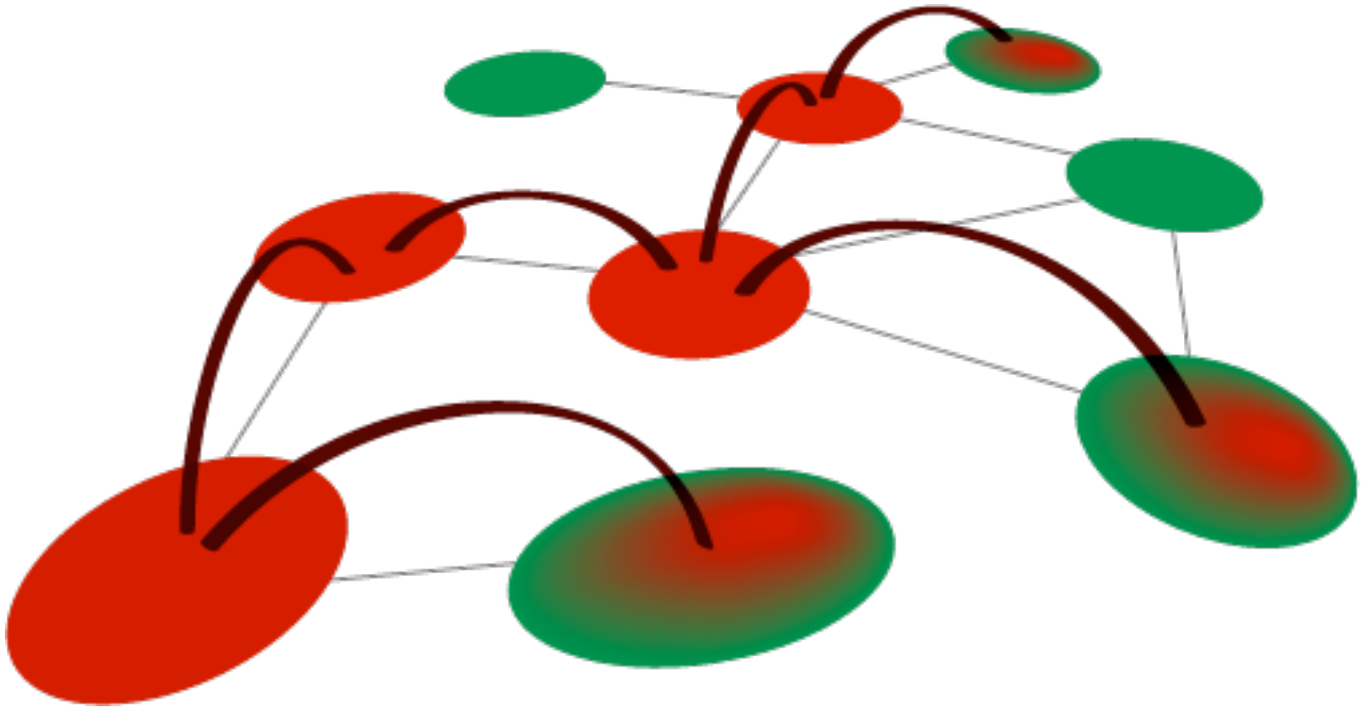
Barrat et al. PNAS (2004)

coarse-grained view

branching process

$D_k^0, D_k^1, \ldots$

\# of ***diseased*** subpops
of degree *k*
at generation *n=0, 1, ...*



coarse-grained view

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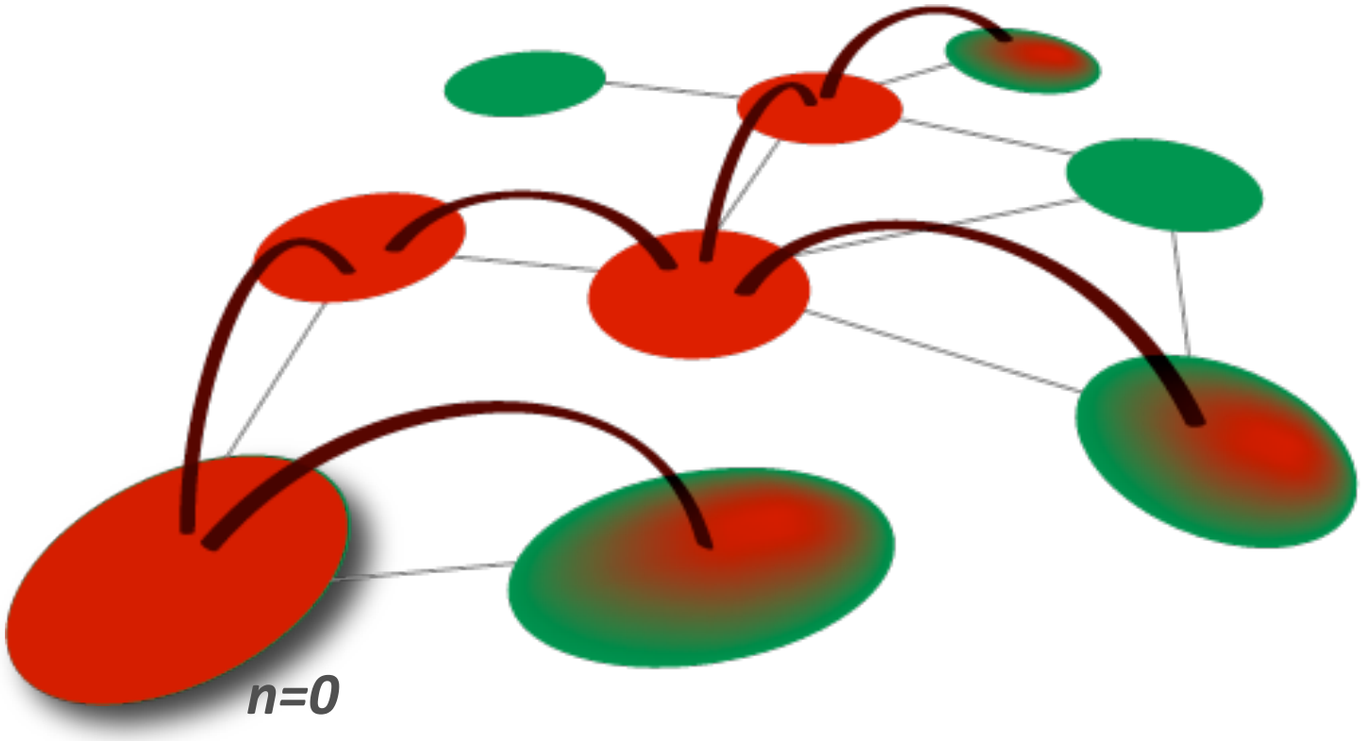

coarse-grained view

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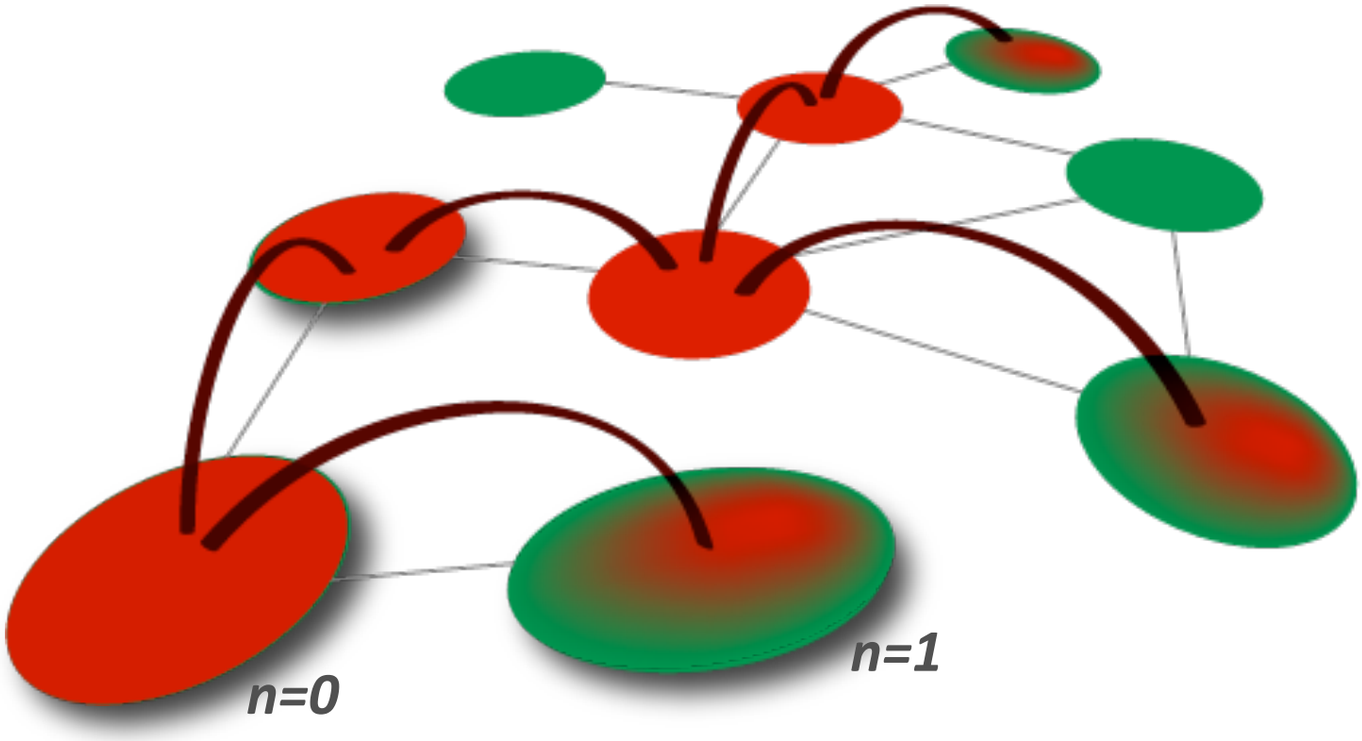

coarse-grained view

branching process

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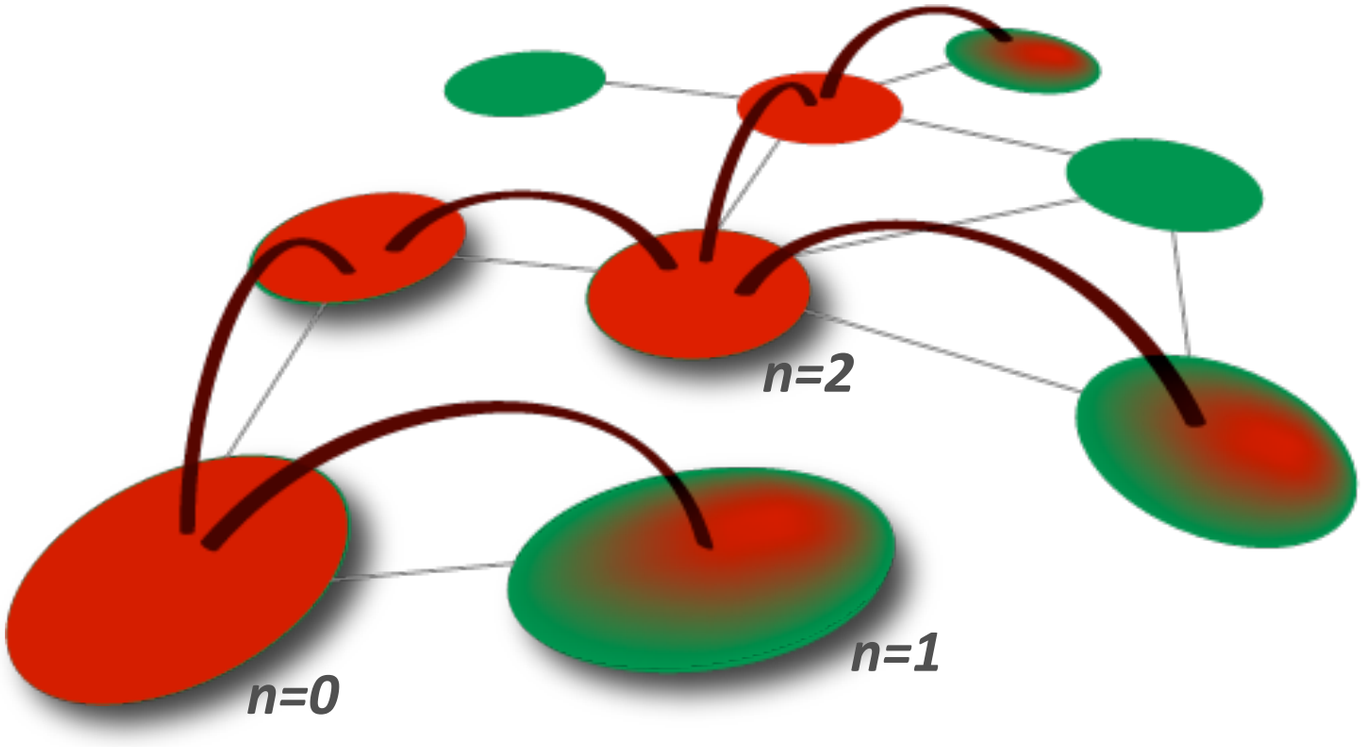

coarse-grained view

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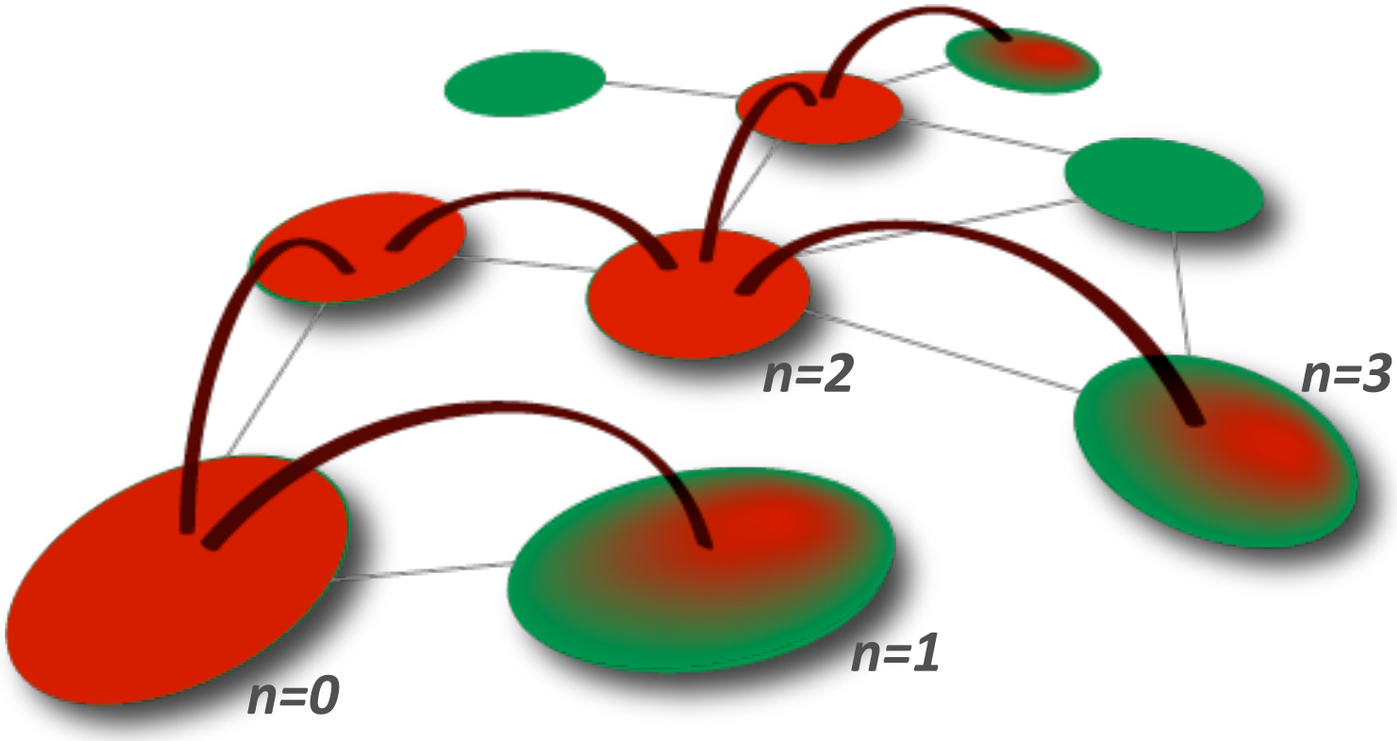
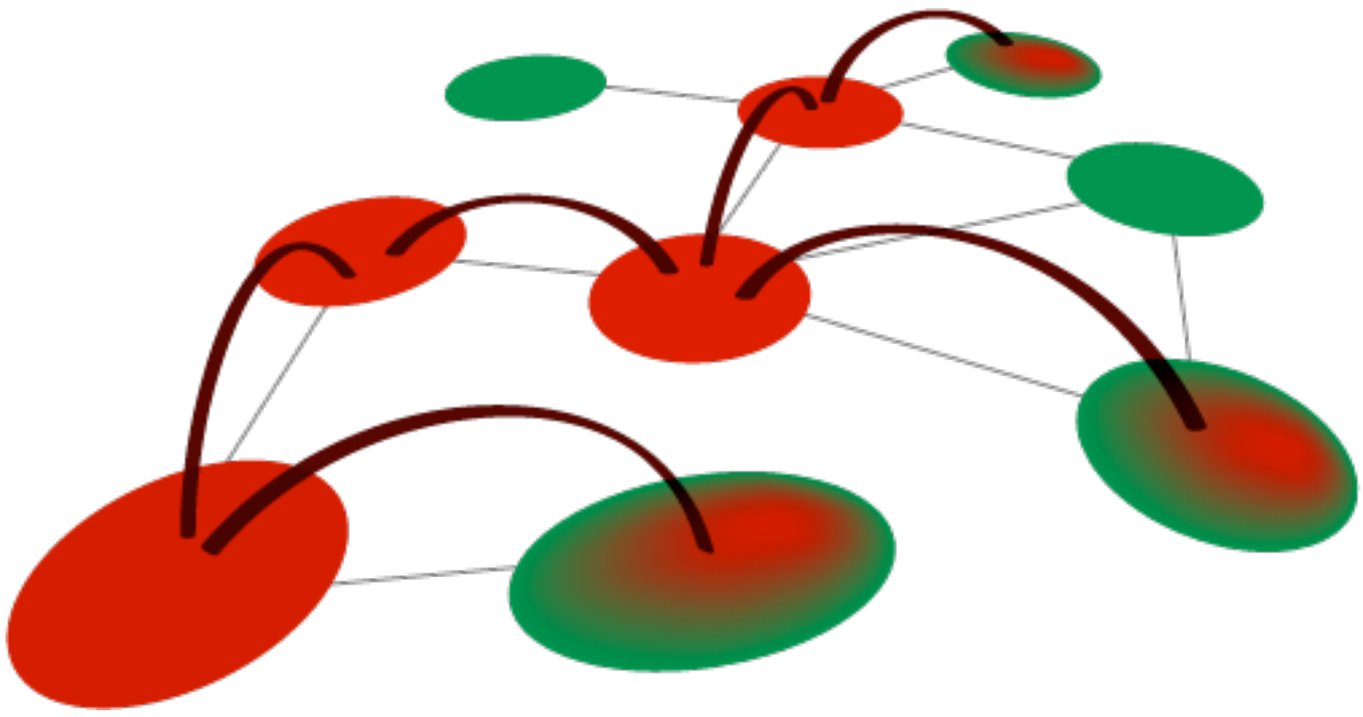
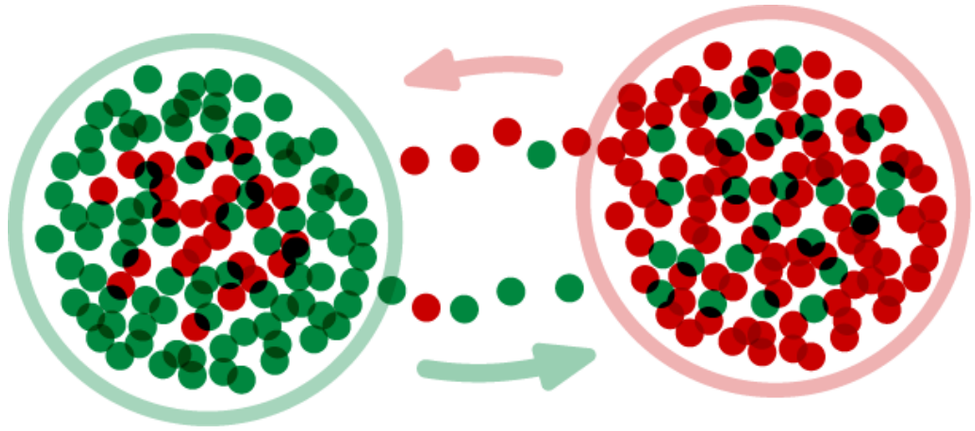


analytical treatment

$$D_k^n = \sum_{k'} D_{k'}^{n-1} P(k|k')(k'-1)\left(1 - \frac{D^{n-1}}{V}\right)\left(1 - R_0^{-\lambda_{kk'}}\right)$$

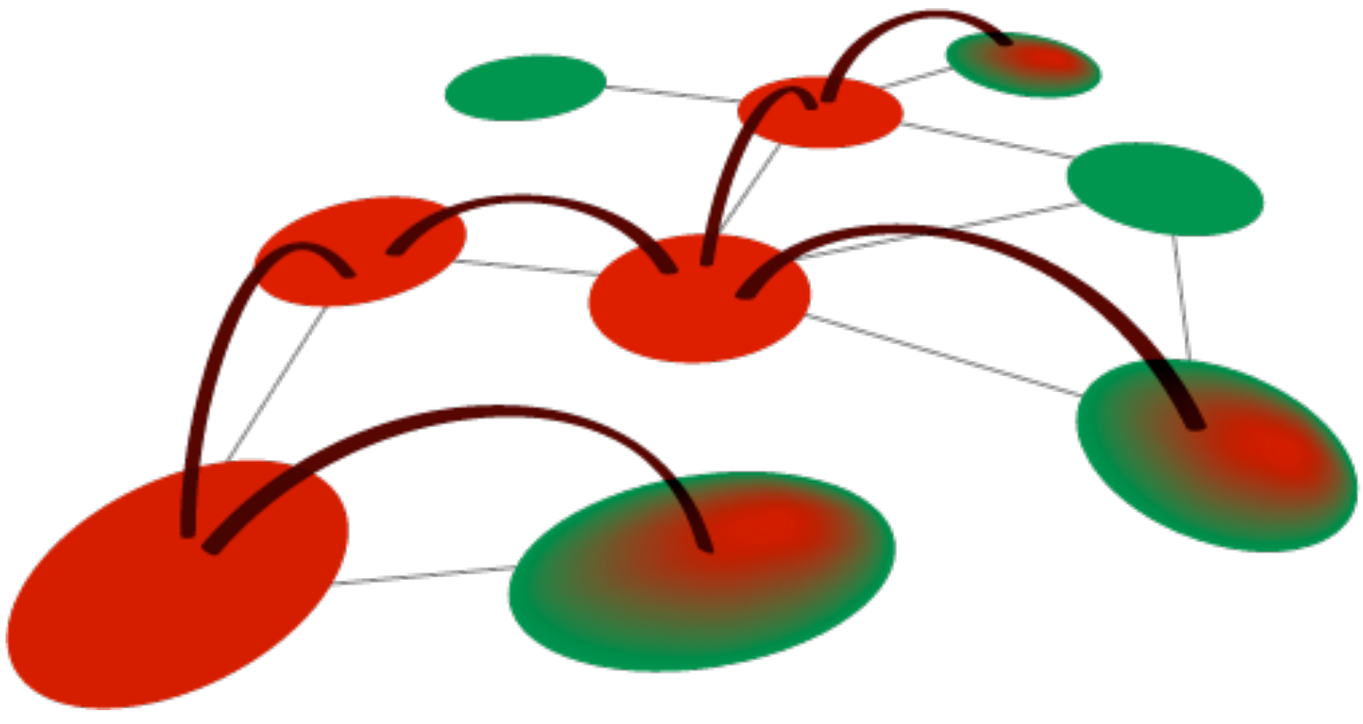


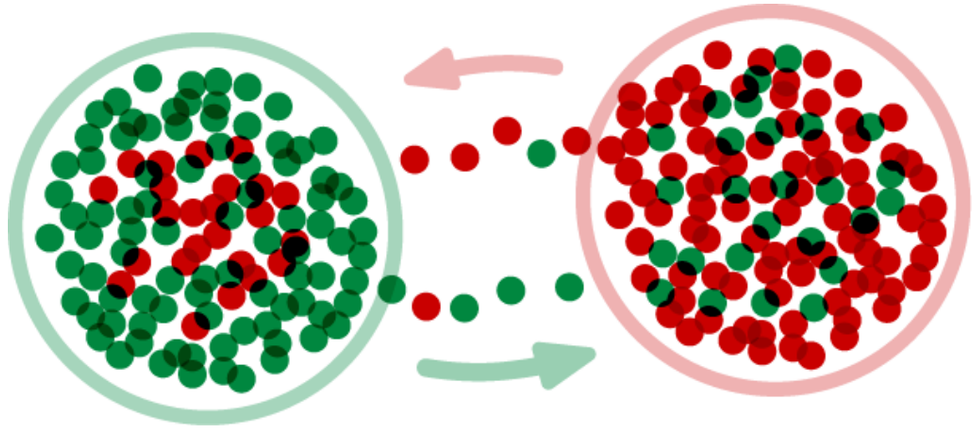


Colizza & Vespignani, PRL 2007, JTB 2008

analytical treatment

$$D_k^n = \sum_{k'} D_{k'}^{n-1} \overbrace{P(k|k')}^{\text{connection } k'\text{-}k} \overbrace{(k'-1)}^{\text{possible paths of infection}} \underbrace{\left(1 - \frac{D^{n-1}}{V}\right)}_{\text{probability of finding uninfected subpopulation}} \underbrace{\left(1 - R_0^{-\lambda_{kk'}}\right)}_{\text{from micro to macro}}$$



