COLUMBIA UNIVERSITY | MAILMAN SCHOOL of PUBLIC HEALTH

ENVIRONMENTAL HEALTH SCIENCES

Transmission Dynamics of SARS-CoV-2: Inference and Projection

Jeffrey Shaman

January 21, 2021

Funders

NIH (NIGMS)/NSF (DMS) joint initiative to support research at the interface of the biological and mathematical sciences

MIDAS

Models of Infectious Disease Agent Study

Funded by the National Institutes of Health

DARPA

DEFENSE THREAT REDUCTION AGENCY · UNITED STATES OF AMERICA

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY · BARDA

NSF

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- ***Cohort*** — 214 individuals from October 2016 to April 2018.

  (two daycares, CUMC, pediatric and adult ED, high school). Weekly swabs + daily symptoms .

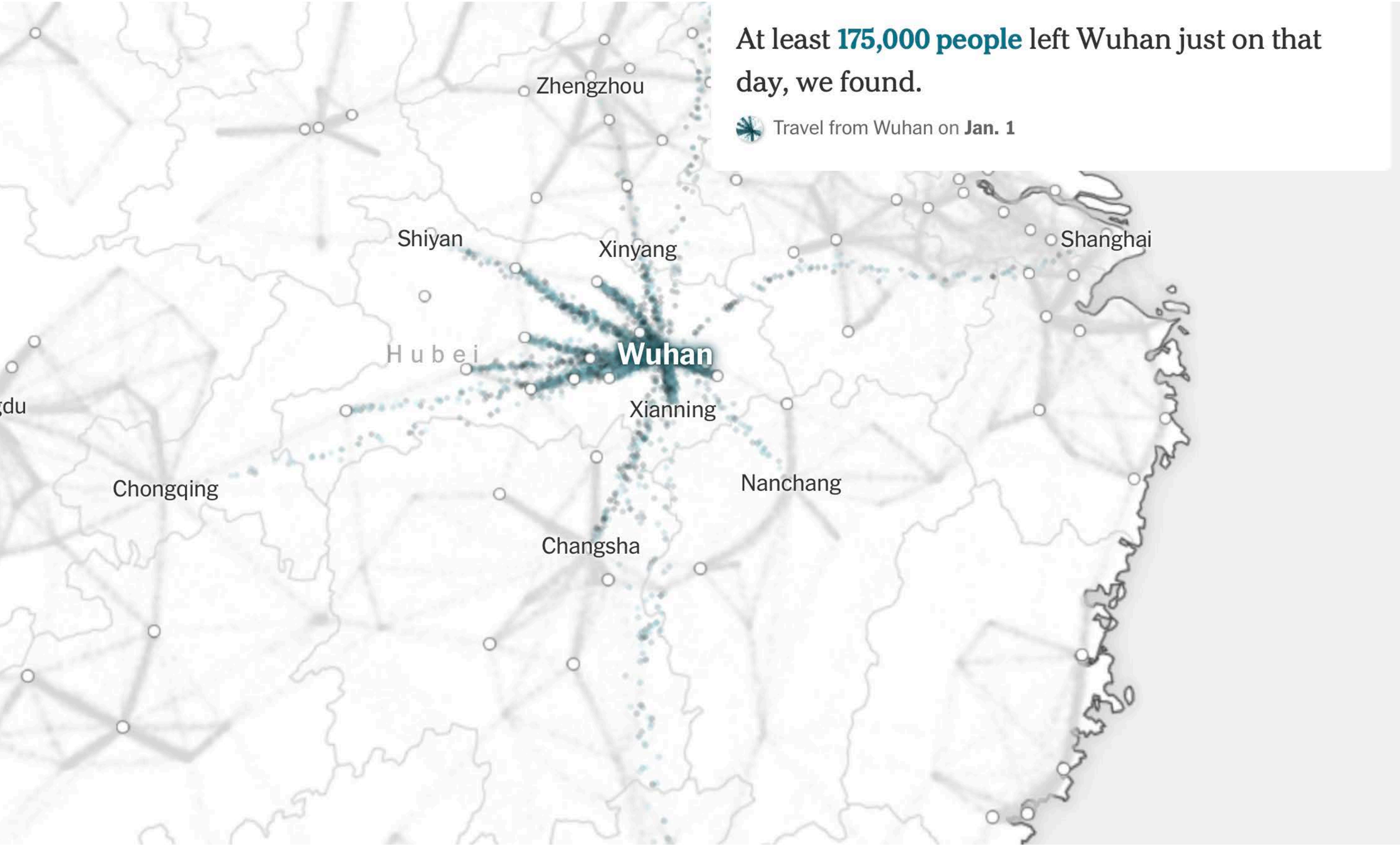
Virome of Manhattan

Most Infections Undocumented

VIRUS	EPISODES*	MA	P(MA|v_i)	HOME	P(HOME|v_i)	MEDS	P(MEDS|v_i)
Influenza	32	7	0.22	14	0.44	18	0.56
RSV	30	2	0.07	6	0.20	12	0.40
PIV	30	3	0.10	4	0.15	9	0.30
HMPV	20	4	0.20	7	0.35	10	0.50
HRV	275	24	0.09	31	0.11	70	0.25
Adenovirus	63	9	0.14	10	0.16	14	0.22
Coronavirus	137	6	0.04	13	0.09	36	0.25

*group of consecutive weekly specimens from a given individual that were positive for the same v
(allowing for a one-week gap to account for false negatives and temporary low shedding).