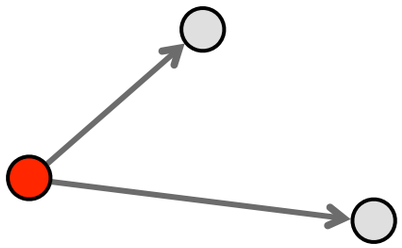


Colizza & Vespignani, PRL 2007, JTB 2008

invasion threshold

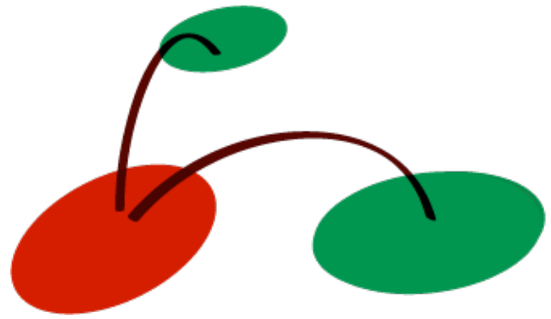
individual level

R_0



subpopulation level

R_*

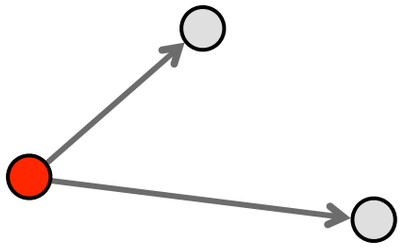


Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

invasion threshold

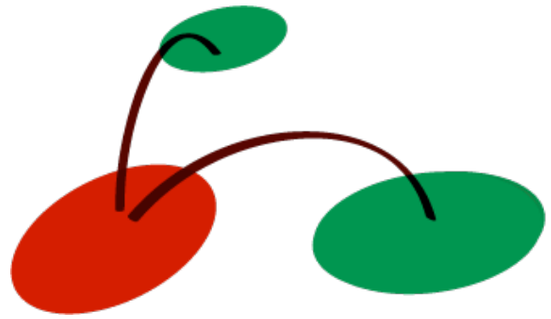
individual level

R_0



subpopulation level

R_*



$$R_* = (R_0 - 1)\frac{\langle k^{2+2\theta}\rangle - \langle k^{1+\theta}\rangle}{\langle k\rangle}\frac{w_0\alpha}{\mu}$$

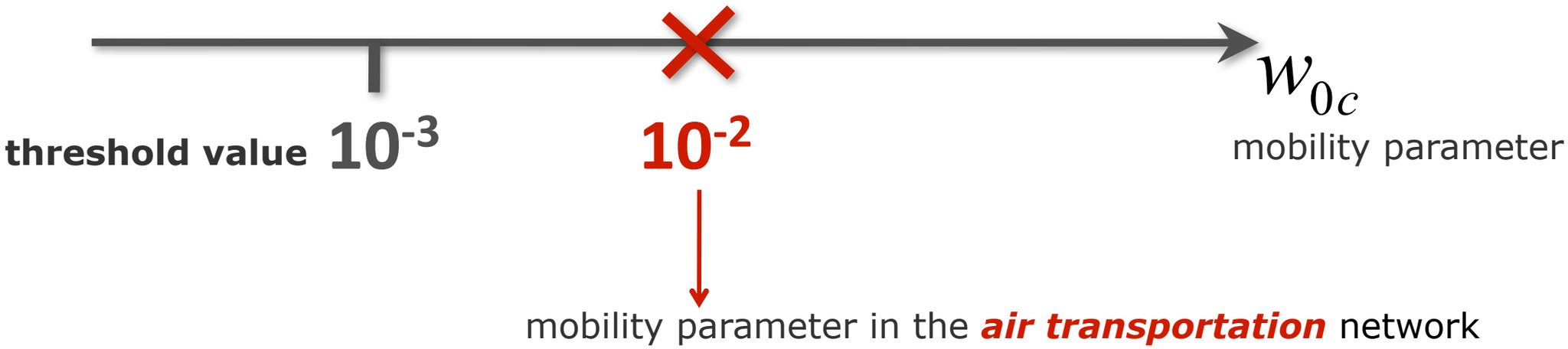
$$w_0 \geq \frac{\mu R_0^2}{2(R_0-1)^2}\frac{\langle k\rangle}{\langle k^{2+2\theta}\rangle - \langle k^{1+\theta}\rangle}$$

Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

critical mobility

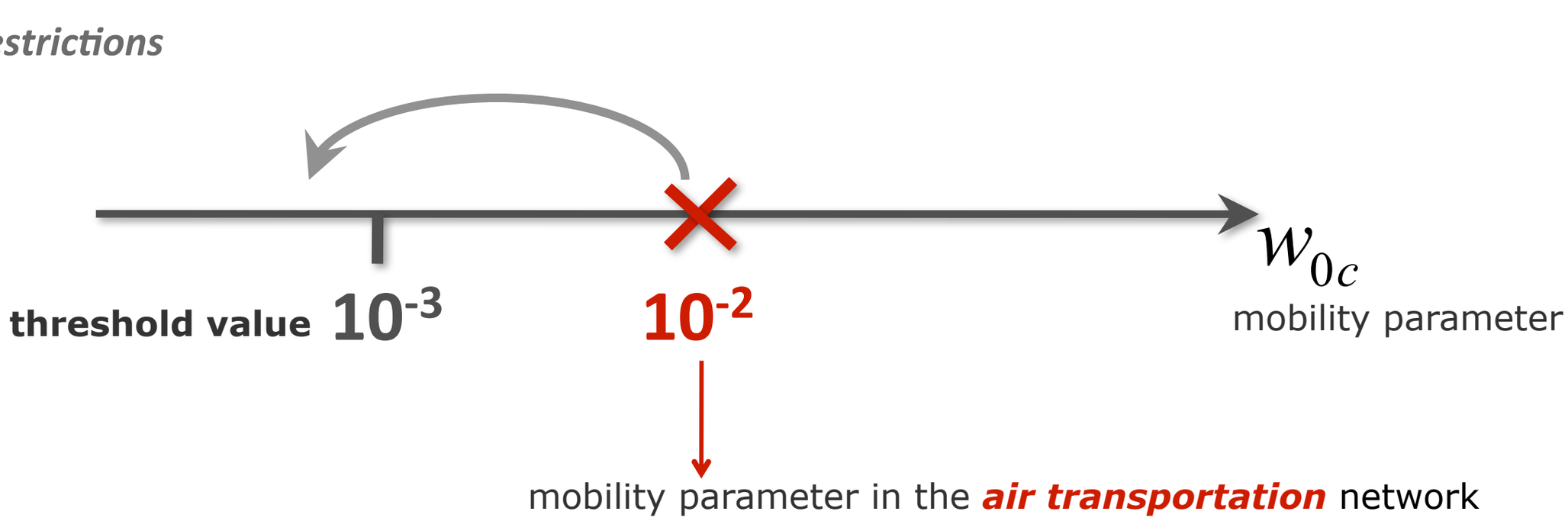
Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

critical mobility



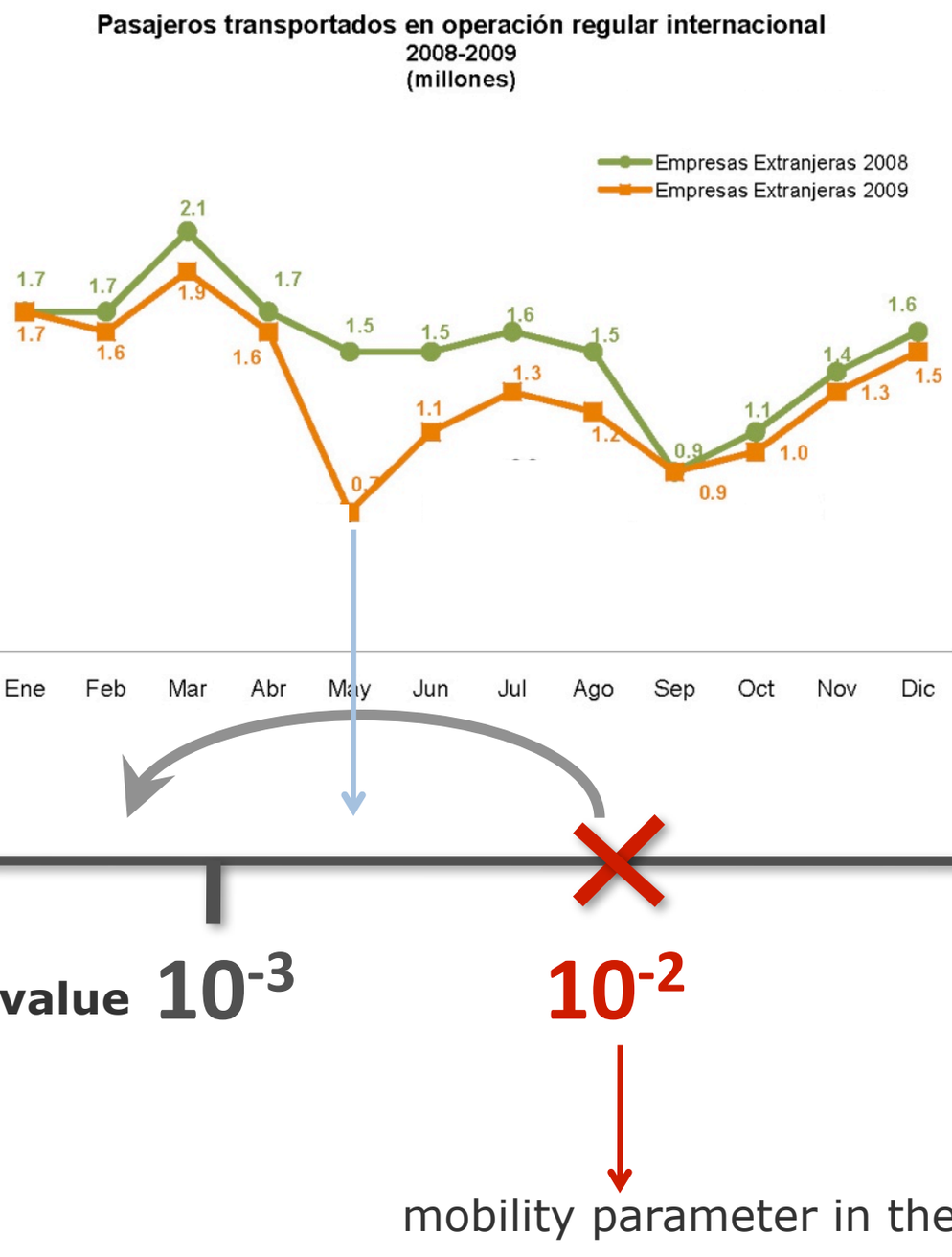
Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

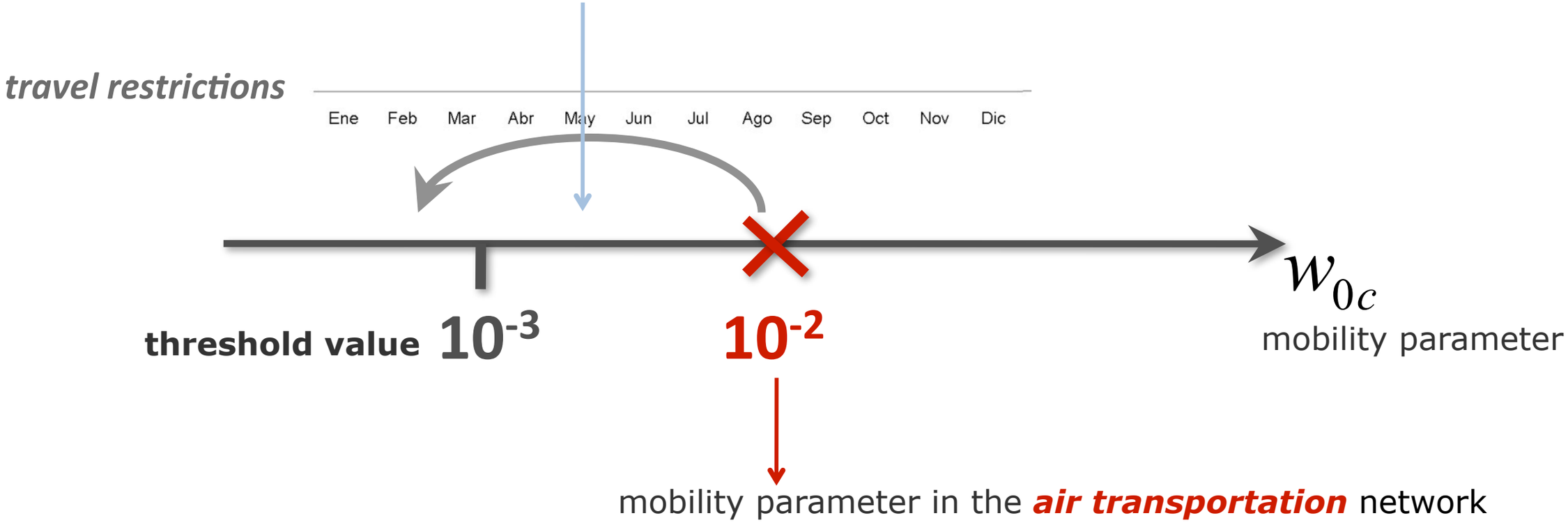
critical mobility



Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

critical mobility



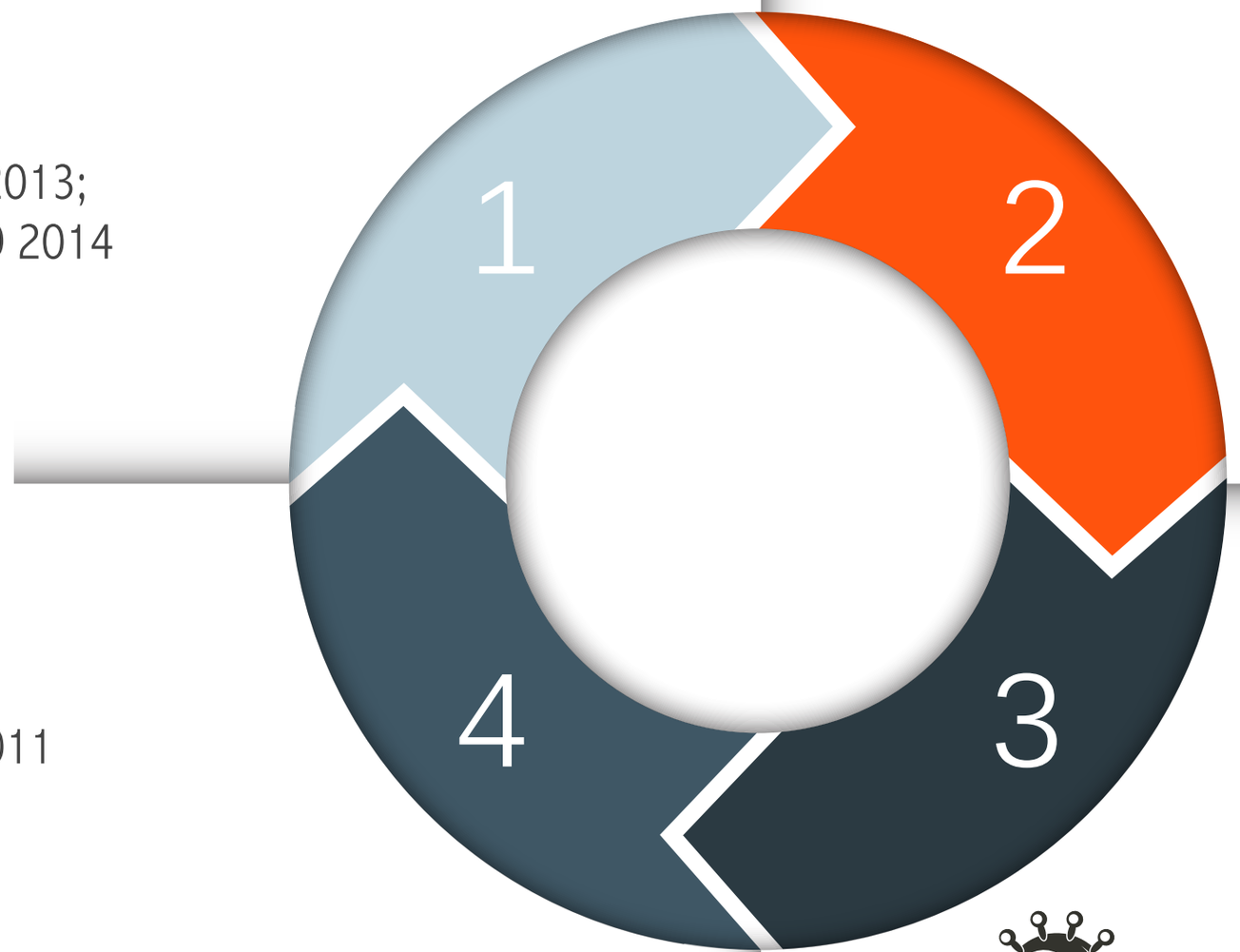


Colizza & Vespignani, PRL 2007, JTB 2008; Bajardi et al PLoS ONE 2011

going beyond

MIXING & TRAVEL

LENGTH OF STAY



Apolloni et al. BMC ID 2013;
Apolloni et al. TBIOMED 2014

Poletto et al, Sci Rep 2012;
Poletto et al, JTB 2013

Meloni et al. Sci Rep 2011

Poletto et al. PLOS CB 2013

CHANGE OF BEHAVIOR

MULTI-STRAINS

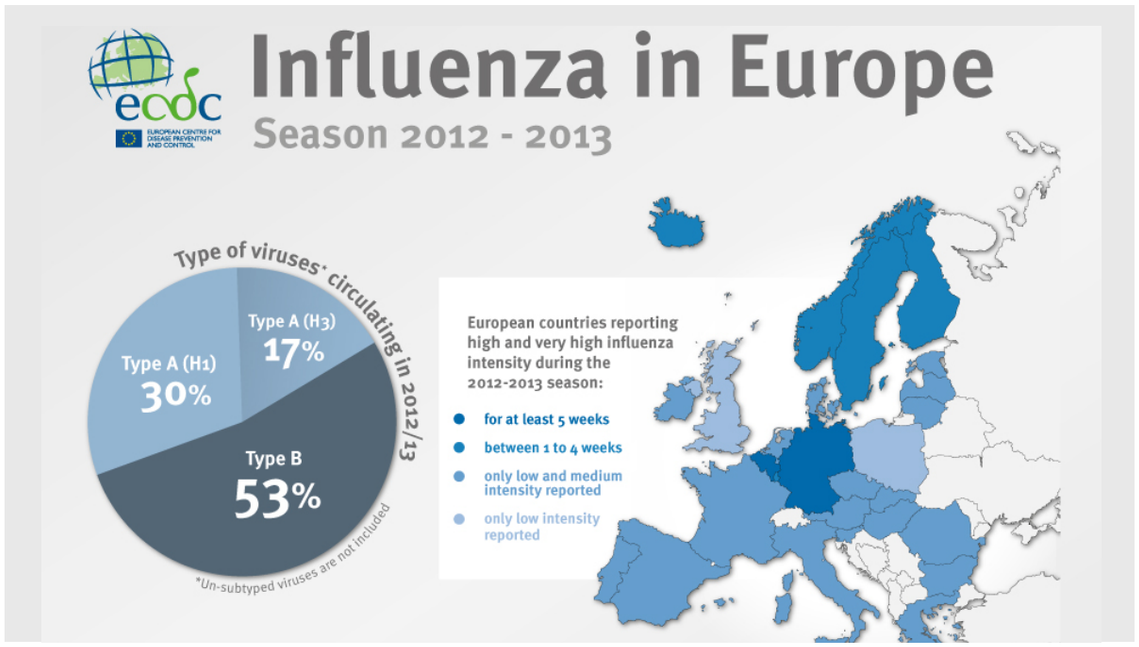
infectious diseases: surveillance

flu by the numbers

pandemic influenza

Balcan et al, BMC Med 2009
Tizzoni et al, BMC Med 2012
www.gleamviz.org

seasonal influenza

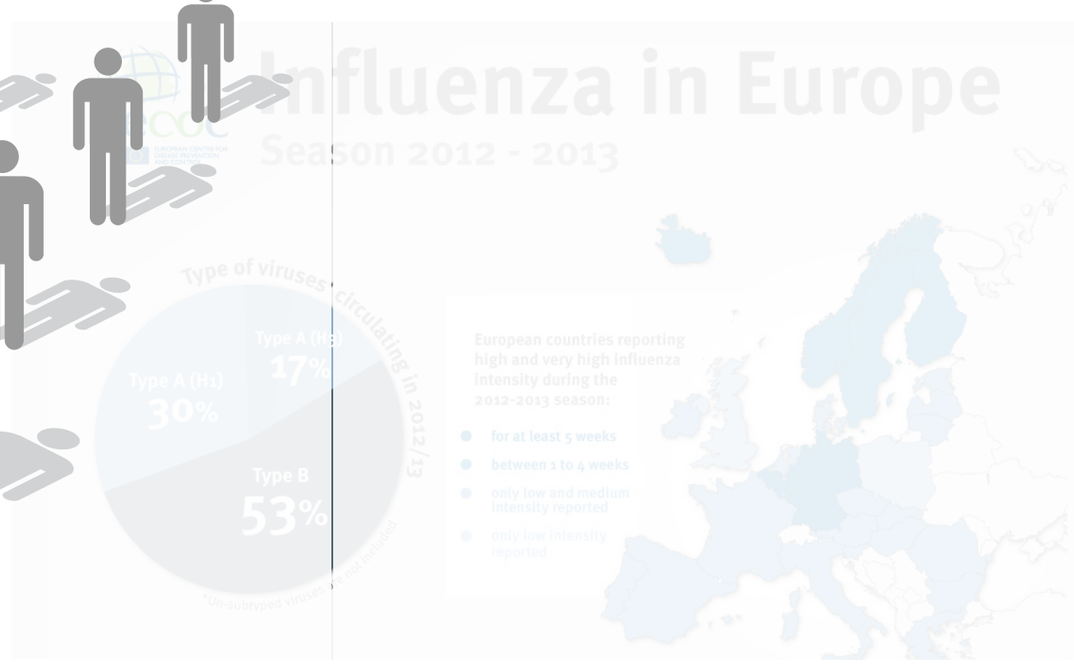


flu by the numbers

pandemic influenza

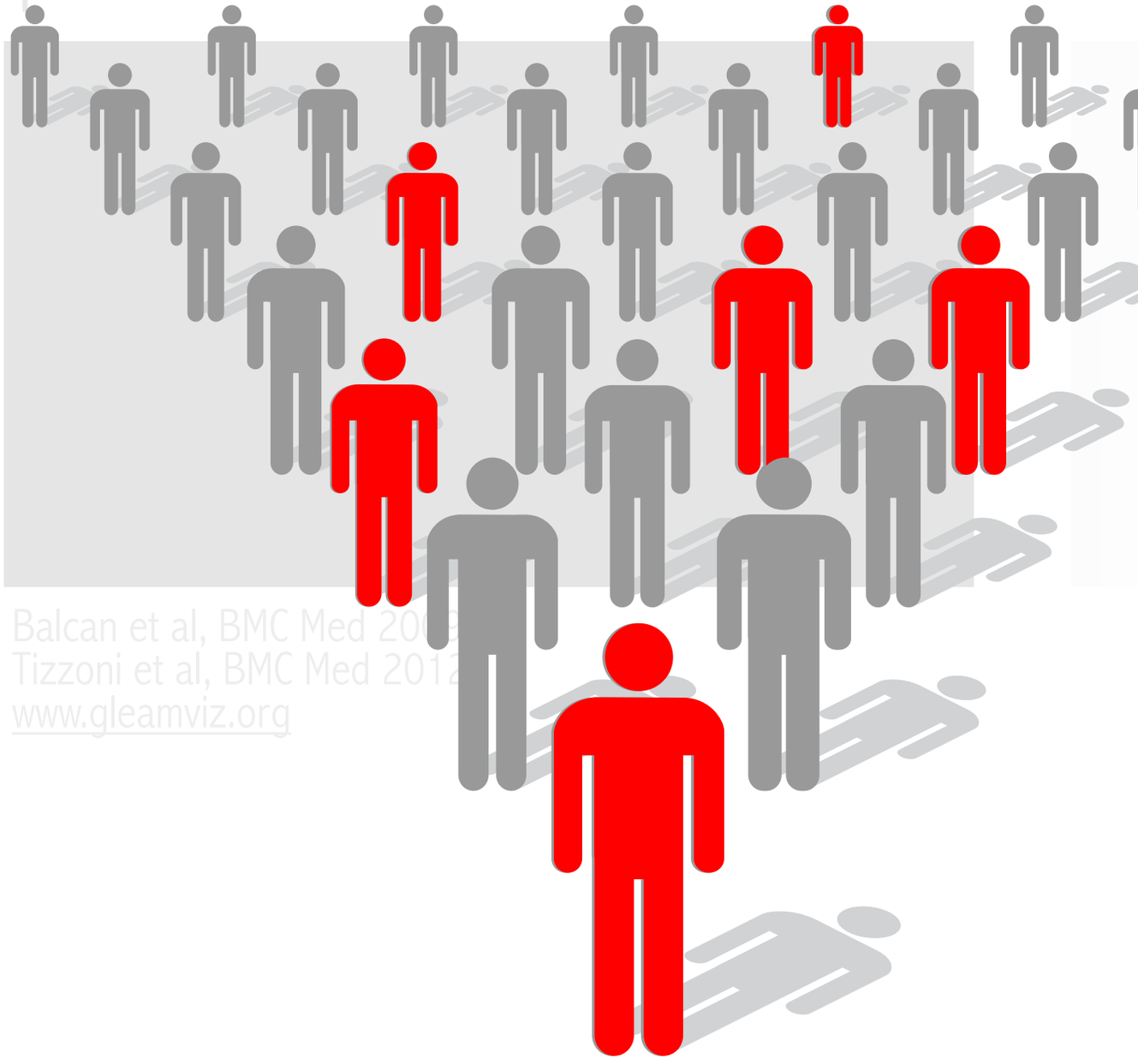
Balcan et al, BMC Med 200
Tizzoni et al, BMC Med 201
www.gleamviz.org

seasonal influenza



flu by the numbers

pandemic influenza



Balcan et al, BMC Med 200
Tizzoni et al, BMC Med 201
www.gleamviz.org

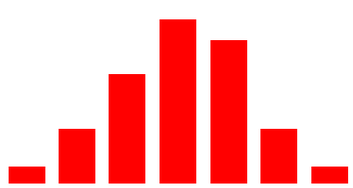
seasonal influenza

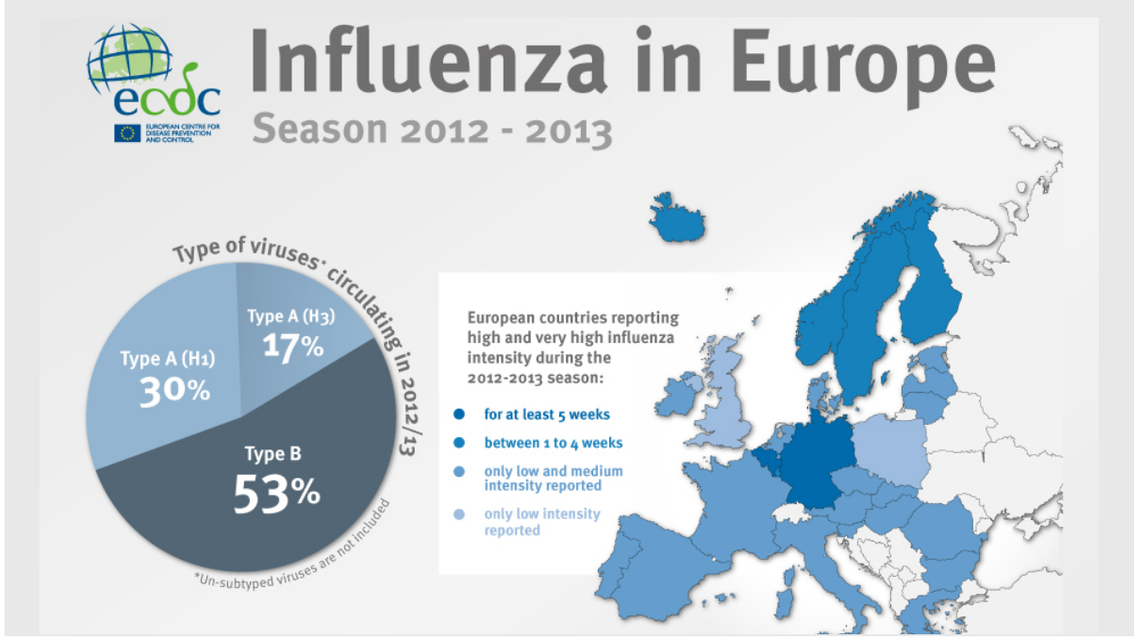
1 IN 5
WILL CATCH
THE FLU

counting flu cases

GP consultations

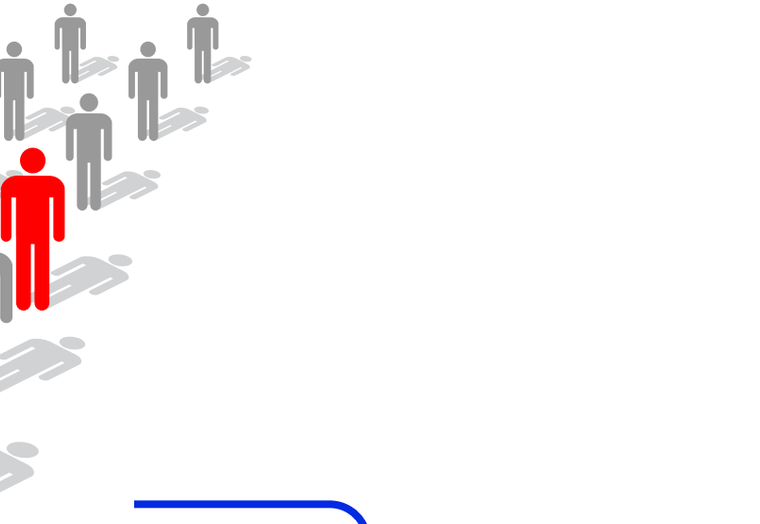
sentinel GPs





counting flu cases

digital surveillance



GP consultations

sentinel GPs

OPEN ACCESS Freely available online

PLoS one

The Use of Twitter to Track Levels of Disease Activity and Public Concern in the U.S. during the Influenza A H1N1 Pandemic

Alessio Signorini[1], Alberto Maria Segre[1], Philip M. Polgreen[2,3]*

1 Department of Computer Science, University of Iowa, Iowa City, Iowa, United States of America, **2** Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, Iowa, United States of America, **3** Department of Internal Medicine, Carver College of Medicine, University of Iowa, Iowa City, Iowa, United States of America

- disease activity
- public sentiment

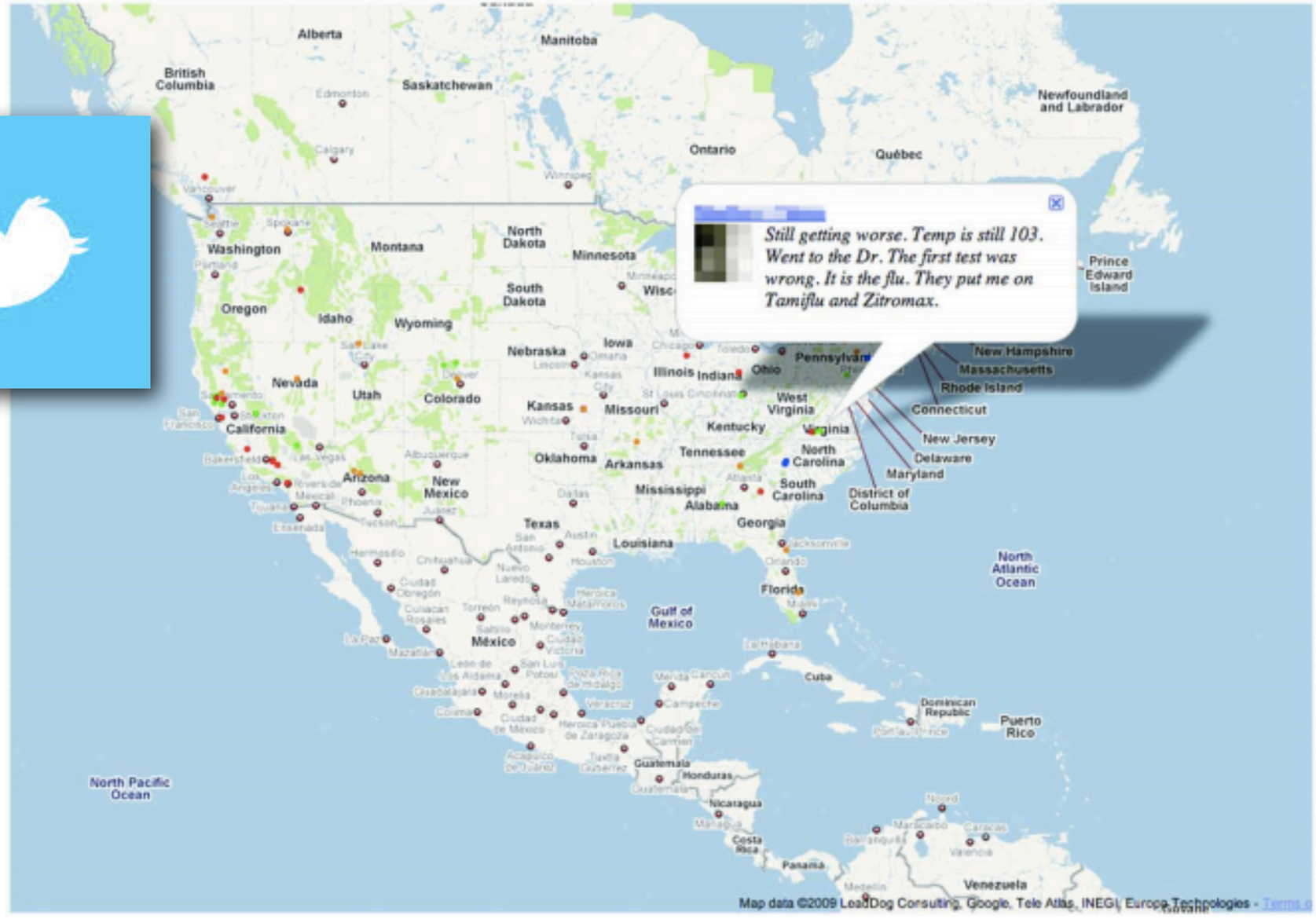
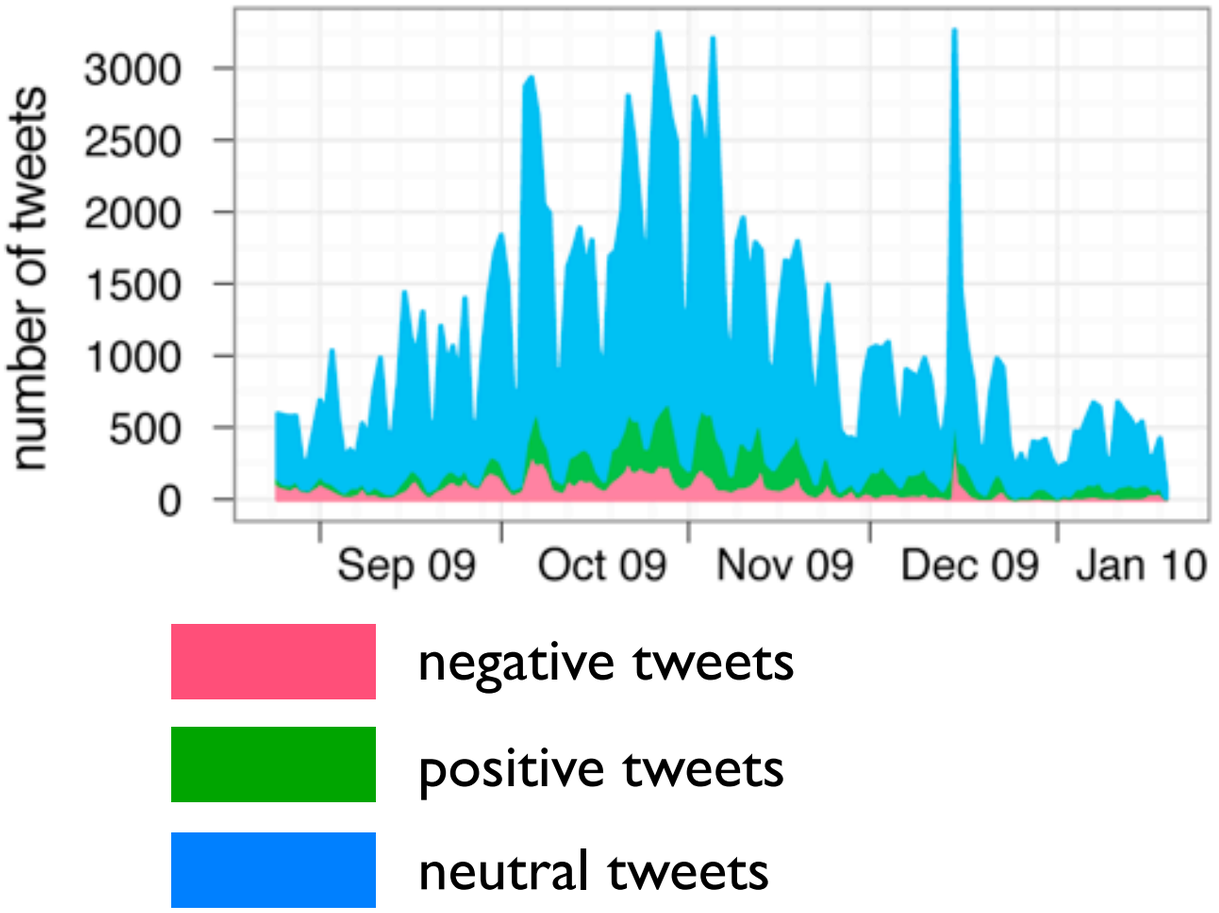
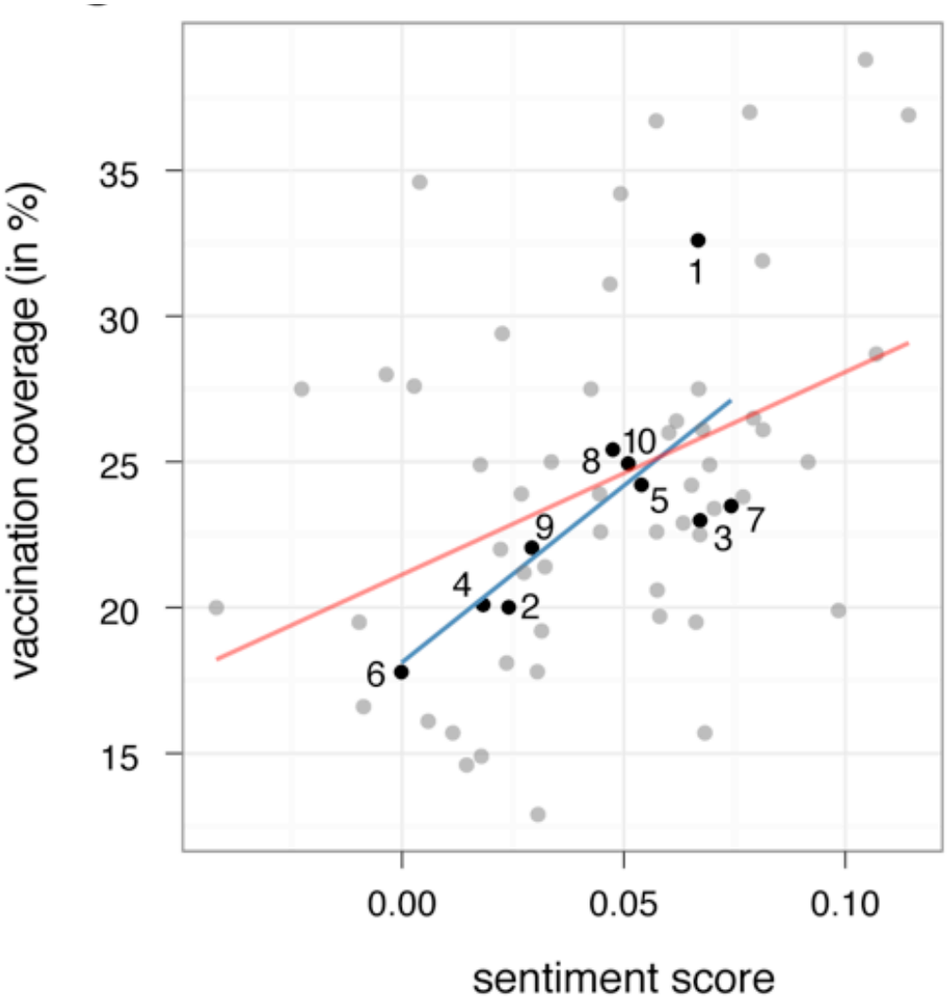


Figure 1. Influenza-Related Twitter Map. Color-coded dots represent tweets issued by users (shown at the users' self-declared home location). Hovering over the dot displays the content of the tweet; here, the user name is intentionally obscured. A client-side JavaScript application updates the map in near-real time, showing the 500 most recent tweets matching the preselected influenza-related keywords.
doi:10.1371/journal.pone.0019467.g001

assessing vaccination sentiment





- information flows more often among people sharing same opinion
- communities ~ opinion >> target specific intervention
- exposure to negative sentiment is contagious >> new communication?

Salathe et al. PLOS CB 2011; EPJ Data Science 2013

nature Vol 457|19 February 2009|doi:10.1038/nature07634

LETTERS

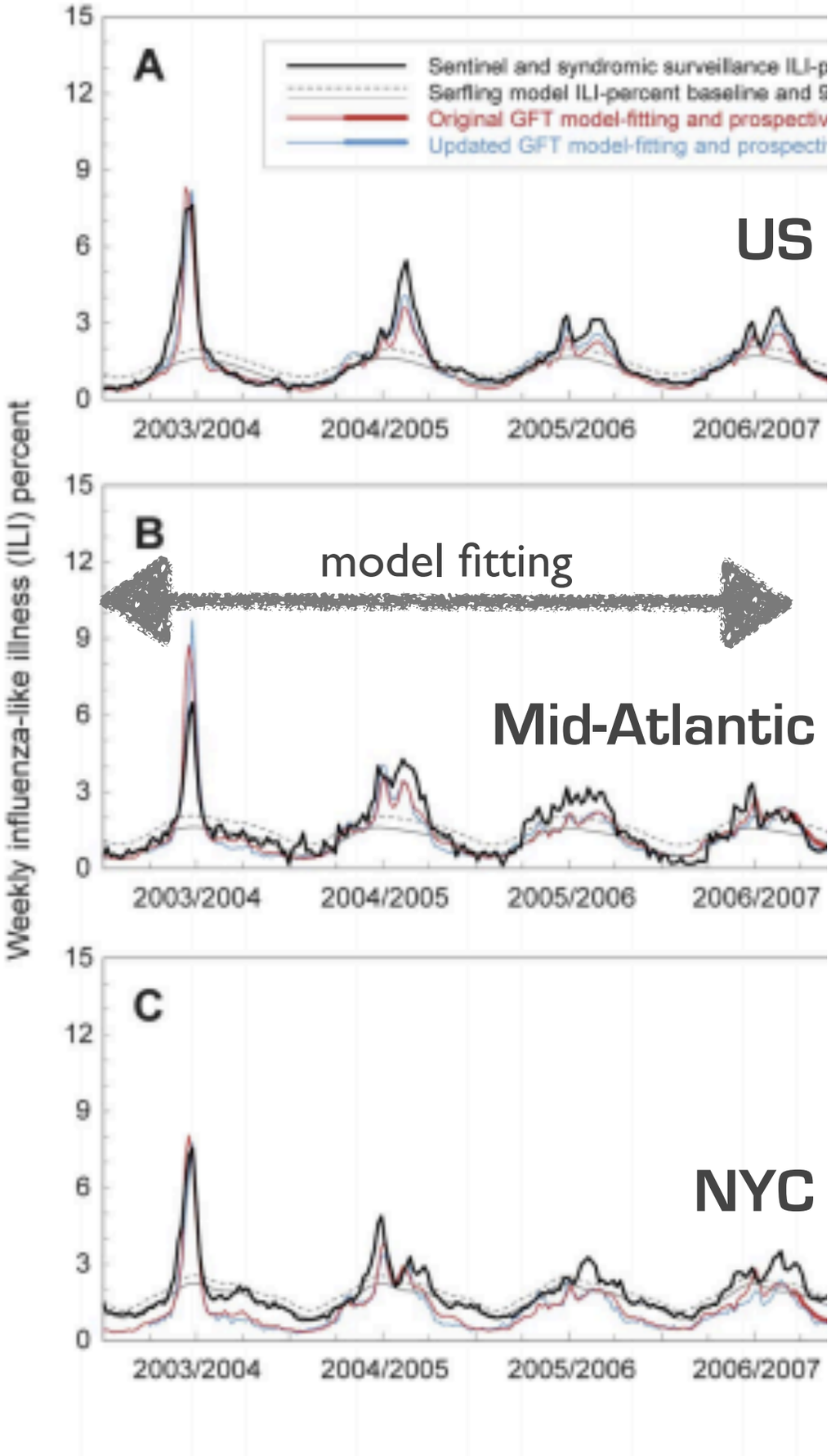
Detecting influenza epidemics using search engine query data

Jeremy Ginsberg[1], Matthew H. Mohebbi[1], Rajan S. Patel[1], Lynnette Brammer[2], Mark S. Smolinski[1] & Larry Brilliant[1]

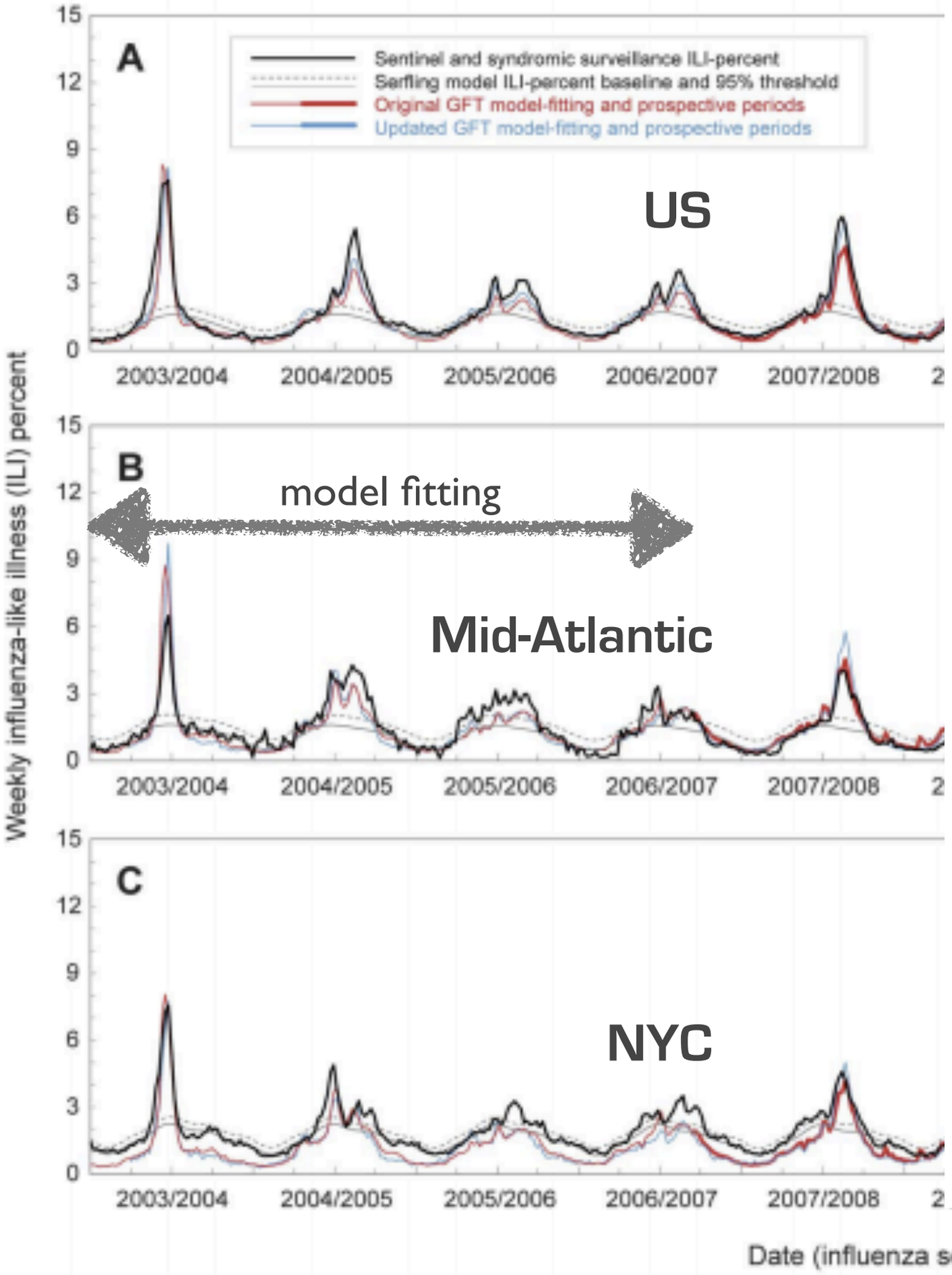
google.org Flu Trends

Search Query Topic	Top 45 Queries N	Top 45 Queries Weighted	Next 55 Queries N	Next 55 Queries Weighted
Influenza Complication	11	18.15	5	3.40
Cold/Flu Remedy	8	5.05	6	5.03
General Influenza Symptoms	5	2.60	1	0.07
Term for Influenza	4	3.74	6	0.30
Specific Influenza Symptom	4	2.54	6	3.74
Symptoms of an Influenza Complication	4	2.21	2	0.92
Antibiotic Medication	3	6.23	3	3.17
General Influenza Remedies	2	0.18	1	0.32
Symptoms of a Related Disease	2	1.66	2	0.77
Antiviral Medication	1	0.39	1	0.74
Related Disease	1	6.66	3	3.77
Unrelated to Influenza	0	0.00	19	28.37
	45	**49.40**	**55**	**50.60**

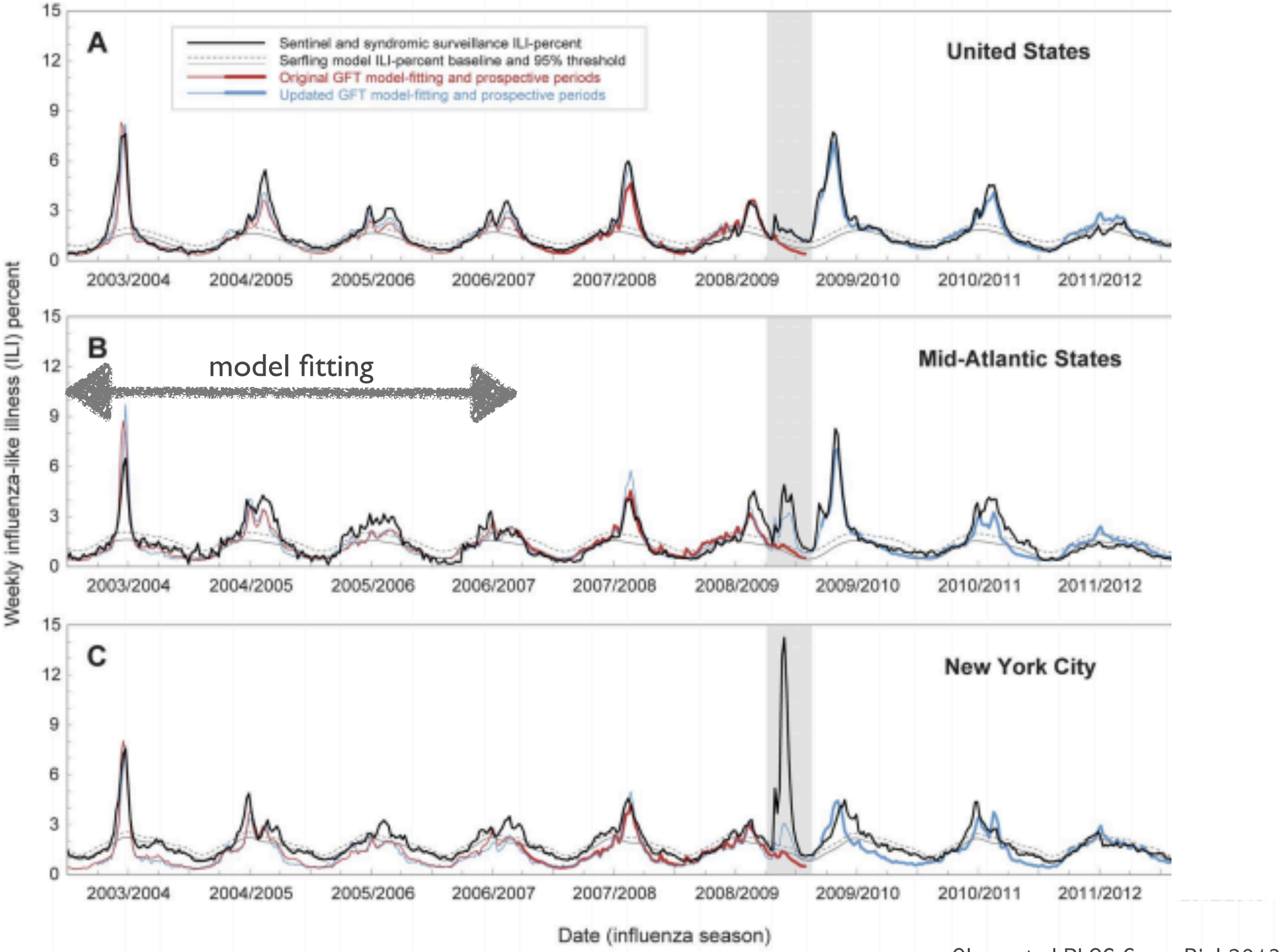
Table 1: Topics found in search queries which were found to be most correlated with CDC ILI data. The top 45 queries were used in our final model; the next 55 queries are presented for comparison purposes. The number of queries in each topic is indicated, as well as query volume-weighted counts, reflecting the relative frequency of queries in each topic.