COVID-19 Rapid Spread



New York Times, March 22, 2020

Inference of Undocumented COVID-19 Infections

Are contagious, undocumented infections supporting the rapid spread of disease?

$$\frac{dS_i}{dt} = -\frac{\beta S_i I_i^r}{N_i} - \frac{\mu\beta S_i I_i^u}{N_i} + \theta \sum_j \frac{M_{ij} S_j}{N_j - I_j^r} - \theta \sum_j \frac{M_{ji} S_i}{N_i - I_i^r}$$

$$\frac{dE_i}{dt} = \frac{\beta S_i I_i^r}{N_i} + \frac{\mu\beta S_i I_i^u}{N_i} - \frac{E_i}{Z} + \theta \sum_j \frac{M_{ij} E_j}{N_j - I_j^r} - \theta \sum_j \frac{M_{ji} E_i}{N_i - I_i^r}$$

$$\frac{dI_i^r}{dt} = \alpha \frac{E_i}{Z} - \frac{I_i^r}{D}$$

$$\frac{dI_i^u}{dt} = (1-\alpha)\frac{E_i}{Z} - \frac{I_i^u}{D} + \theta \sum_j \frac{M_{ij} I_j^u}{N_j - I_j^r} - \theta \sum_j \frac{M_{ji} I_i^u}{N_i - I_i^u}$$

$$N_i = N_i + \theta \sum_j M_{ij} - \theta \sum_j M_{ji}$$

- Metapopulation network model representing 375 cities in China
- Use Tencent travel records during the Chunyun spring festival
- Coupled with data assimilation methods
- Use daily observations from all 375 cities
- Simulate January 10-23

Li et al., 2020

Inference of Undocumented COVID-19 Infections

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$$\frac{dI_i^r}{dt} = \alpha \frac{E_i}{Z} - \frac{I_i^r}{D}$$