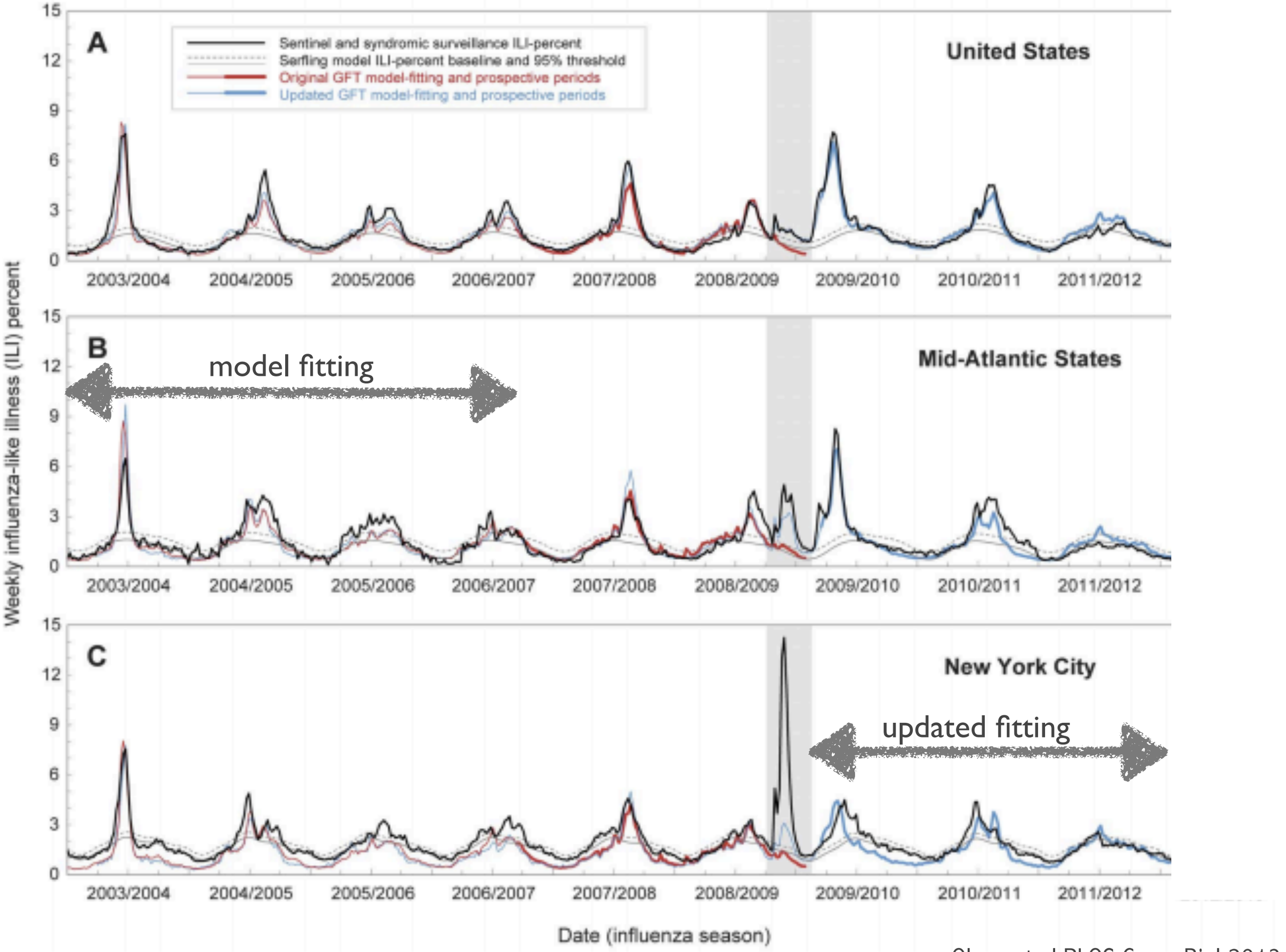
Olson et al PLOS Comp Biol 2013



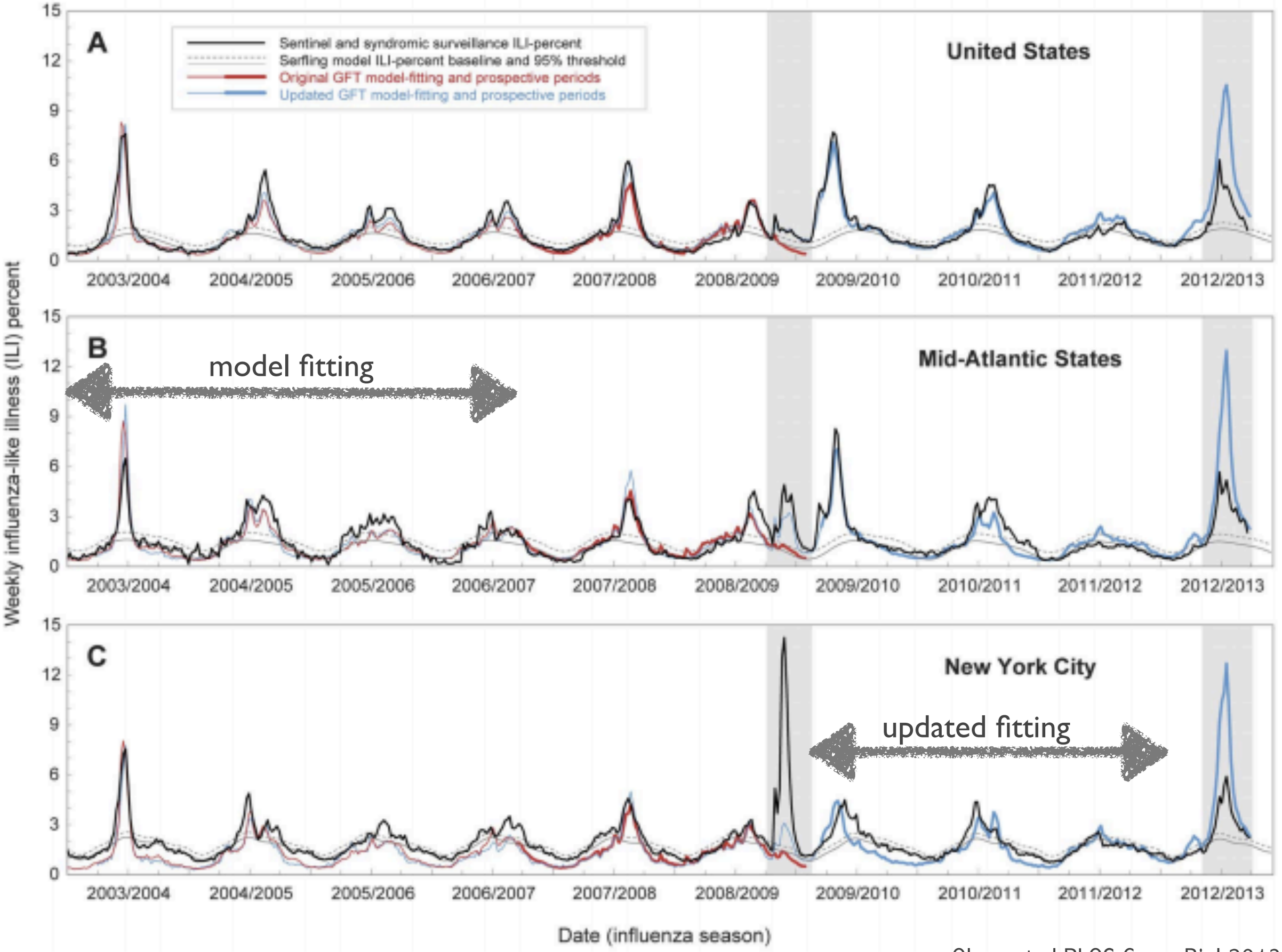
Olson et al PLOS Comp Biol 2013



Olson et al PLOS Comp Biol 2013



Olson et al PLOS Comp Biol 2013



Olson et al PLOS Comp Biol 2013

JOHN ANGELILLO/UPI/NEWSCOM

The latest US influenza season is more severe and has caused more deaths than usual.

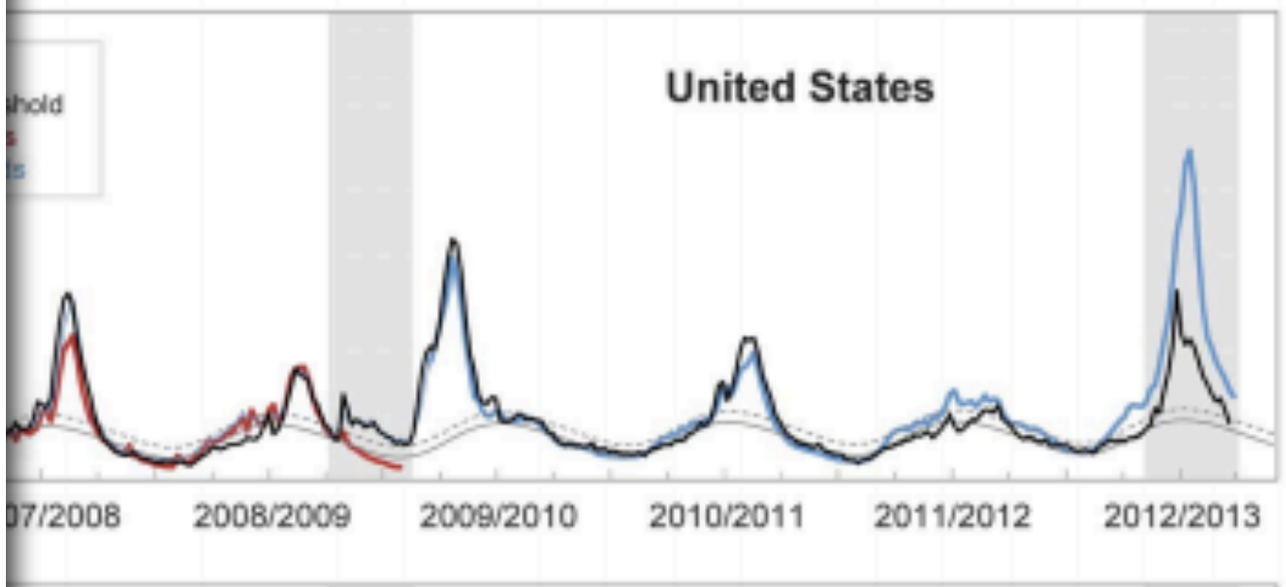
EPIDEMIOLOGY

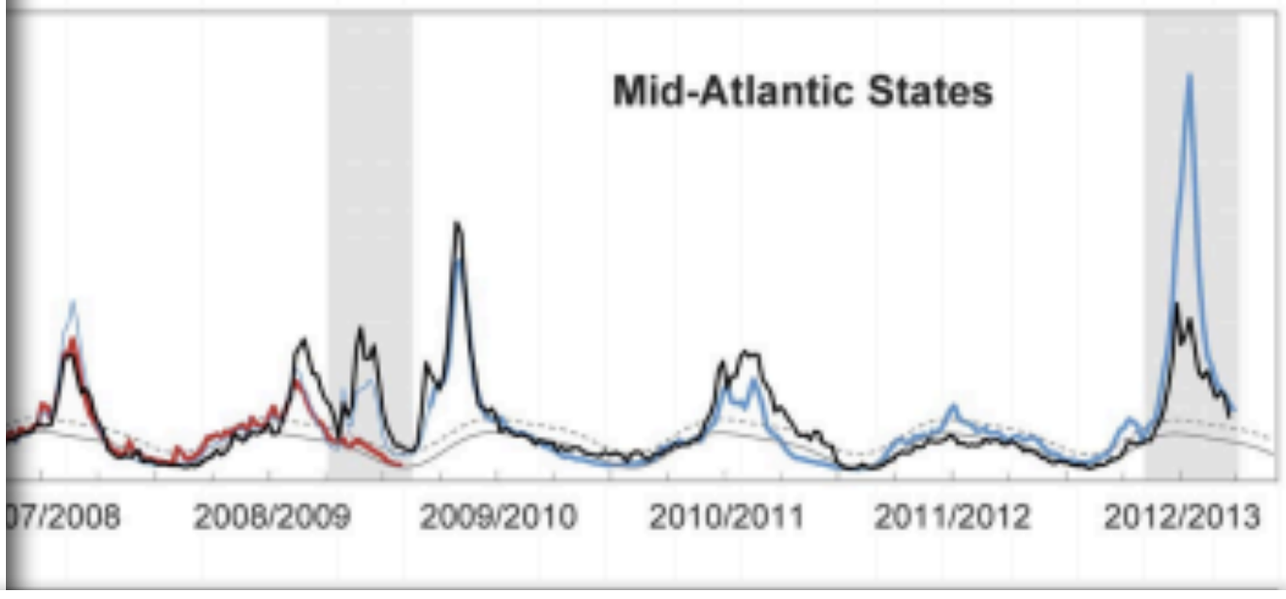
When Google got flu wrong

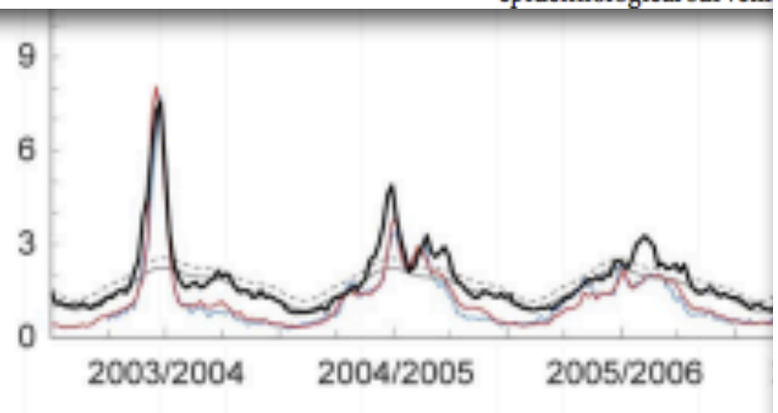
US outbreak foxes a leading web-based method for tracking seasonal flu.

BY DECLAN BUTLER

complement, but not sub
epidemiological surveill





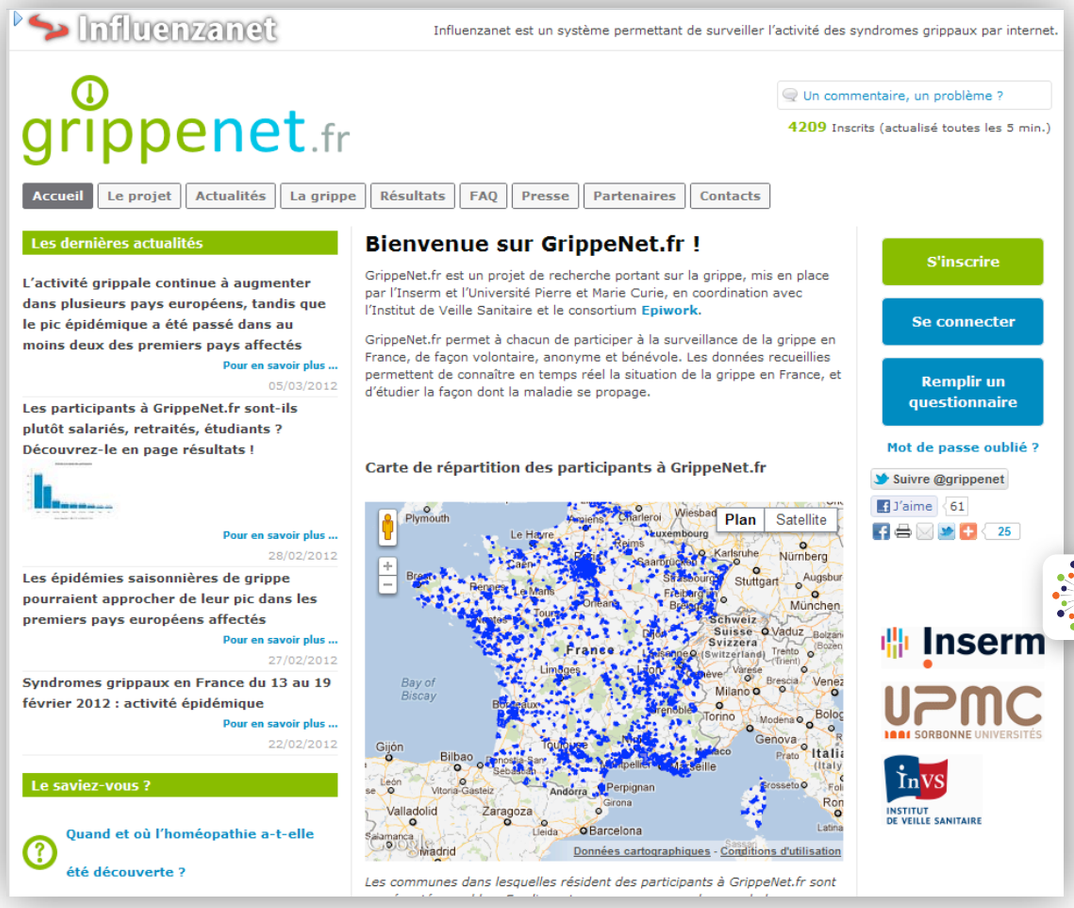


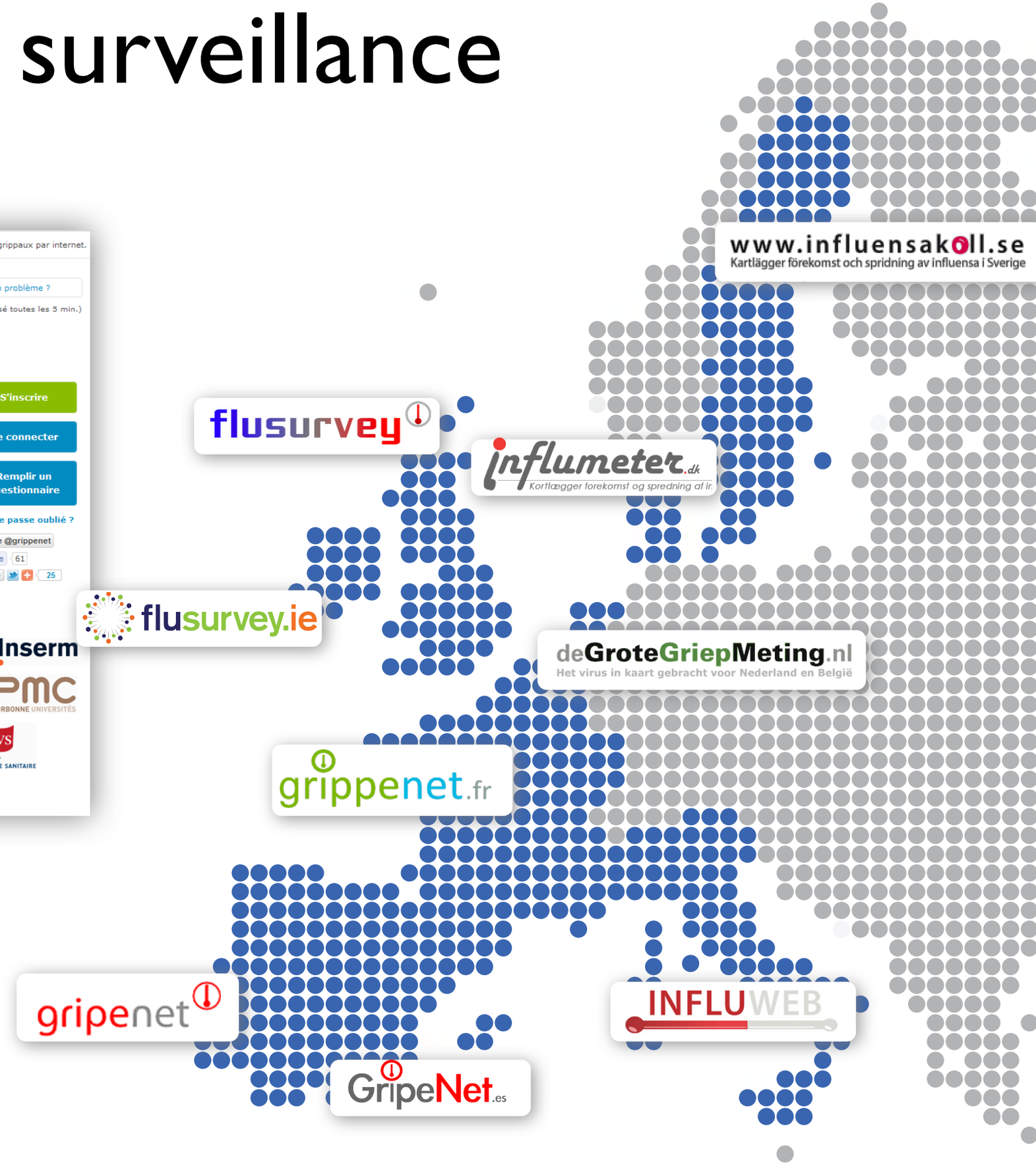
BIG DATA

The Parable of Google Flu: Traps in Big Data Analysis

David Lazer,[1,2]* Ryan Kennedy,[1,3,4] Gary King,[3] Alessandro Vespignani[3,5,6]

participatory surveillance



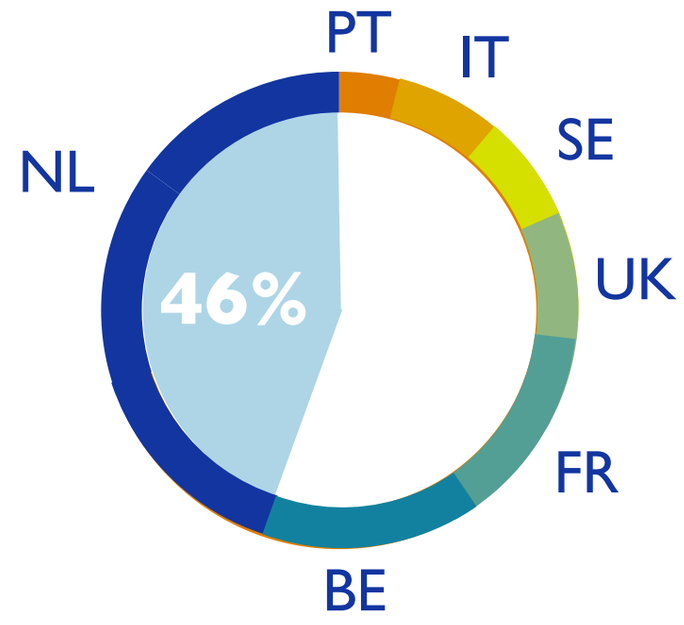


www.influenzanet.eu

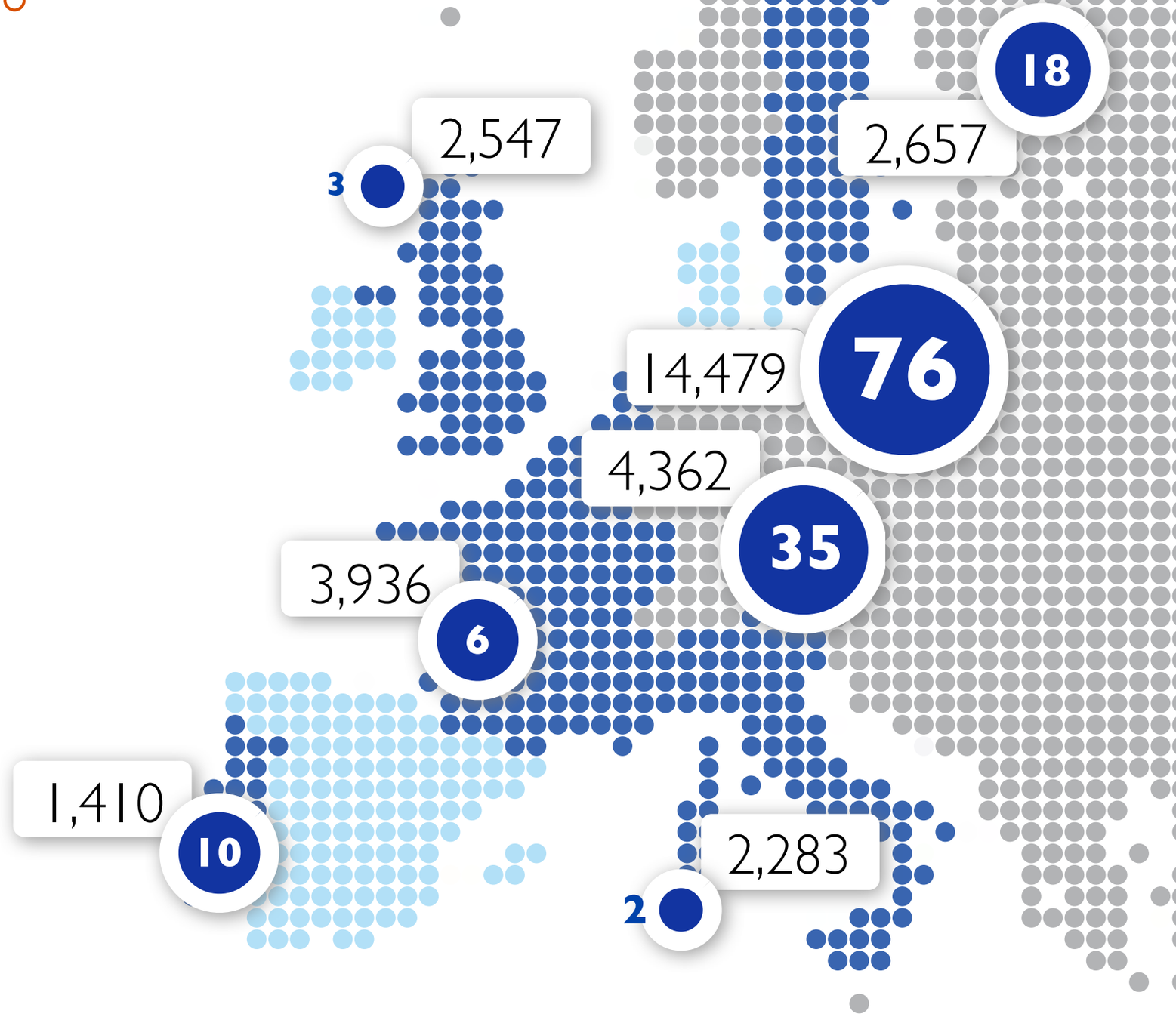
influenzanet

31,674 European residents

80% : *active* [55-90]%

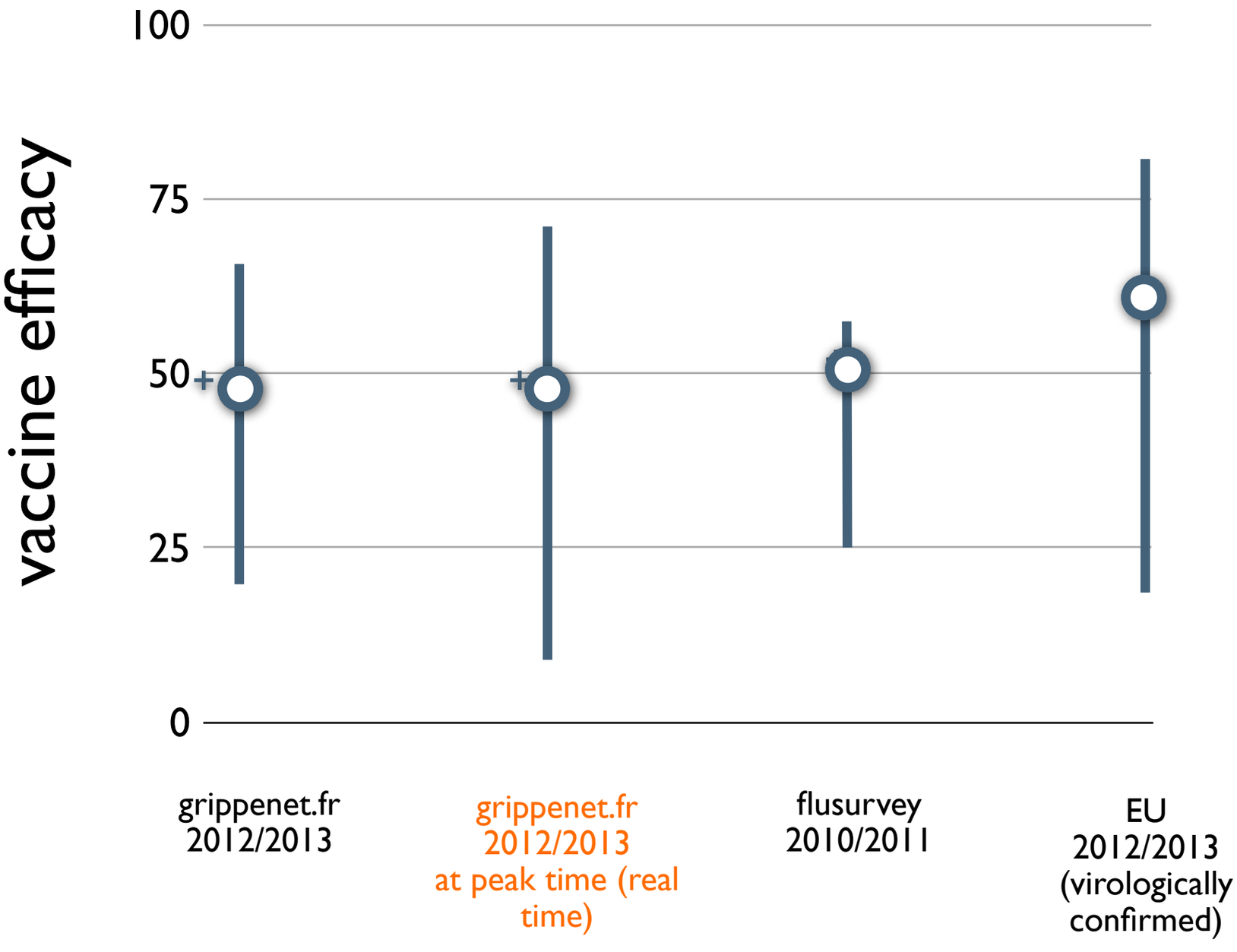


participants per 100,000 individuals in the country



Debin et al, PLOS One 2013
Paolotti et al, Clin Microbiol Inf 2014

real-time predictions

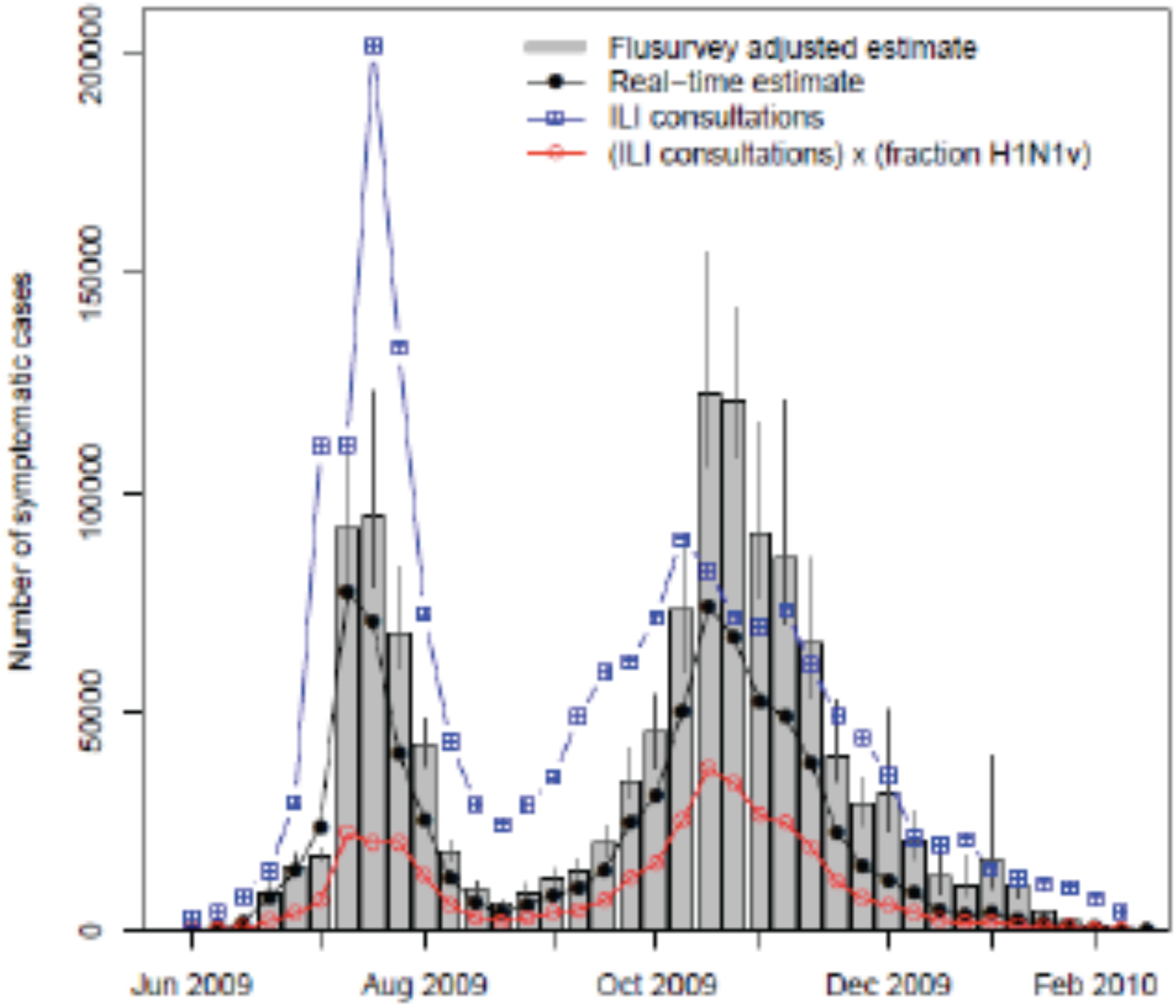


Debin et al, Human Vaccine & Therap 2014

re-assessment of surveillance data

- ILI seeking medical attention:
start: 43%
end: 32% ($p<10^{-4}$)

- fall epidemic wave: 45% bigger than initially thought

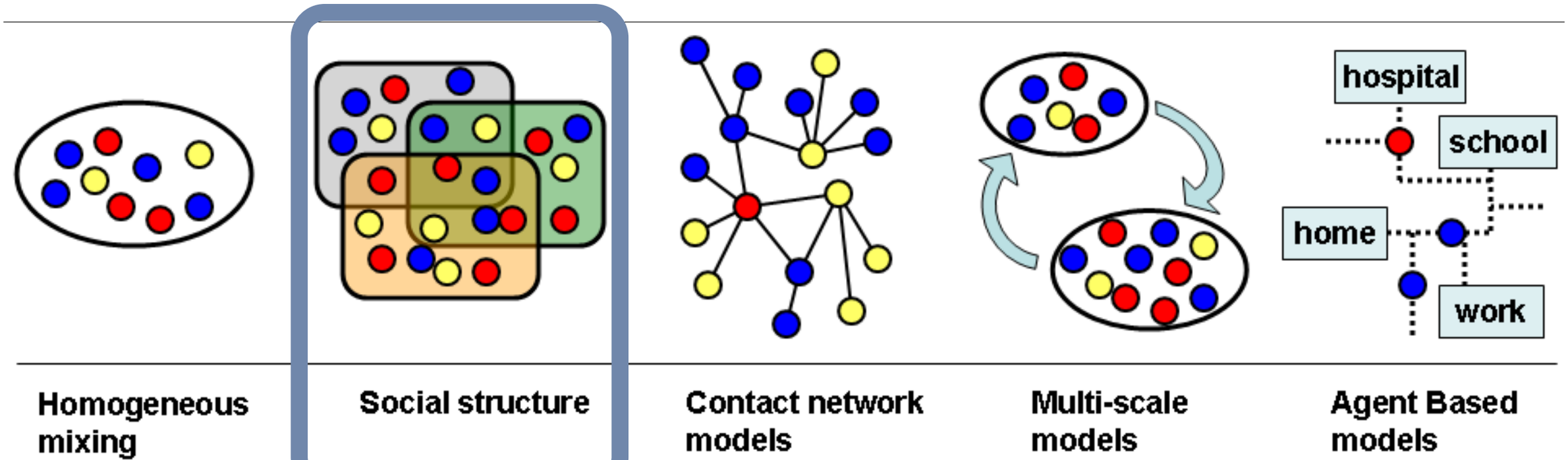


Brooks-Pollock et al, BMC Inf Dis 2011

infectious diseases:

modeling H1N1 pdm

1st application to H1N1pdm



Eames et al.: Measured Dynamic Social Contact Patterns Explain the Spread of H1N1v Influenza. PLOS Comput Biol (2012)

Eames et al.'s study

THE PROBLEM

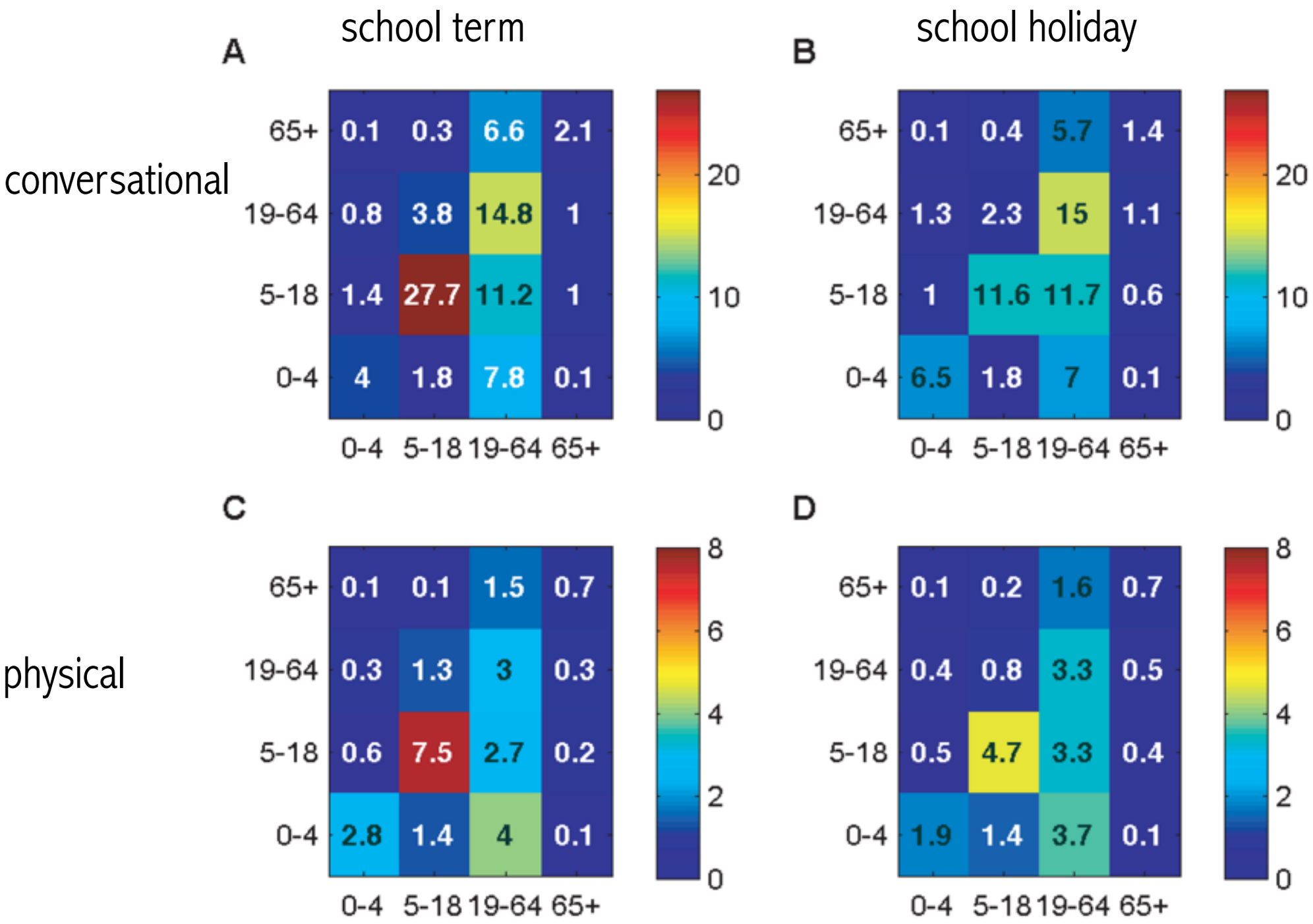
- changes in disease incidence in the 2009 H1N1 pdm in the UK
- occurrence of summer wave in the UK

THE APPROACH

- age-structured model
- contacts among age classes during school term and school holidays
- fit to the surveillance data

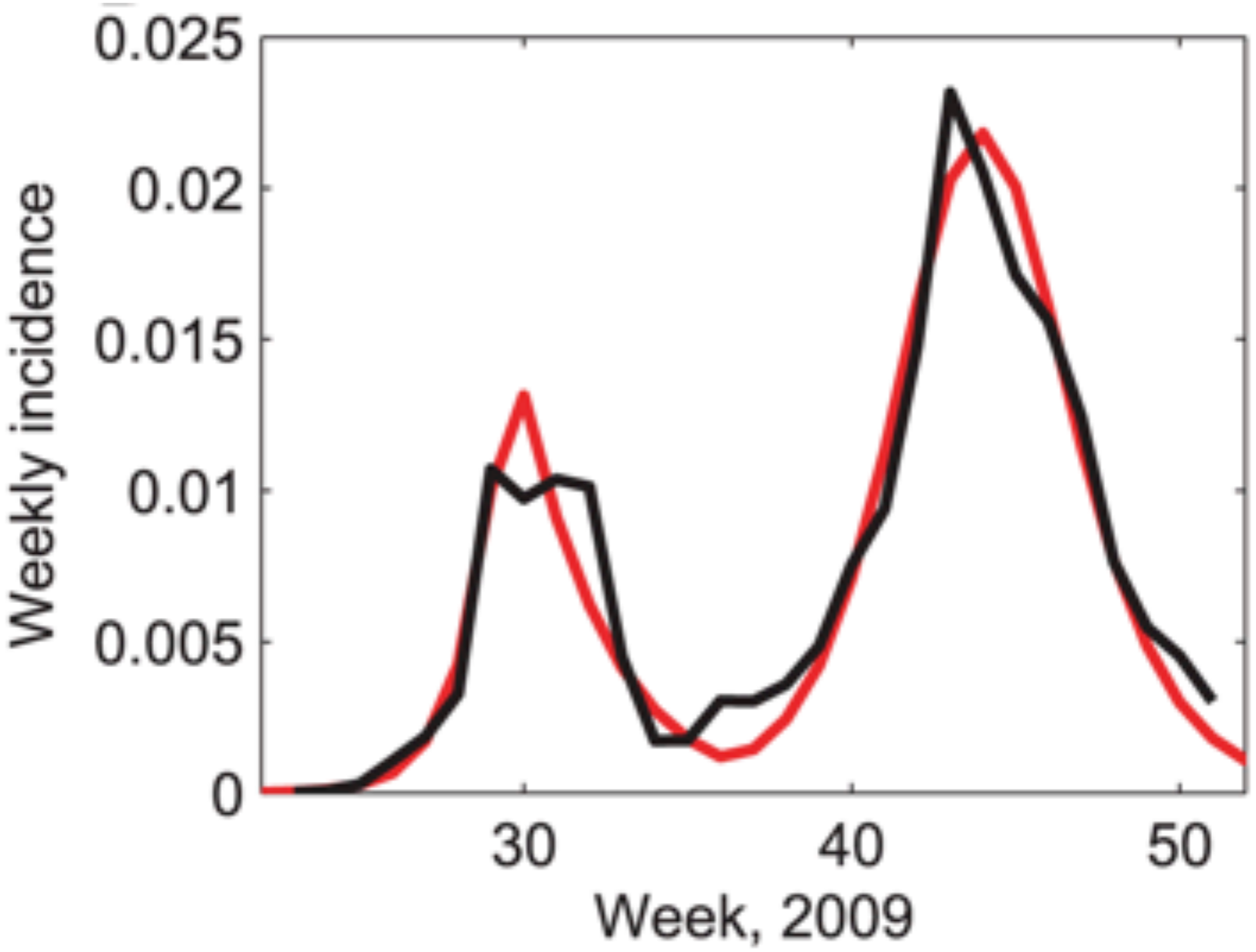
Eames et al. PLOS CB 2012

contacts: schools on/off



Eames et al. PLOS CB 2012

results



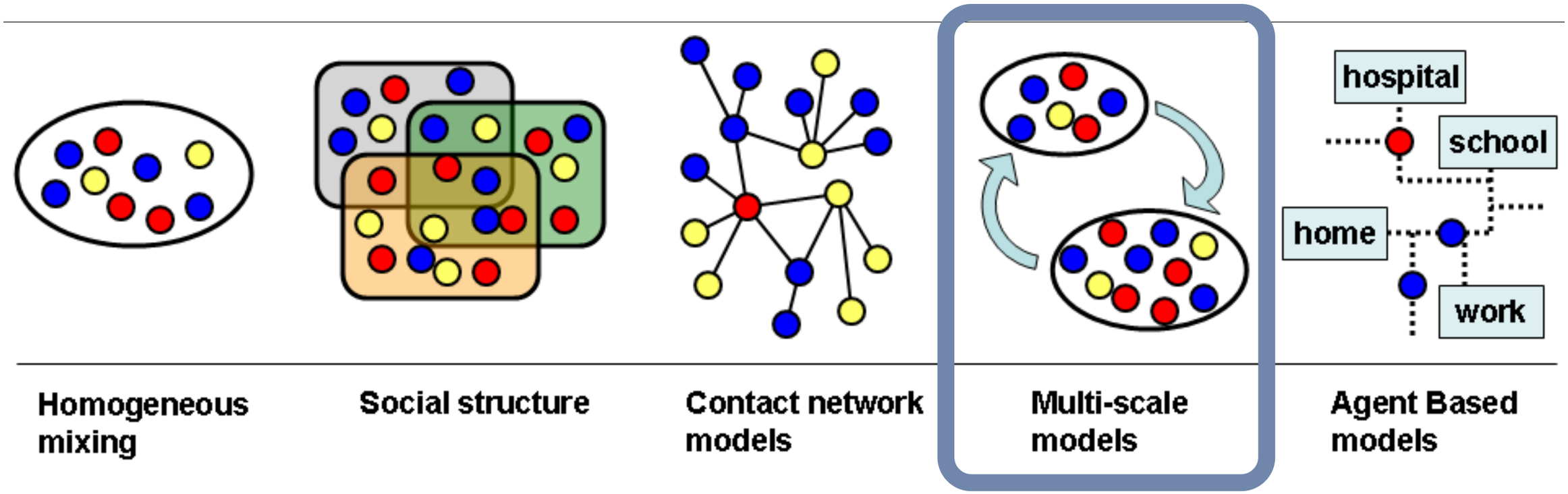
- fall of ~35% of R_0 during school holidays

Eames et al. PLOS CB 2012

some limitations...

- data needs: *difficult to parameterize in real-time*
- homogeneous mixing with age structure at country level, but *space is missing*

2nd application to H1N1pdm

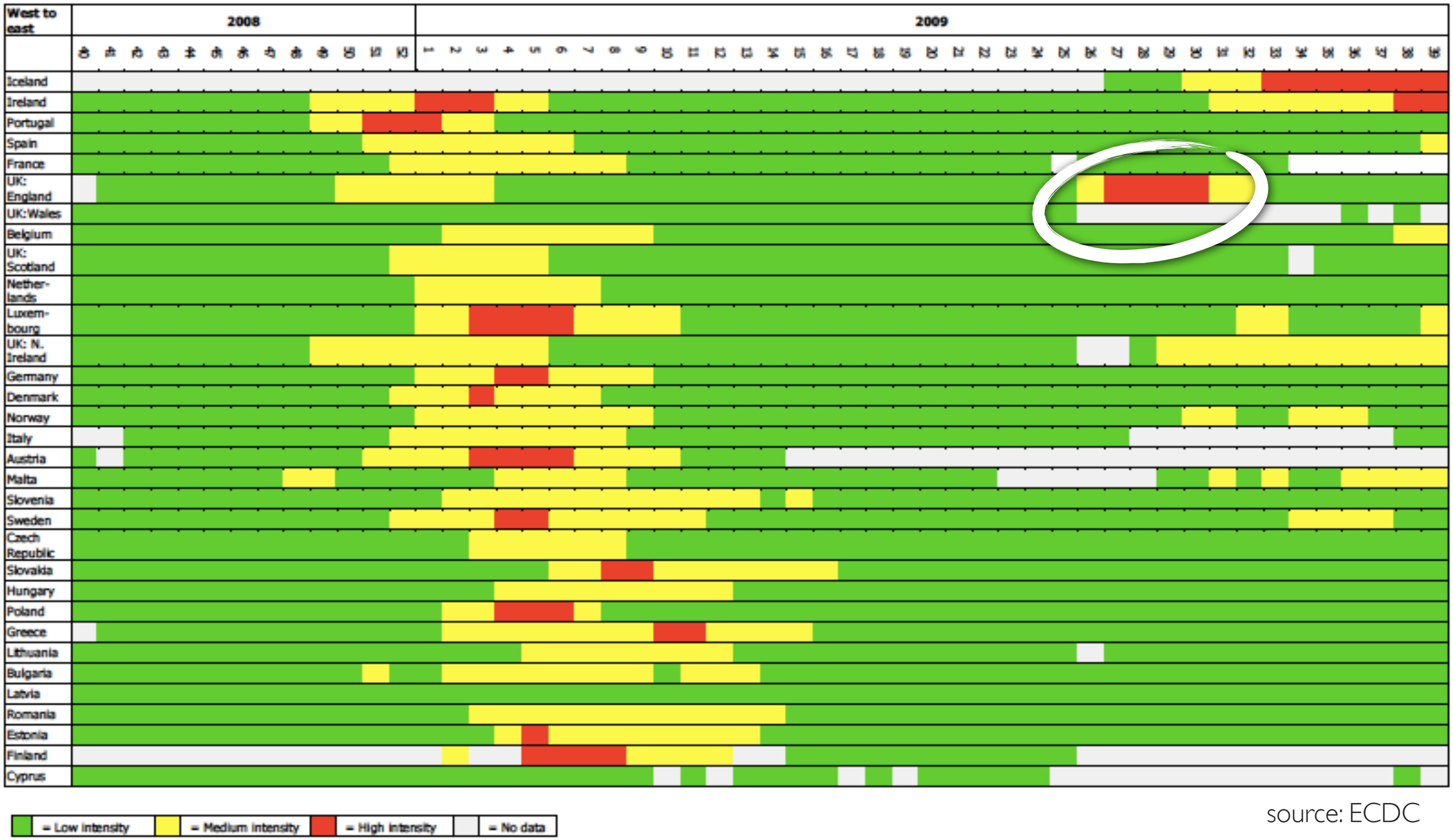


Apolloni et al.: Age-specific contacts and travel patterns in the spatial spread of 2009 H1N1 influenza pandemic.
BMC Inf Dis (2013)

and in the rest of Europe?