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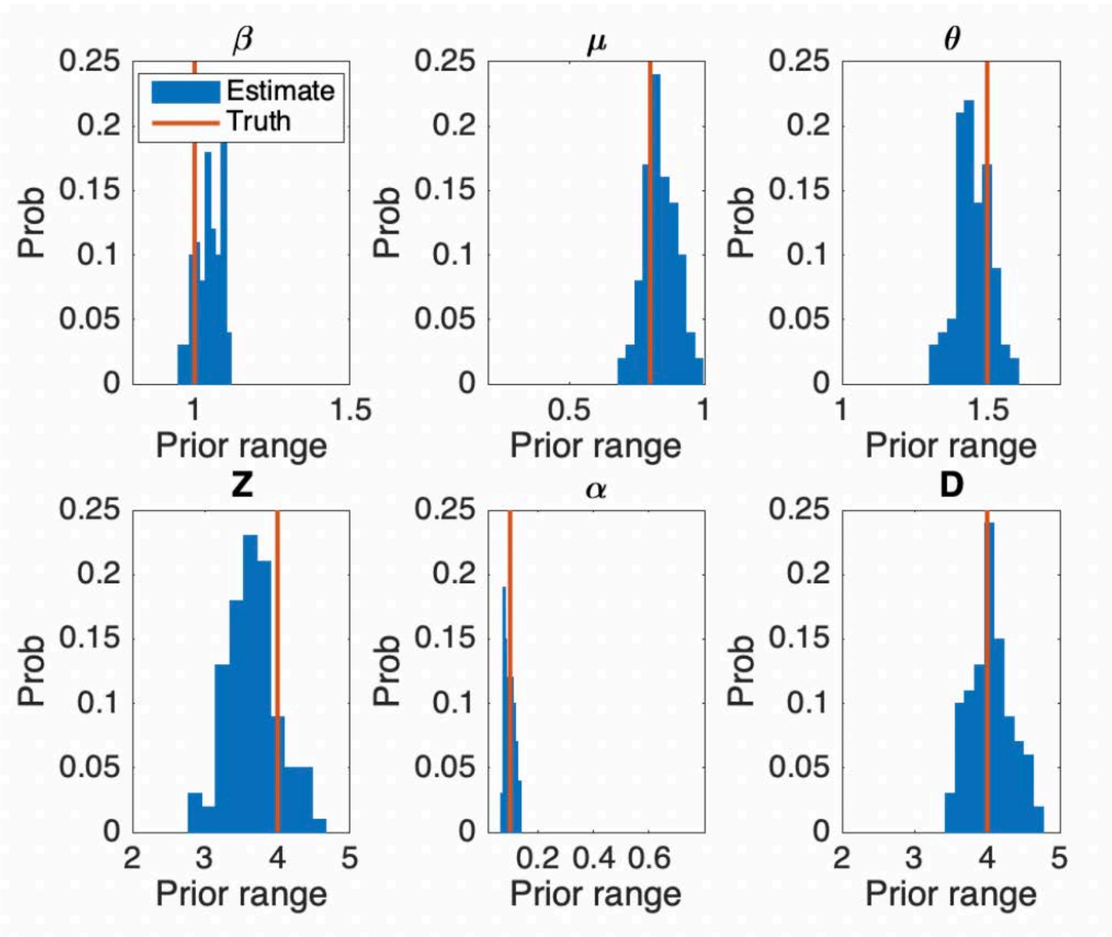
$$N_i = N_i + \theta \sum_j M_{ij} - \theta \sum_j M_{ji}$$

Li et al., 2020

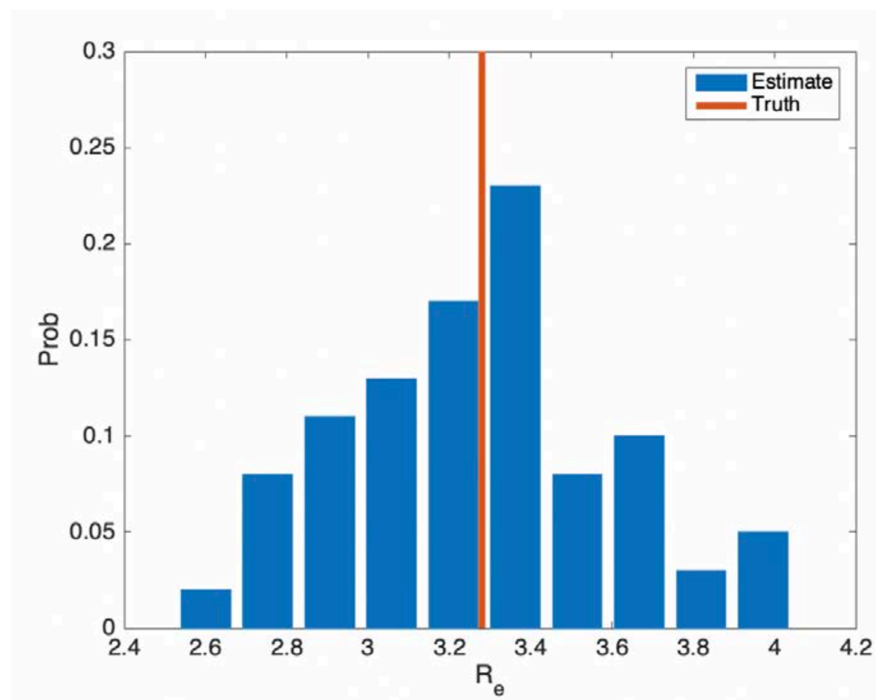
- Simulate January 10-23
- Prior to travel restrictions
- The model separately represents documented and undocumented infections
- The model has a separate contagiousness for documented/ undocumented infections

Inference of Undocumented COVID-19 Infections

Are contagious, undocumented infections supporting the rapid spread of disease?