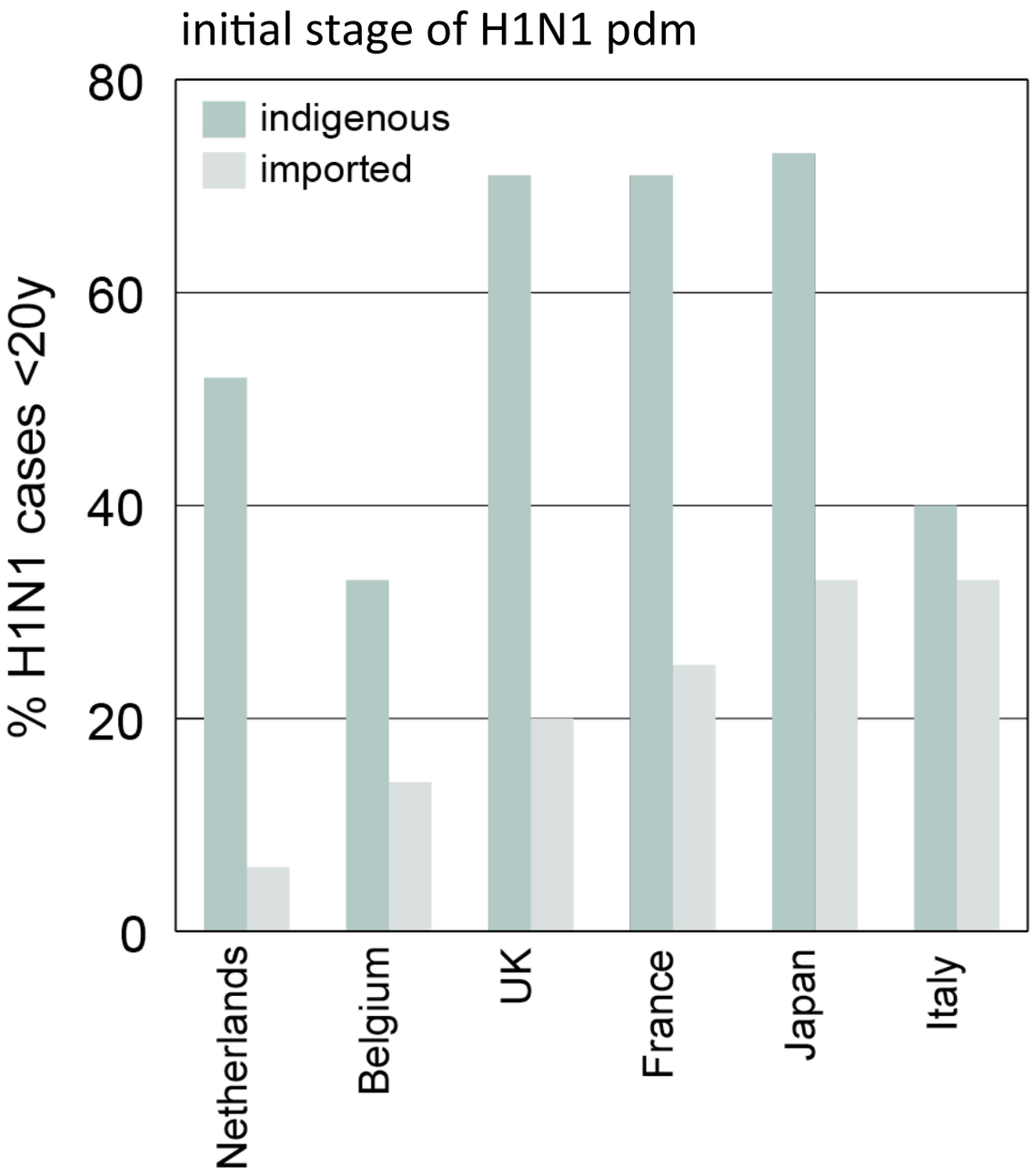
and in the rest of Europe?

Table 2: **Intensity of influenza activity in the EU, Iceland and Norway during the 2008/09 season, by country (ordered by geographical longitude) and week of reporting**



source: ECDC

evidence from H1N1 pdm



- *local outbreak:* (mainly) children

- see*ding:* (mainly) adults

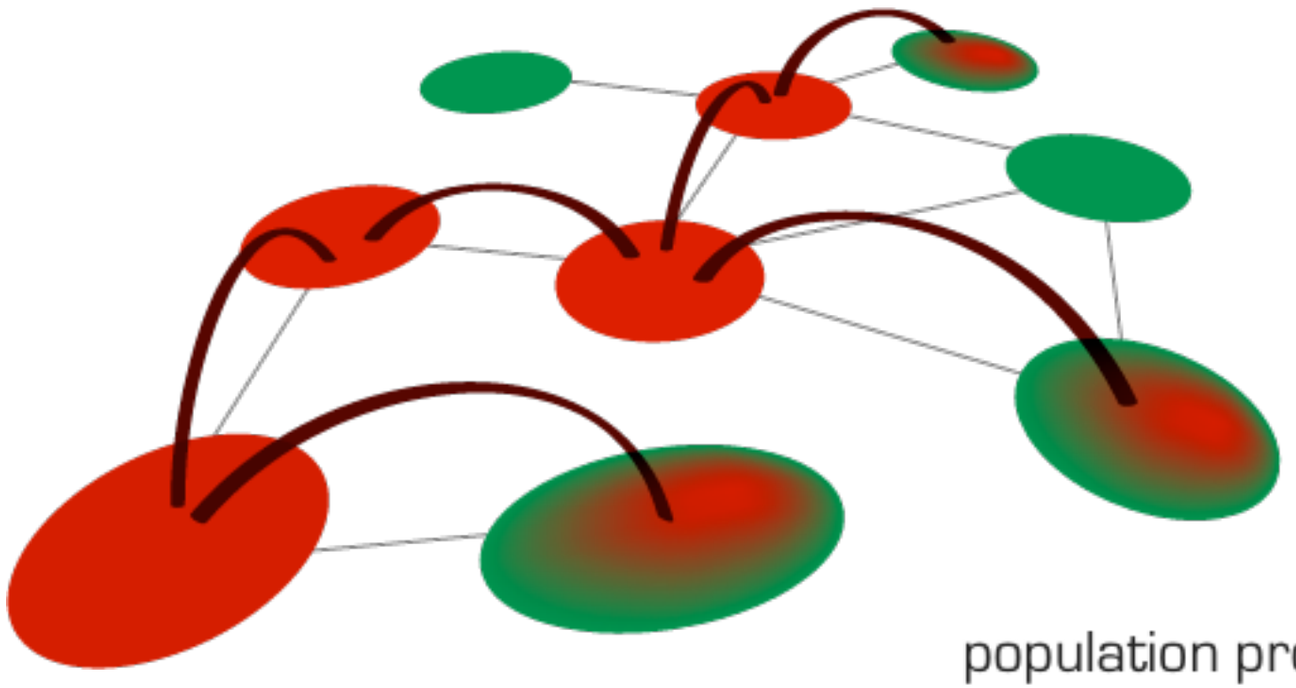
the problem

age-specific { contacts, travel behavior

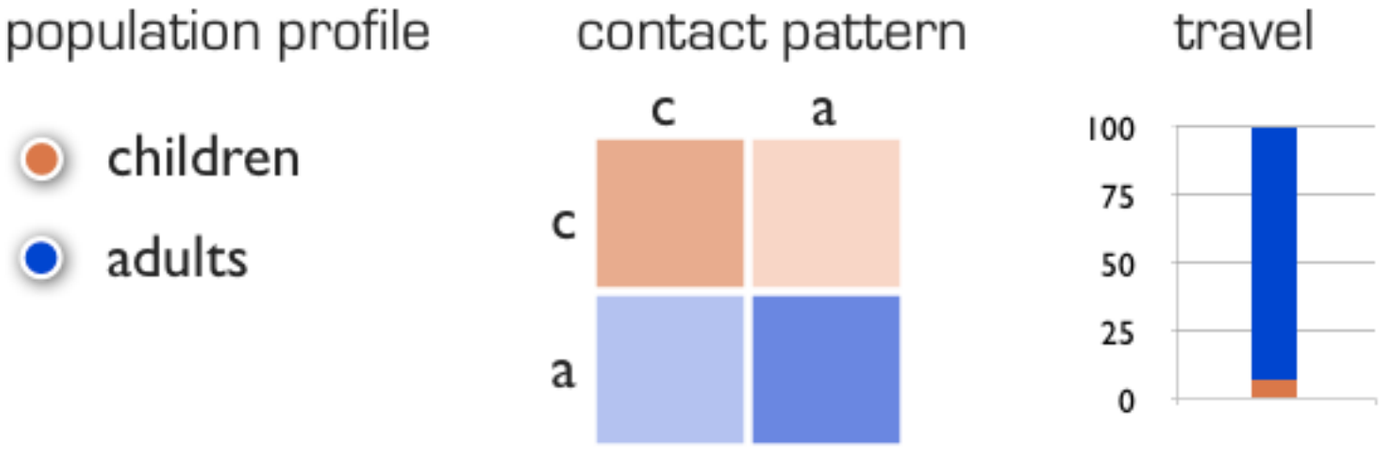
CONDITIONS FOR SPATIAL INVASION

	analytical approaches	numerical approaches
single population (no space)	✓	✓
multiple populations (space)		✓

multi-host metapopulation



multi-host metapopulation approach



$$D_k^n = \sum_{k\prime} D_{k'}^{n-1}(k'-1)P(k|k')\left(1-\sum_{m=0}^{n-1}\frac{D_k^m}{V_k}\right)\cdot\Omega_{k\prime k}\left(\lambda_{k'k,c}\,,\lambda_{k'k,a}\right)$$

Apolloni et al., BMC Inf Dis 2013

invasion threshold

- multi-host branching process
- degree-block approximation
- small values of R_0
- no topological correlations
- localized seeding

$$R_* = [(1-\pi_c)rz_c + (1-\pi_a)(1-r)z_a]\frac{w_0}{\mu}\frac{\langle k^{2+2\theta}\rangle - \langle k^{1+2\theta}\rangle}{\langle k\rangle}$$

children travel fraction

topology and fluxes of aviation network

prob extinction

infectious period

epidemic sizes

Apolloni et al., BMC Inf Dis 2013

invasion threshold

- multi-host branching process
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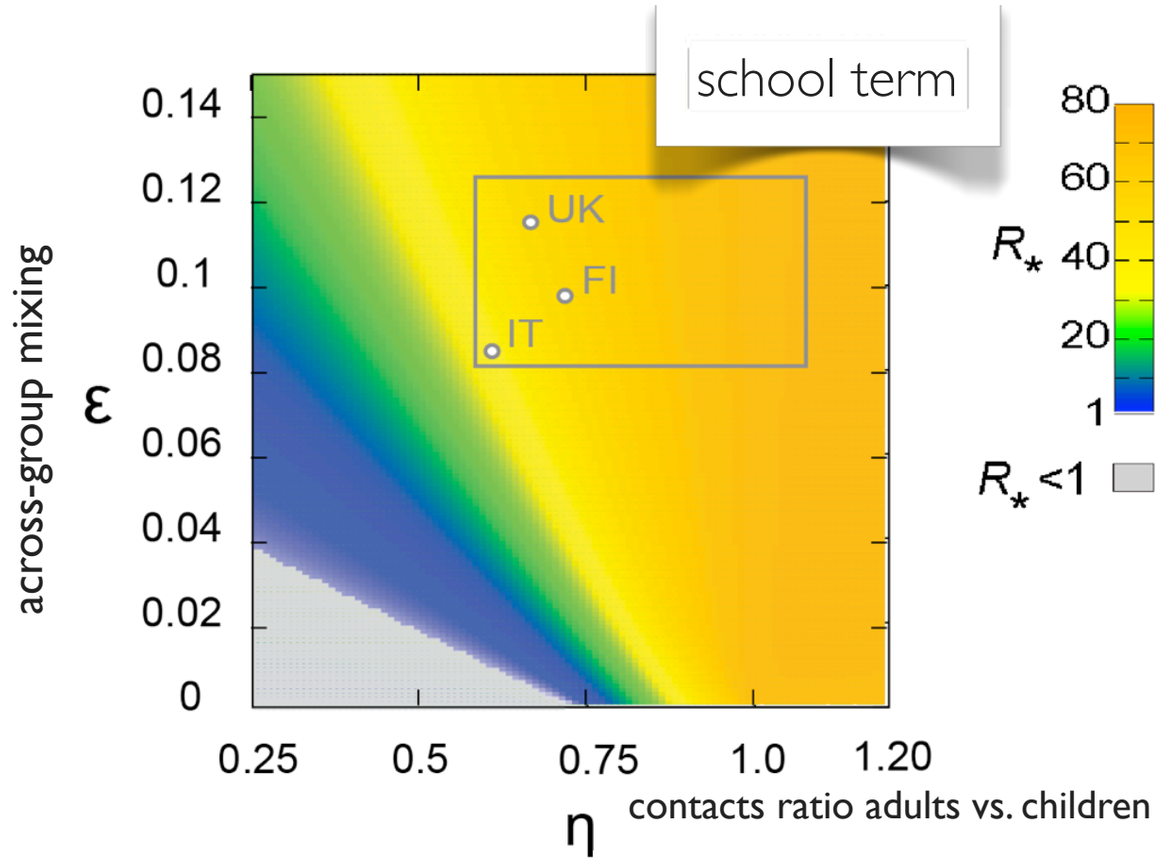
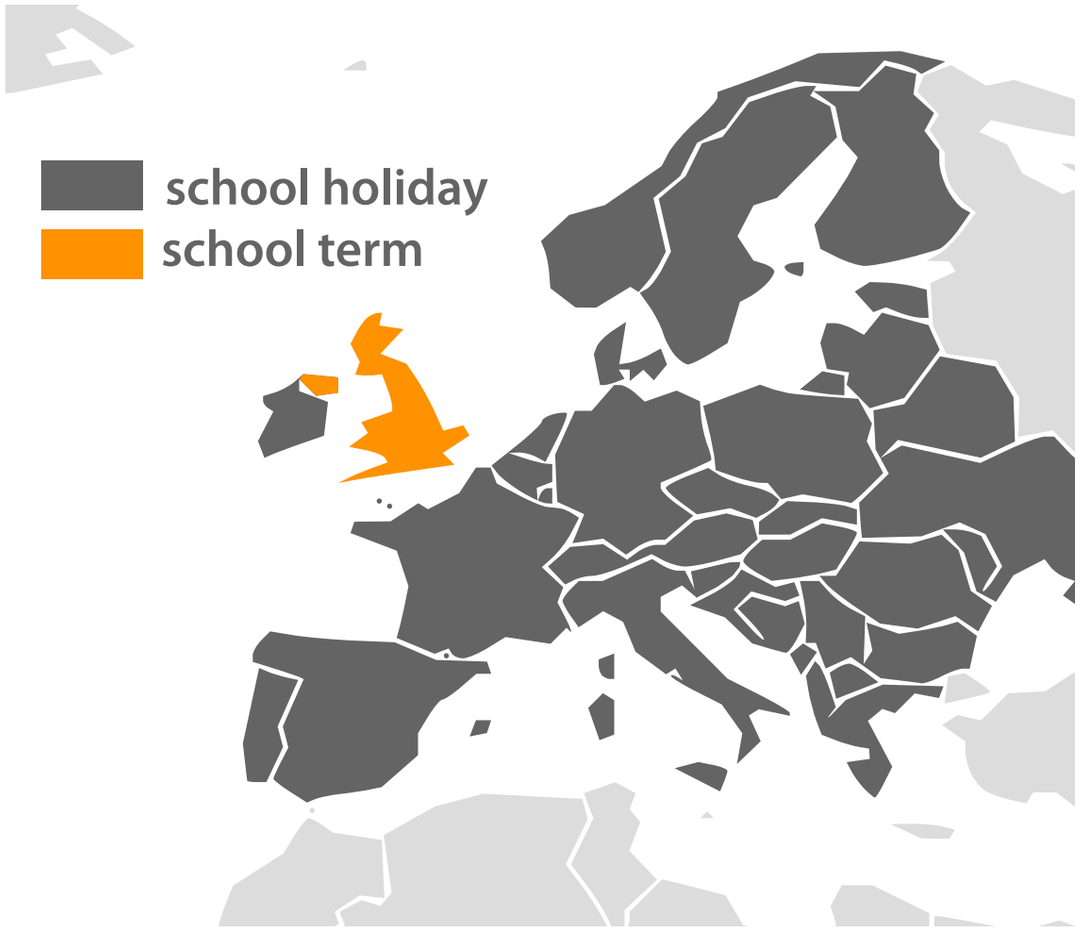
Apolloni et al., BMC Inf Dis 2013

effects of school calendar



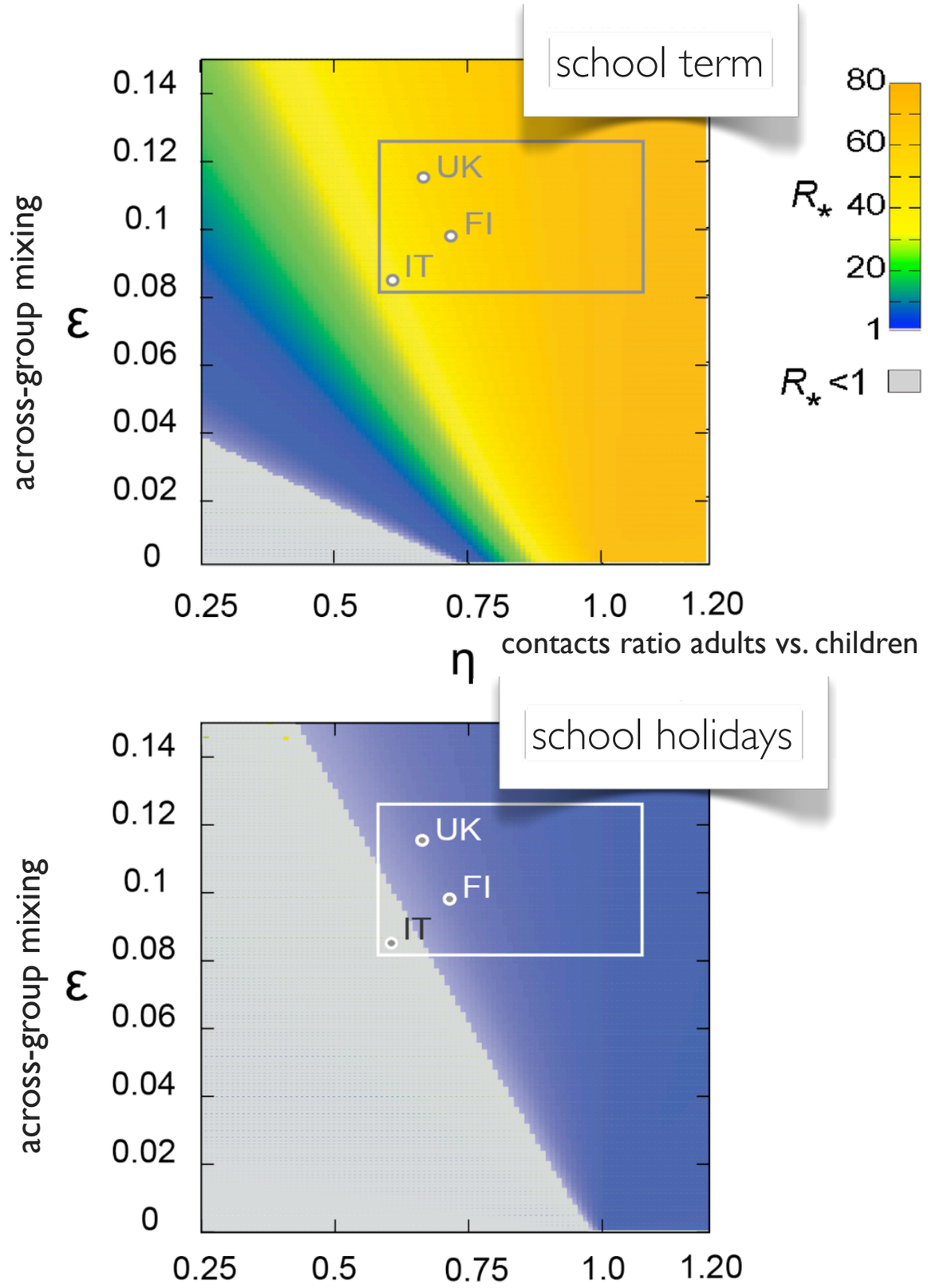
Apolloni et al., BMC Inf Dis 2013

effects of school calendar

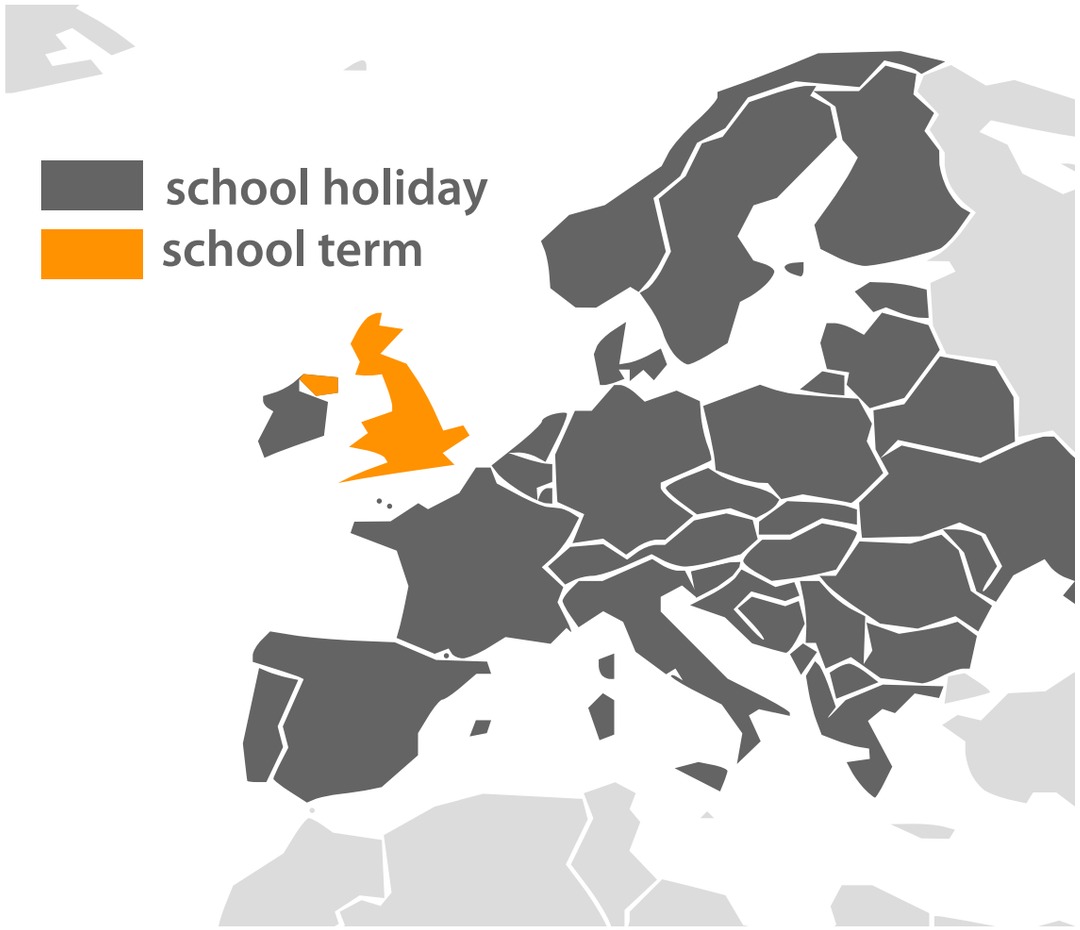


R0 reduction due to school closure: Eames 2012

Apolloni et al., BMC Inf Dis 2013



effects of school calendar



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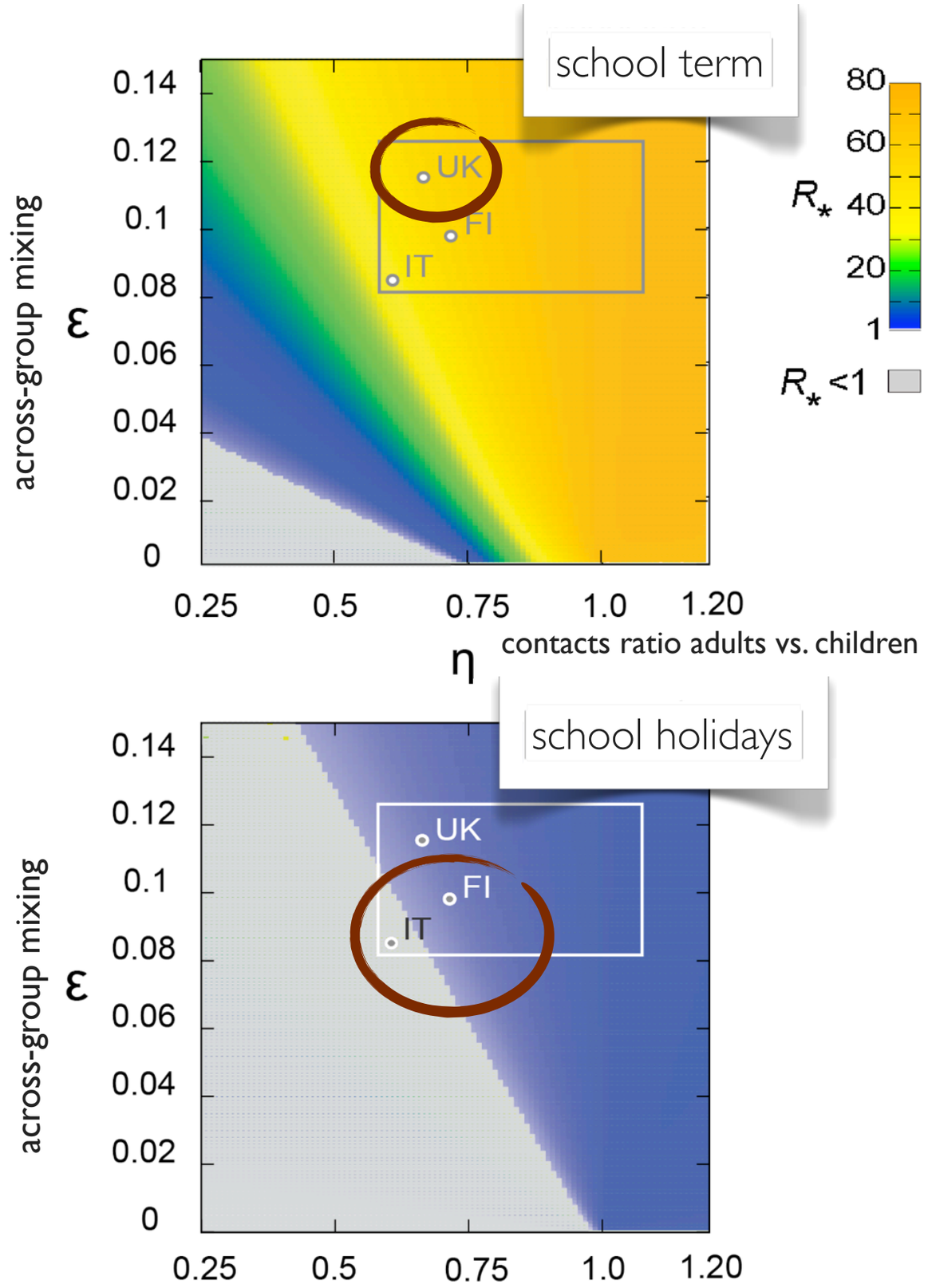
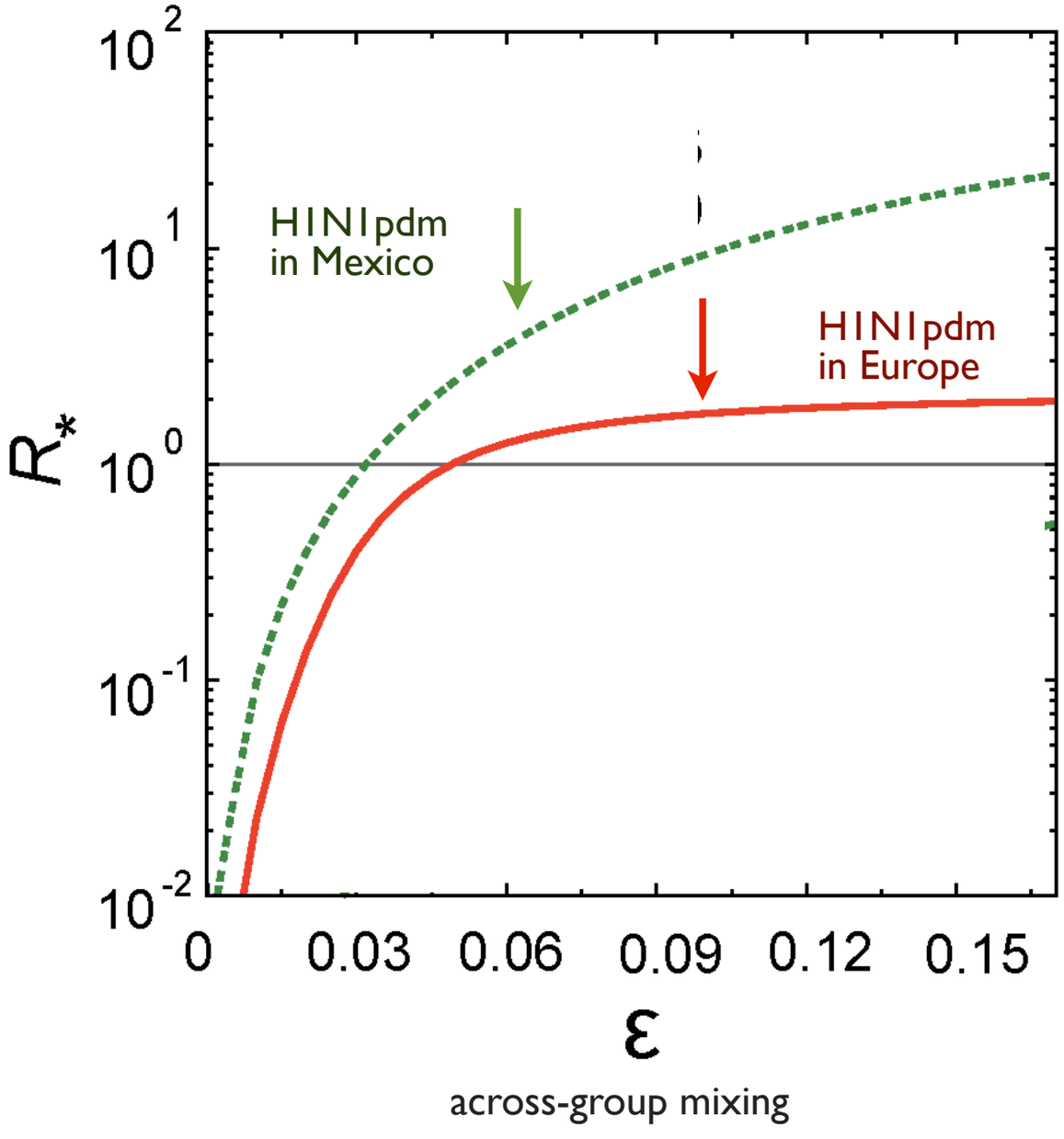
Apolloni et al., BMC Inf Dis 2013



Europe *vs.* Mexico



region	α	η	ε
Europe (average values)	0.2	0.79	0.097
Mexico	0.32	0.32	0.063

fraction of children

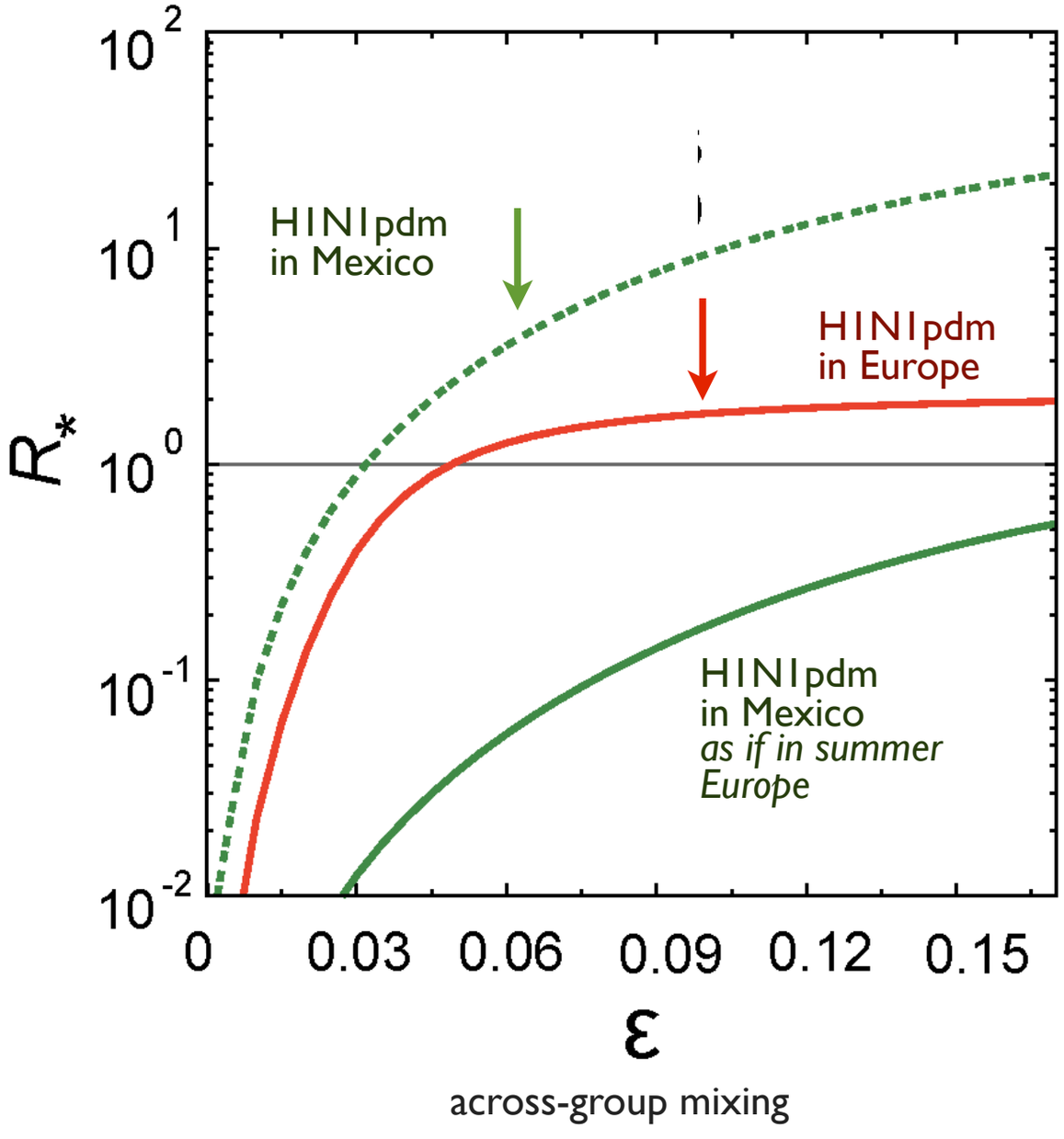
contacts ratio adults vs. children

across-groups mixing

Apolloni et al. 2013

data for Mexico: Fraser 2009

Europe *vs.* Mexico



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fraction of children

contacts ratio adults vs. children

across-groups mixing

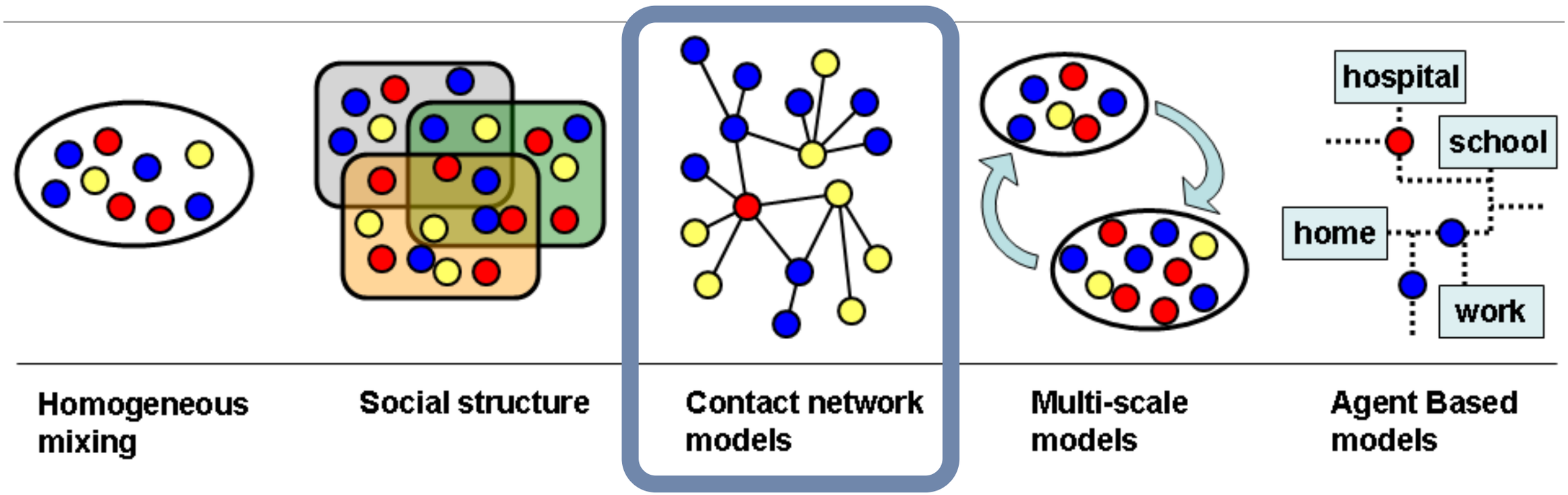
Apolloni et al. 2013

data for Mexico: Fraser 2009

some limitations...

- simplified representation
- invasion prediction, not dynamics

3rd application to H1N1pdm



Homogeneous mixing | Social structure | **Contact network models** | Multi-scale models | Agent Based models

Carrat et al.: Planning for the next influenza H1N1 season: a modelling study.
BMC Inf Dis (2010)

Carrat et al.'s study

THE PROBLEM

use surveillance data of the first pandemic season in France to:

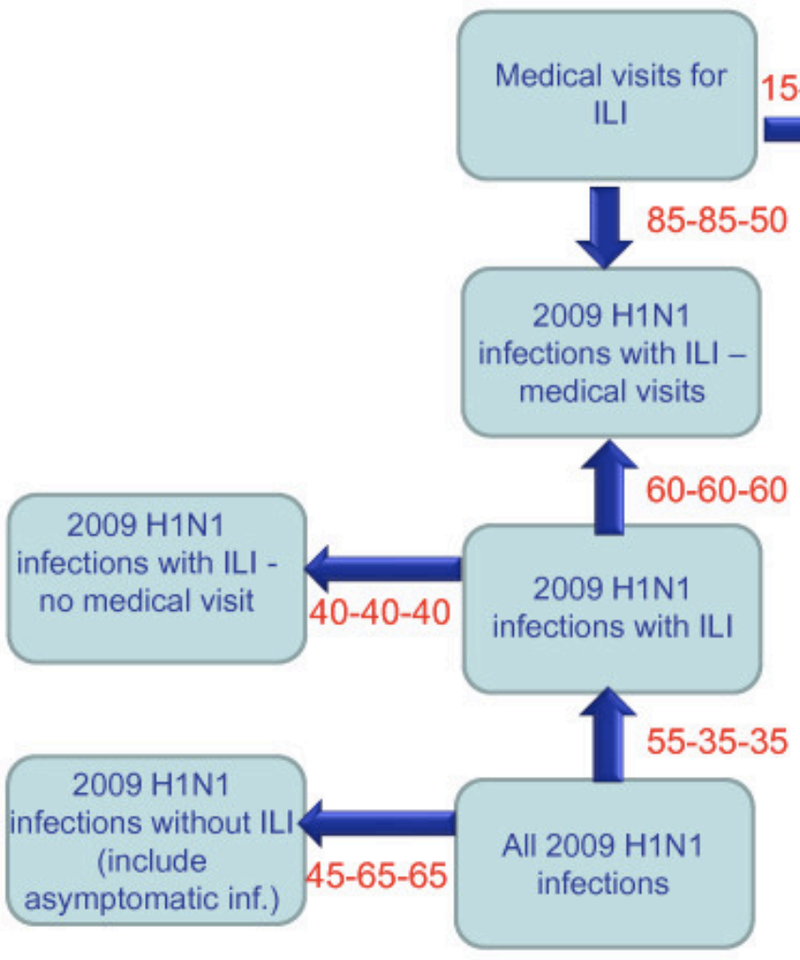
- estimate attack rates, rates of pre- and post-exposure immunity
- explore hypothetical scenarios of virus reintroduction with varying levels of cross-immunity

THE APPROACH

- individual-centered model
- demographic characteristics (children, young adults, elderly) and household sizes
- network of contacts
- detailed description of health-care seeking behavior, treatment

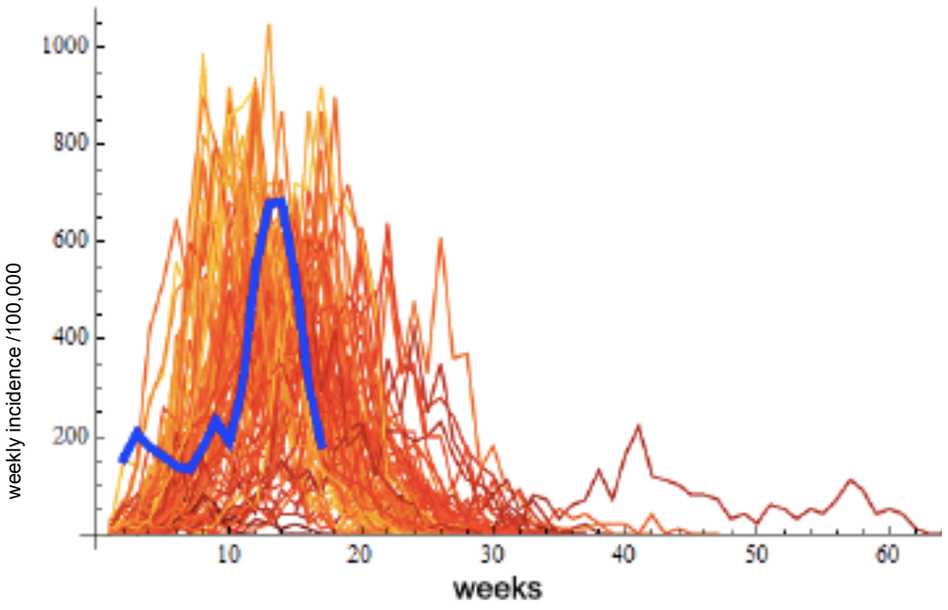
Carrat et al. BMC Inf Dis 2010

Carrat et al.'s study



- complete bidirectional networks inside households
- BA networks for other contacts
- high clustering
- <k>=13.9 overall (15.3 children, 14.6 young adults, 5.1 elderly)

results



pre-exposure immunity	**predicted attack rates**
young adults=36% elderly=85%	children=39% young adults=15% elderly=1.5%
postulating: young adults=0 elderly=0	children=64% young adults=48% elderly=27%

hypothesized second pandemic season
(circulation, re-introduction, modified antigenic properties)
with variable cross protection

70% cp: small epidemic size
50% cp: disease burden ~ 1st season
30% cp: substantial burden

Carrat et al. BMC Inf Dis 2010

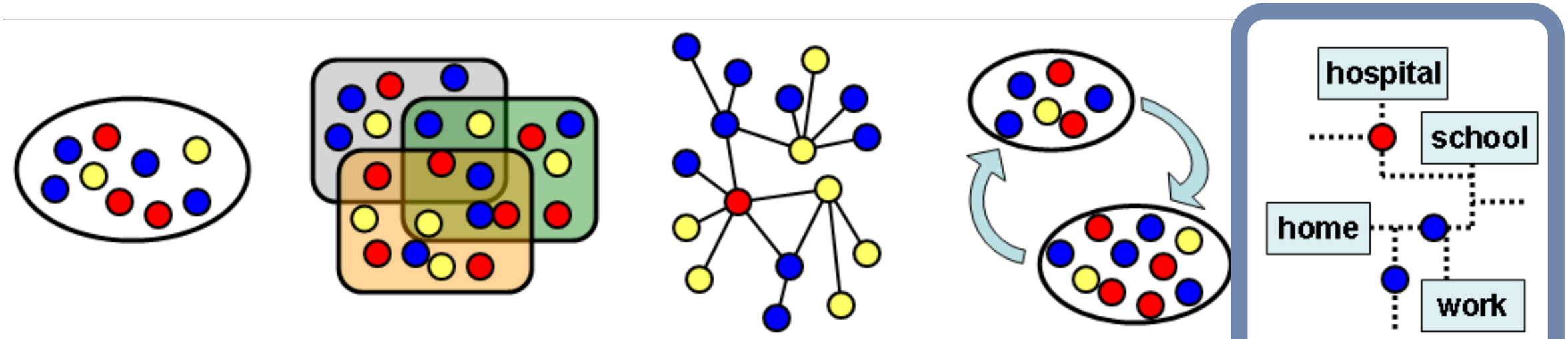
some limitations...

- sensitivity to assumed networks of contacts?

- *difficult to parameterize in real-time*

- highly detailed for single population, but *space is missing*

4th application to H1N1pdm



Determinants of the spatiotemporal dynamics of the 2009 H1N1 pandemic in Europe: implications for real-time modelling.
PLOS Comp Biol (2011)

Merler et al.

Merler et al.'s study

THE PROBLEM

use epidemic data and available estimates up to June 2009 to:

- evaluate the role of EU socio-demographic structures, school calendars, intra-EU mobility in shaping the spatio-temporal spread

THE APPROACH

- agent-based model informed with EU synthetic population
- explicit spatial structure restricted to EU + model for seeding events
  - school calendars
  - available epidemic estimates

Merler et al. PLOS Comp Biol 2011

synthetic population: household type

Each individual belongs to an **Household** (family)

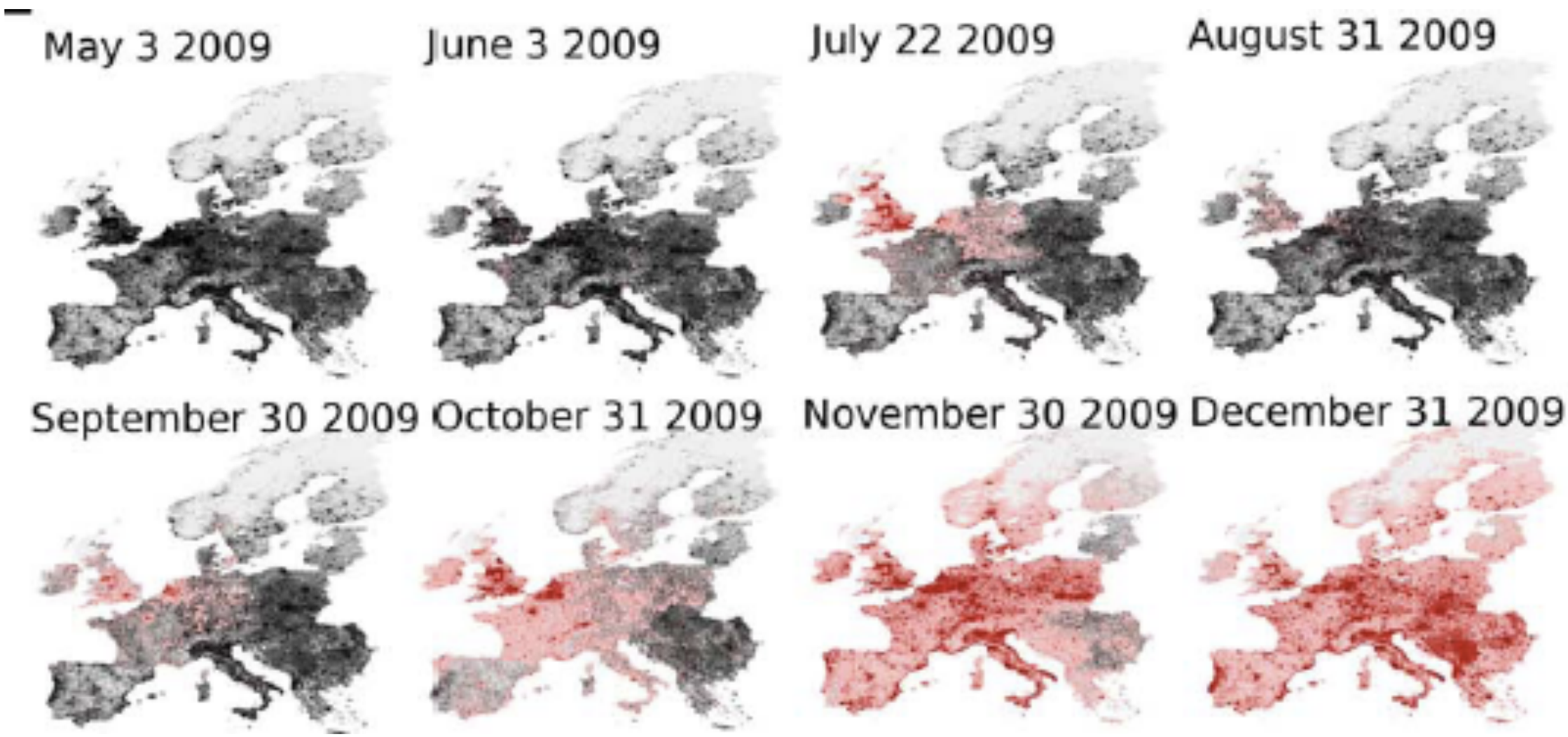
- each Household is located in a **Municipality**

8 Household types

- $5 + 3$ with an *additional member*

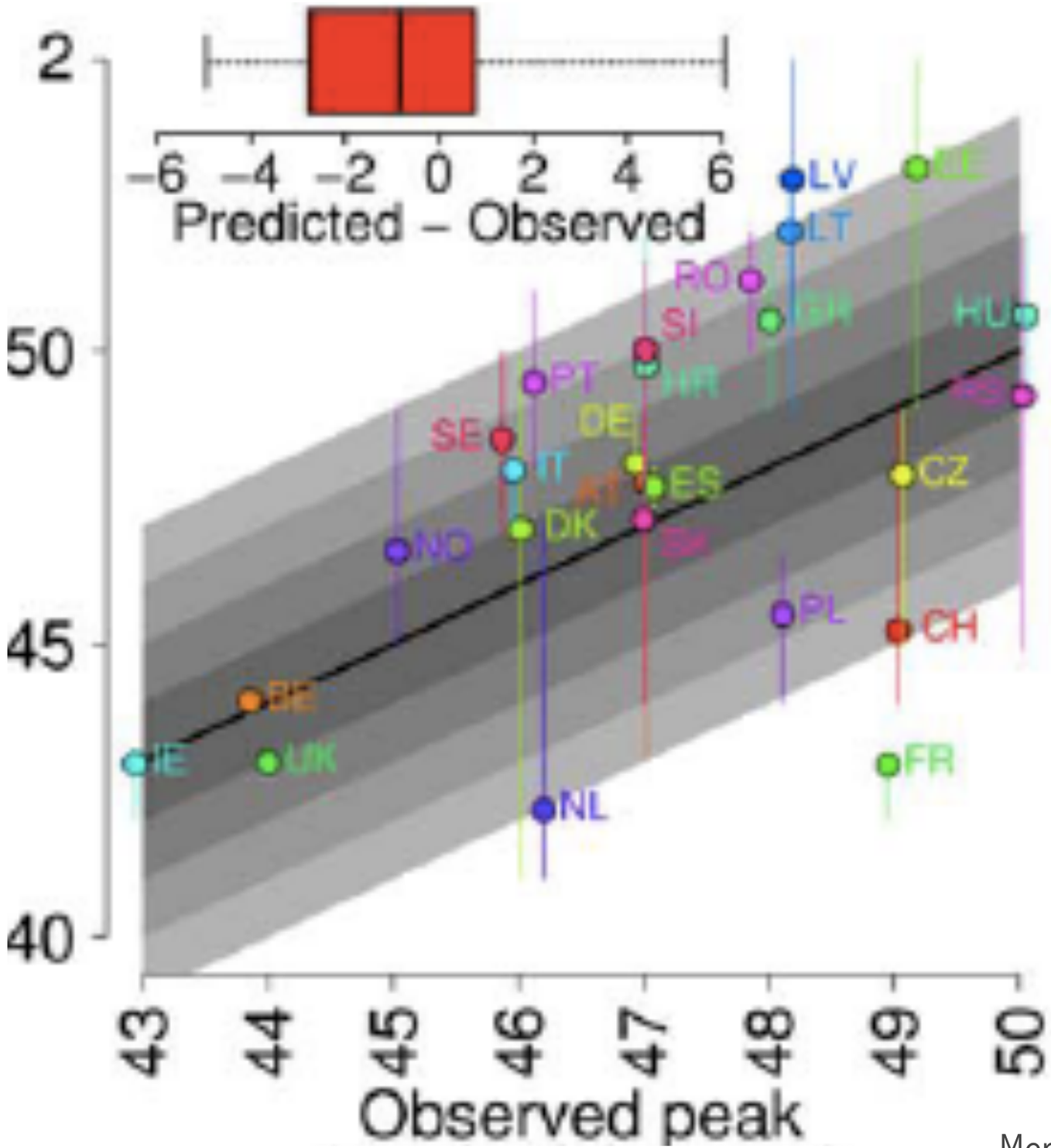
Type	Number	Population	Prob. Add. Member
Single without children	0.338	0.149	—
Couple without children	0.268	0.243	0.010
Couple with children	0.277	0.475	0.020
Single with children	0.09	0.106	0.012
More household groups	0.027	0.028	—
Total	1.000	1.000	—
	27,785,928	63,126,802	

results (I)