- Synthetic test of model-inference parameter estimation using model-generated observations



Li et al., 2020

Inference of Undocumented COVID-19 Infections

Are contagious, undocumented infections supporting the rapid spread of disease?

Parameter	Median (95% CIs)
Transmission rate (β, days^{-1})	1.12 (1.04, 1.18)
Relative transmission rate (μ)	0.55 (0.46, 0.62)
Latency period (Z, days)	3.69 (3.28, 4.03)
Infectious period (D, days)	3.48 (3.18, 3.74)
Reporting rate (α)	0.14 (0.10, 0.18)
Basic reproductive number (R_e)	2.38 (2.04, 2.77)
Mobility factor (θ)	1.36 (1.28, 1.43)

- Estimate that 14% of infections are documented
- 86% are undocumented
- Per person, undocumented infections are on average half as contagious (55%) as documented infections
- 2.38 reproductive number

Li et al., 2020

Inference of Undocumented COVID-19 Infections

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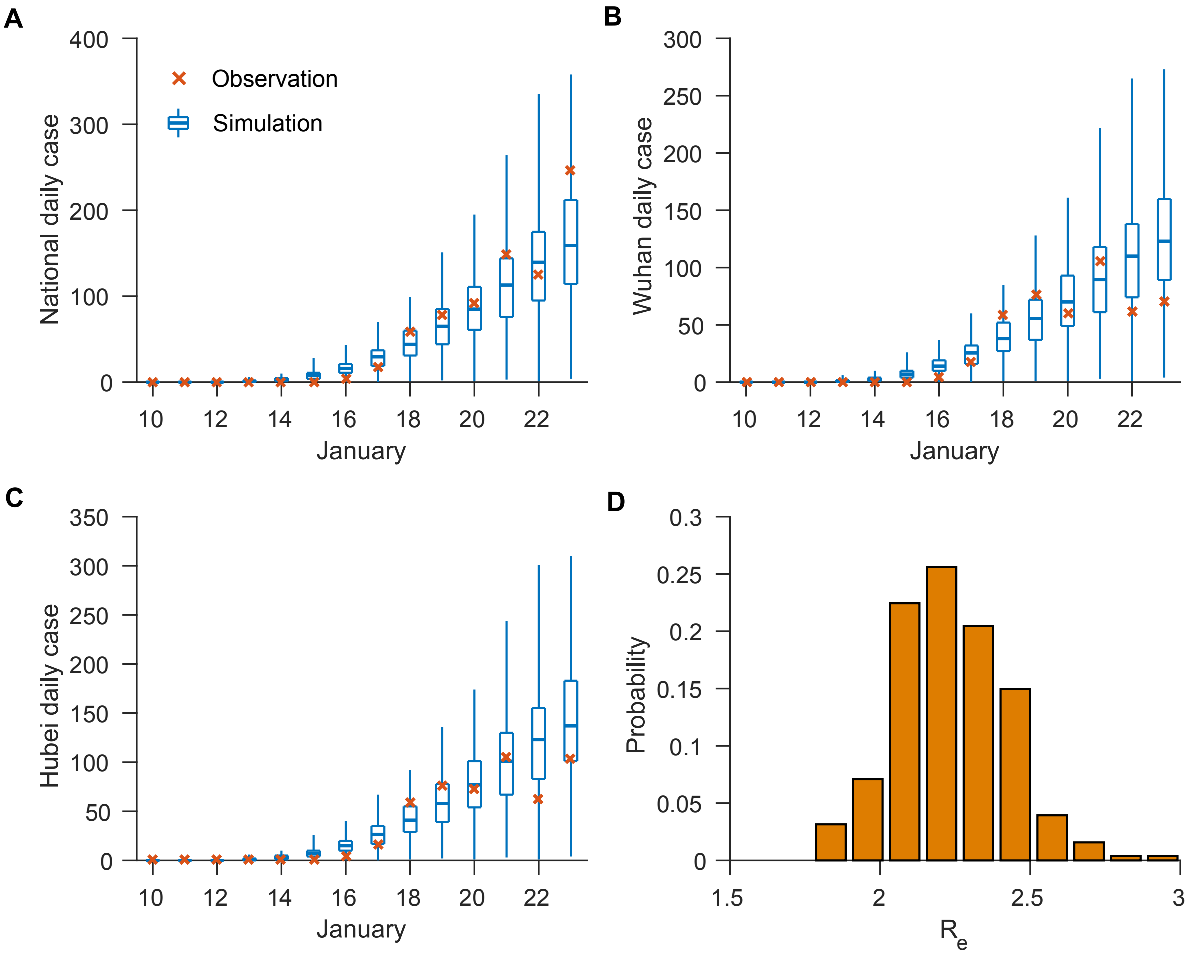
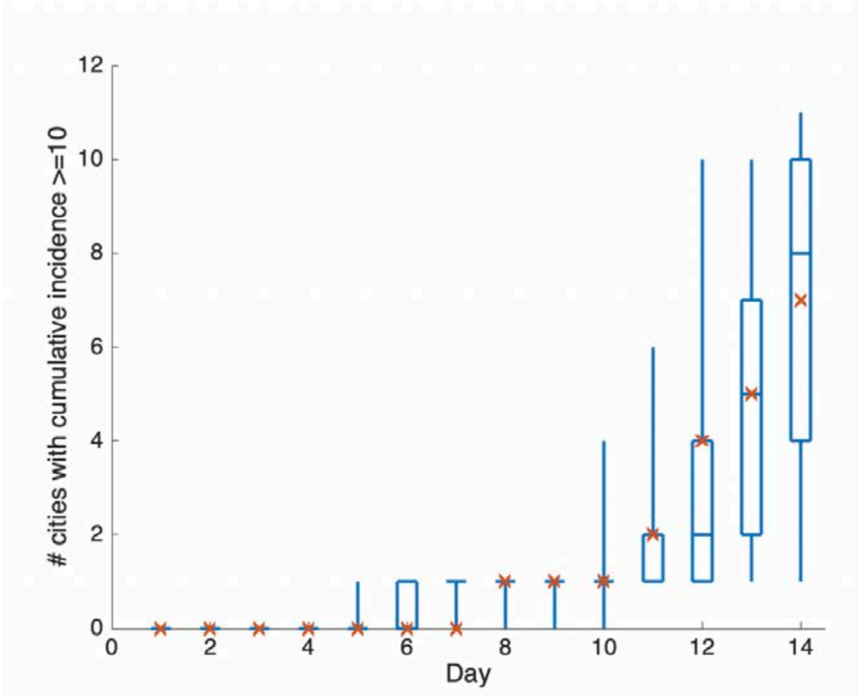


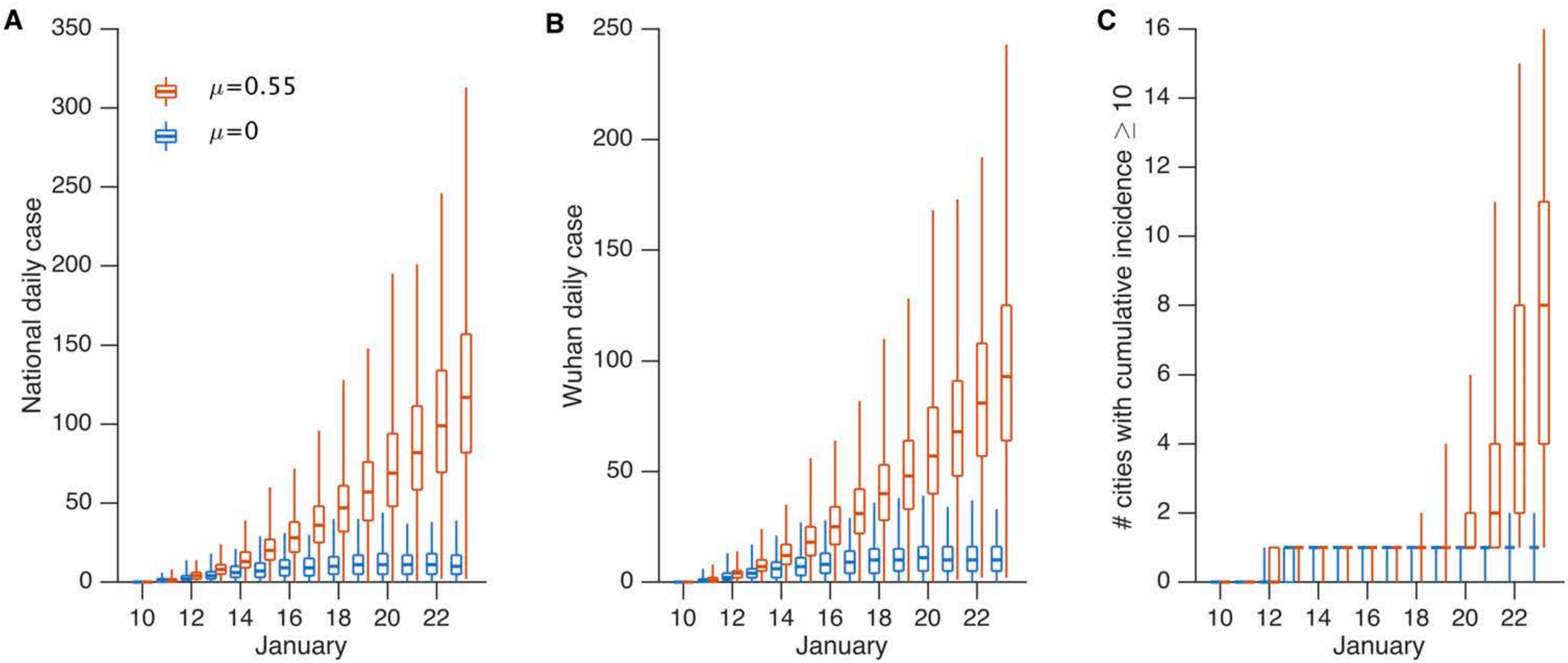
- Simulations with the parameter estimates match the observed outbreak



Li et al., 2020

Inference of Undocumented COVID-19 Infections

Are contagious, undocumented infections supporting the rapid spread of disease?