Merler et al. PLOS Comp Biol 2011

results (2)

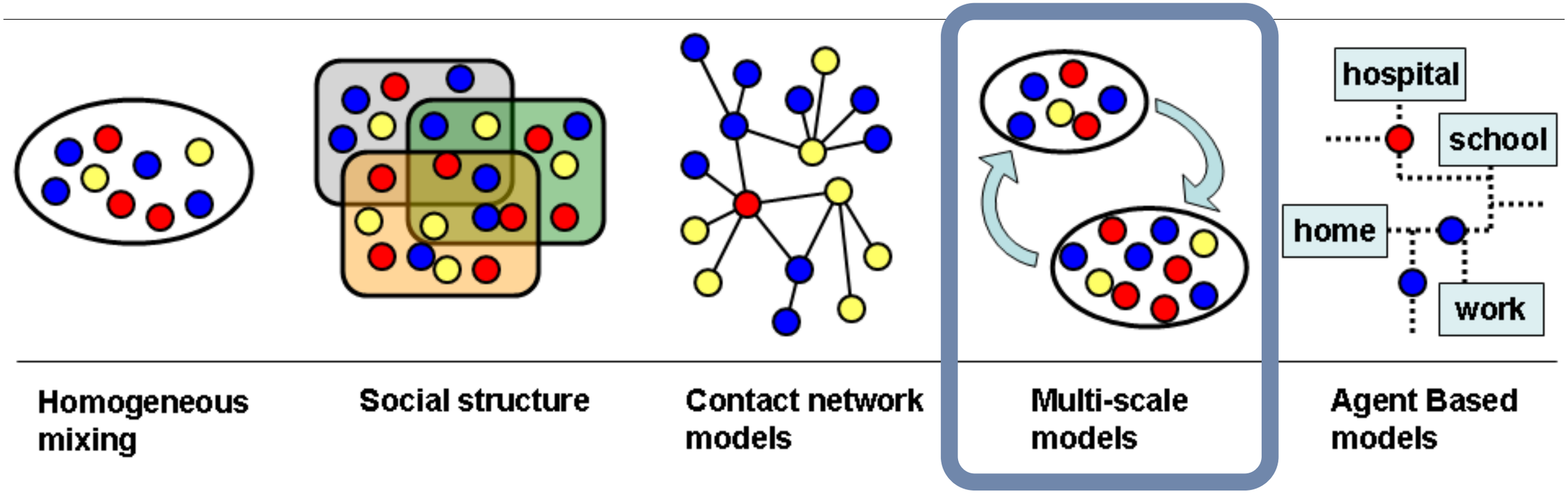


Merler et al. PLOS Comp Biol 2011

some limitations

- *difficult to parameterize in real-time*
- high resolution data available for developed countries (and few developing countries)

5th application to H1N1pdm



Seasonal transmission potential and activity peaks of the new influenza A/H1N1: a Monte Carlo likelihood analysis based on human mobility. *BMC Med* (2009) — Balcan et al.

Real-time numerical forecast of global epidemic spreading: case study of 2009 A/H1N1pdm. *BMC Med* (2012). — Tizzoni et al.

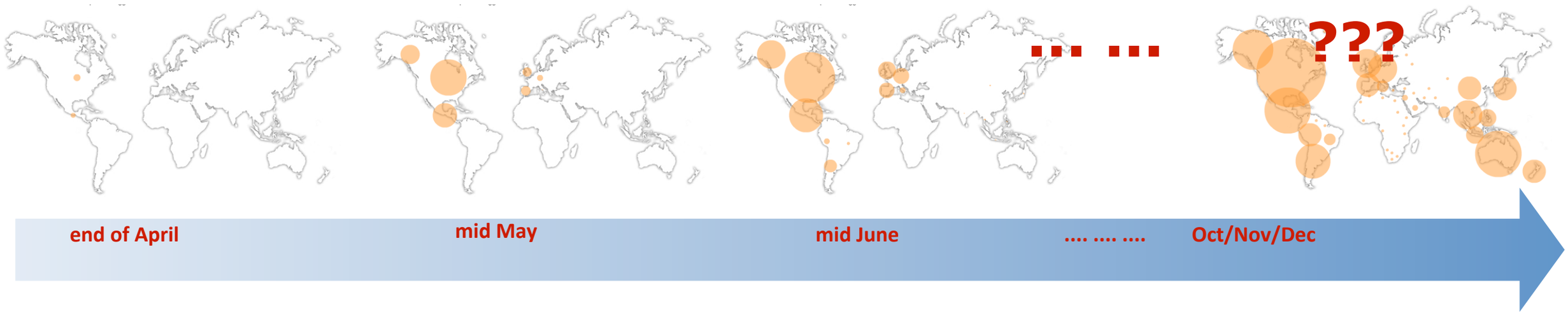
the GLEAM study

THE PROBLEM

use the epidemic data up to June 2009 to:

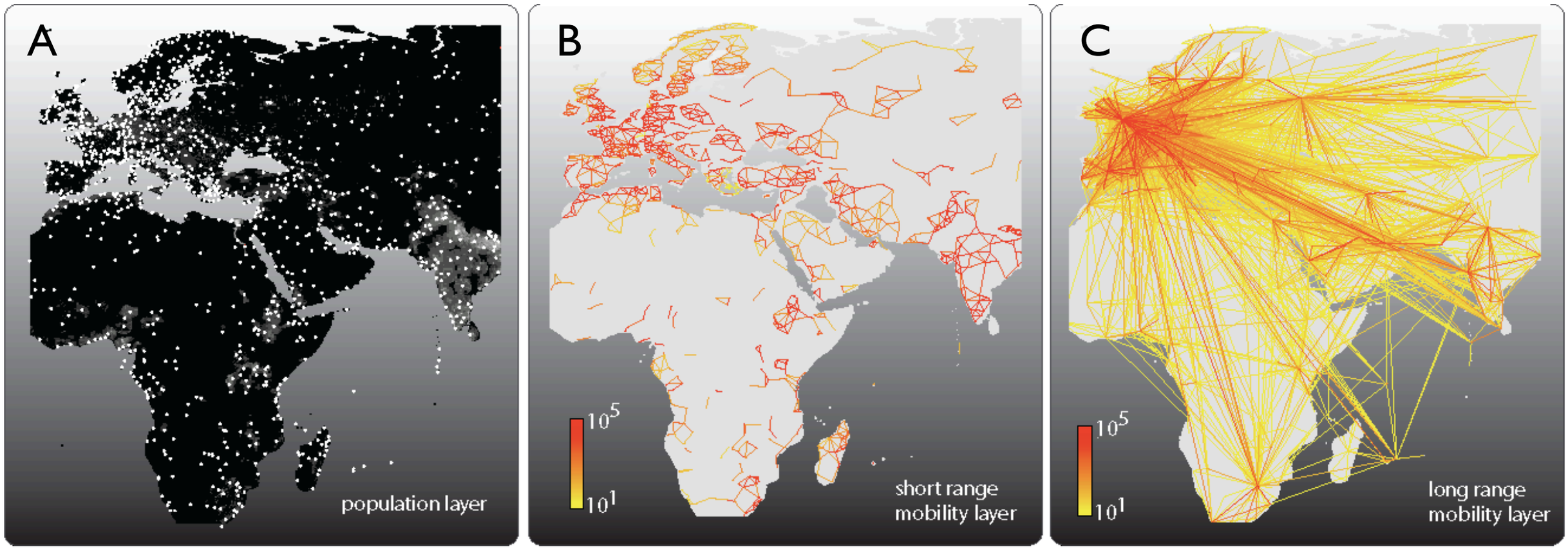
- estimate the seasonal transmission potential of the pandemic

- predict in *real-time* the future spatio-temporal propagation at the *global level* and in particular the peak timing for the upcoming winter season



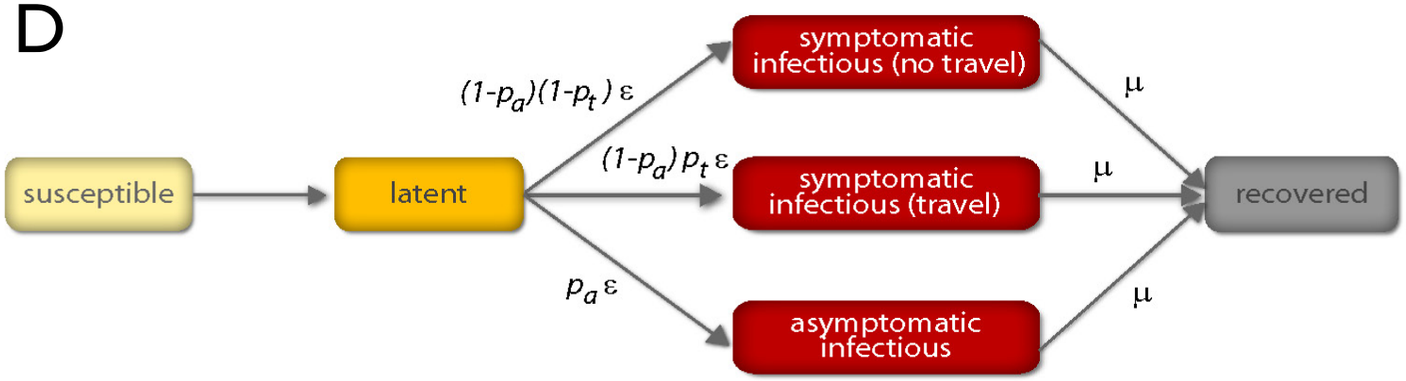
Balcan et al. PNAS 2009

GLEAM approach



- population data in cells ¼° x ¼°
- daily commuting data
- 3400 airports in 220 countries
- 20,000 connections
- traffic data (IATA, OAG)
- >99% commercial traffic

D



customizable compartmental model

Balcan et al. PNAS 2009

GLEAM: how it works (1)

GLEaM is based on

a stochastic metapopulation approach

www.gleamviz.org
Balcan et al. PNAS 2009

GLEAM: how it works (2)

input

demographic data

mobility data

epidemic model

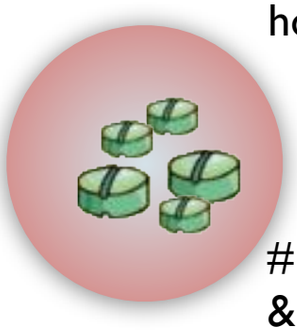
GLEaMviz.org

the model

- individual level simulations
  - intra-population transmission dynamics
    - compartmental natural history of the disease
    - age structure and other determinants
    - response strategies (containment, mitigation, pharmaceutical interventions)
  - inter-population mobility
    - air travel: explicit stochastic simulations based on IATA/OAG data
    - ground movements: effective short-range multimodal mobility
      - time-scale separation & effective force of infection

output

cases (ILI, hospitalized, ICU, ..



drugs & intervention efficacy

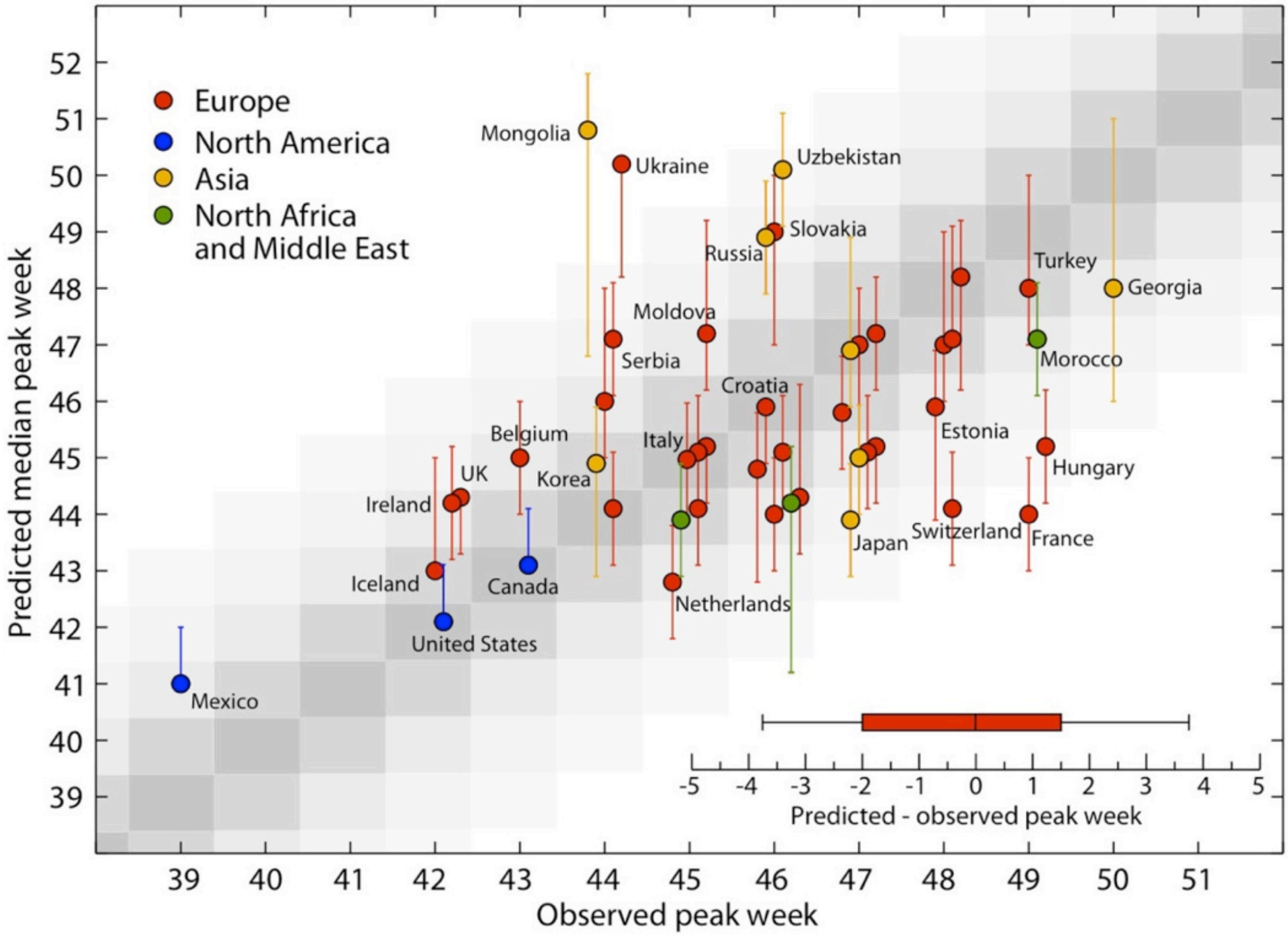
seeding. arrival time, geotemporal spreading

Balcan et al. PNAS 2009

results

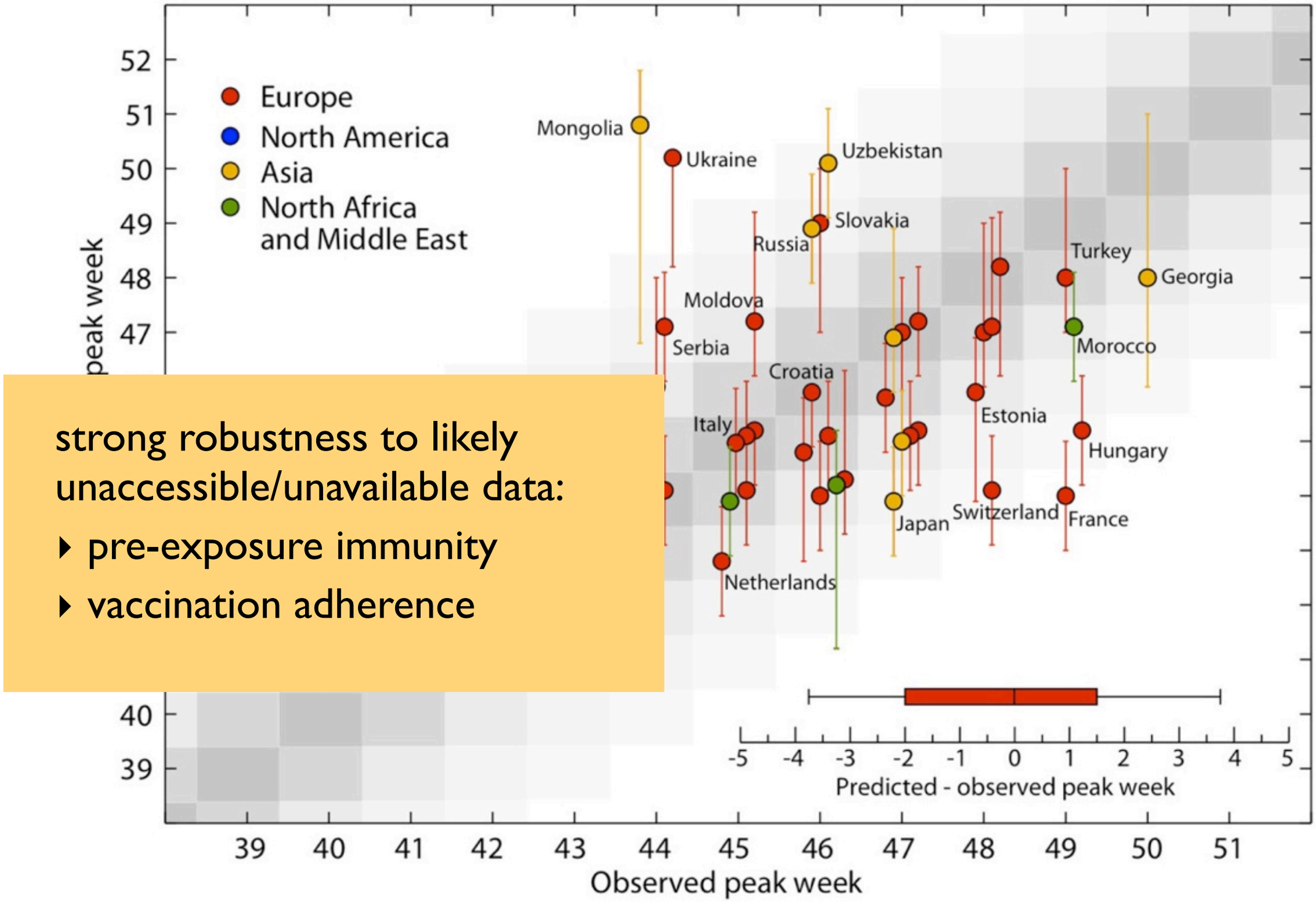
www.gleamviz.org
Balcan et al. BMC Med 2009

validation



Balcan et al. BMC Med 2009
Tizzoni et al BMC Med 2012

validation



strong robustness to likely unaccessible/unavailable data:

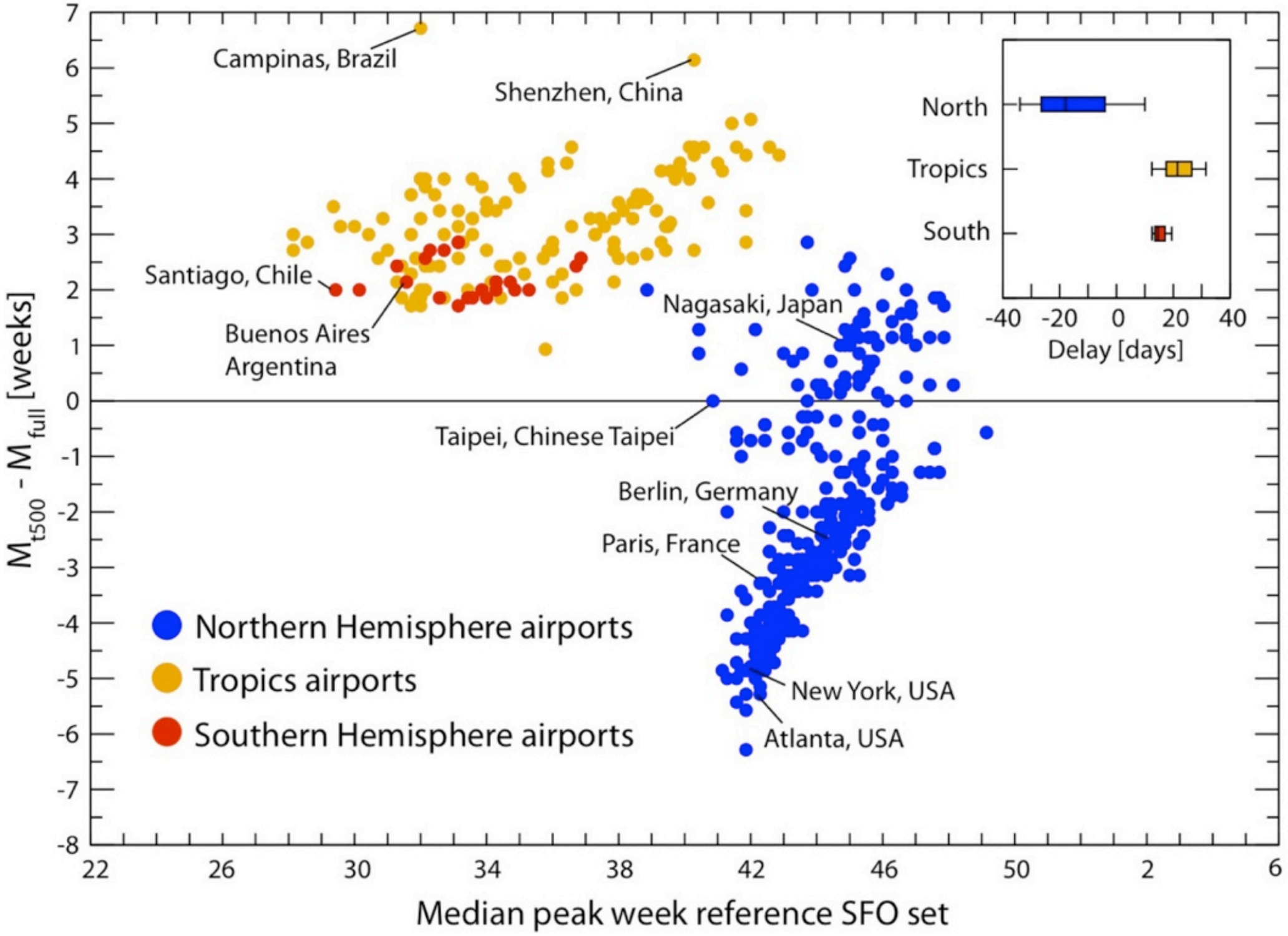
- pre-exposure immunity
- vaccination adherence

Balcan et al. BMC Med 2009
Tizzoni et al BMC Med 2012

importance of resolution

reference	# airports	# countries
Rvachev & Longini, 1985	52	35
Grais et al, 2003; Flahault et al, 2006	52	35
Cooper et al, 2006; Wu et al, 2009	105	
Epstein et al, 2007	155	
Kenah et al, 2011	321	
Hufnagel et al, 2004	500	>100
Colizza et al, 2006-2007	3,100	220
Balcan et al, 2009; Bajardi et al, 2011; Tizzoni et al, 2012	3,362	220

error on predictions



Tizzoni et al BMC Med 2012

some limitations...

- lack of high resolution description of socio-demographic structures (e.g. households, schools/workplaces)

remaining challenges...

➡ models: high resolution demand *vs*. understanding of basic mechanisms; integrating different scales

➡ data to inform models
- ➡ social, behavioral, demographic, mobility...
- ➡ underdeveloped countries?

➡ surveillance: high resolution, same case-definition, health-seeking behavior, ...

➡ sharing

➡ preparedness for emergency (building up collaborative workflows in *peacetime*)

(re-)emerging epidemics

APR 02, 2014

Five more Ebola cases, 3 more dead in Guinea

Lisa Schnirring | Staff Writer | CIDRAP News | Apr 02, 2014

The new Ebola cases push the outbreak total to 127 cases, including 83 fatal ones.

Middle East respiratory syndrome coronavirus (MERS-CoV) – update

Disease Outbreak News

27 MARCH 2014 - On 20 and 21 March 2014, the Ministry of Health of Saudi Arabia announced an additional six laboratory-confirmed cases of infection with Middle East respiratory syndrome coronavirus (MERS-CoV).

Details of the cases provided to WHO are as follows:

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Human infection with avian influenza A(H7N9) virus – update

Disease outbreak news

4 APRIL 2014 - On 3 April 2014, the National Health and Family Planning Commission (NHFPC) of China notified WHO of two additional laboratory-confirmed case of human infection with avian influenza A(H7N9) virus.

Details of the cases reported to WHO are as follows:

- A 28 year-old man from Suzhou City, Jiangsu province. He becam March, and was admitted to hospital on 28 March. He is currently severe condition. The patient has a history of exposure to poultry.
- A 68 year-old man from Guangzhou City, Guangdong province. He ill on 20 March and was admitted to hospital on 24 March. He is c a critical condition. The patient has a history of exposure to poultr

Chikungunya in the French part of the Caribbean isle of Saint Martin

Disease outbreak news
10 December 2013

On 6 December 2013, WHO was notified of two laboratory confirmed cases of locally acquired chikungunya disease in the French part of the Caribbean isle of Saint Martin. The other part of the isle is a country that is part of the Kingdom of the Netherlands (Sint Maarten). These two cases were confirmed by polymerase chain reaction (PCR) test performed by the French National Reference Centre for arboviruses in Marseille.

collaborative workflows

modelers

Public Health officers

policy makers

communication to public