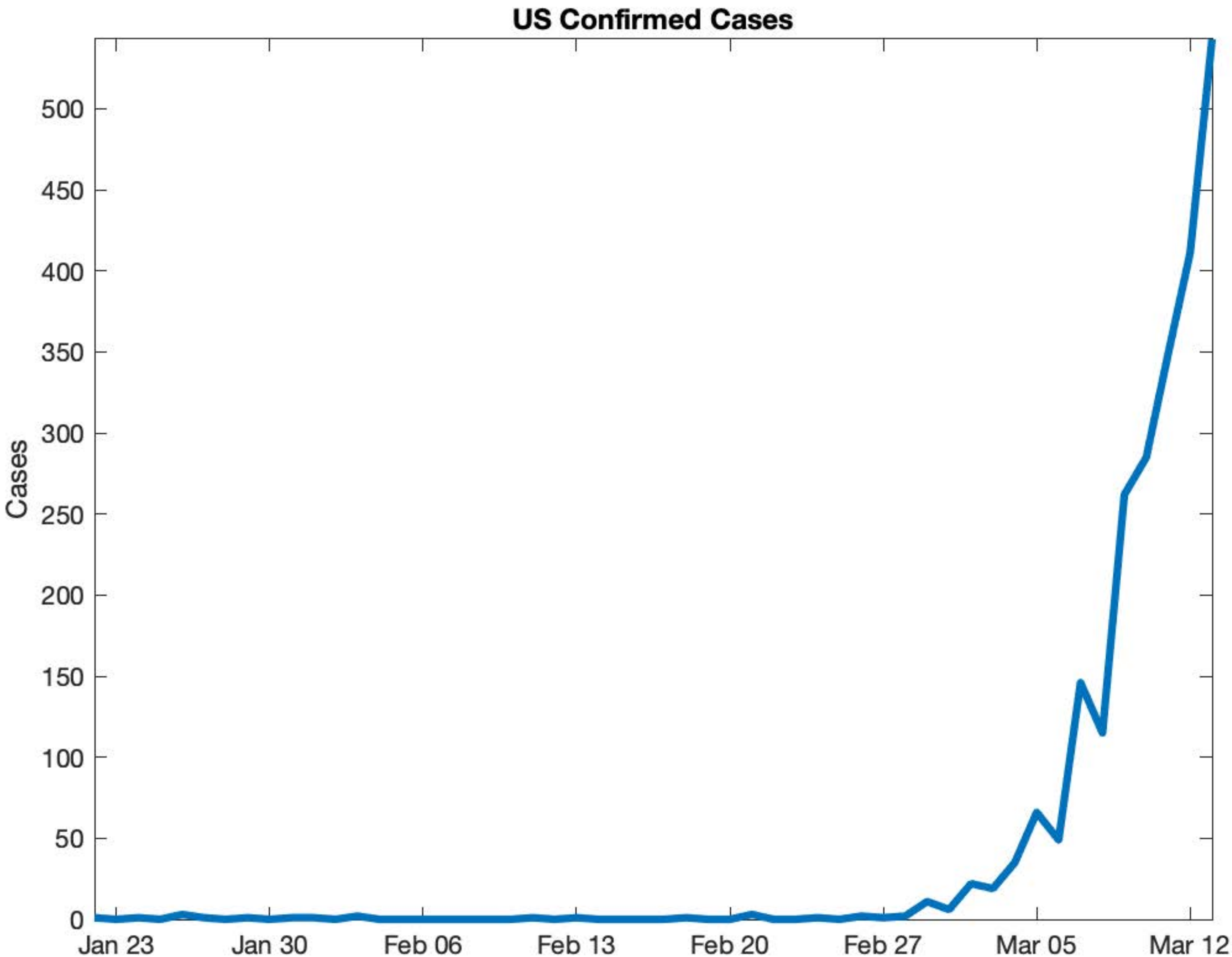


- Simulations show without transmission from undocumented cases, confirmed cases decrease 79%

Li et al., 2020

Documentation History of CoV

- SARS: sub-clinical infection rates believed to be low (WHO, 2003)
- MERS: 21% of laboratory identified cases were mild or asymptomatic (WHO, 2018)
- Seasonal Coronaviruses (229E, OC43, NL63, HKU1)
  - 135 infection events
  - >60% mild or asymptomatic
  - 4% sought medical care (all had either OC43 or HKU1—the two seasonal betacoronaviruses) (Shaman and Galanti, 2020)
- Our model-inference approach identifies a 14% documentation rate prior to travel restrictions (Li et al. 2020) and indicates that undocumented infections contribute substantially to COVID-19 transmission.



US Confirmed Cases
Cases
0
50
100
150
200
250
300
350
400
450
500
Jan 23
Jan 30
Feb 06
Feb 13
Feb 20
Feb 27
Mar 05
Mar 12

Inference of Undocumented COVID-19 Infections and Key Epidemiological Parameters

$$S_{ij}(t+dt_1) = S_{ij}(t) - \frac{\beta S_{ij}(t)\sum_k I_{ki}^r(t)}{N_i^D(t)}dt_1 - \frac{\mu\beta S_{ij}(t)\sum_k I_{ik}^u(t)}{N_i^D(t)}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)}\sum_{k\neq i}\frac{\bar{N}_{ik}\sum_l S_{kl}(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{S_{ij}(t)}{N_i^D(t) - \sum_l I_{li}^r(t)}\sum_{k\neq i}\bar{N}_{ki} \quad (1)$$

$$E_{ij}(t+dt_1) = E_{ij}(t) + \frac{\beta S_{ij}(t)\sum_k I_{ki}^r(t)}{N_i^D(t)} + \frac{\mu\beta S_{ij}(t)\sum_k I_{ik}^u(t)}{N_i^D(t)}dt_1 - \frac{E_{ij}(t)}{Z}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)}\sum_{k\neq i}\frac{\bar{N}_{ik}\sum_l E_{kl}(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{E_{ij}(t)}{N_i^D(t) - \sum_l I_{li}^r(t)}\sum_{k\neq i}\bar{N}_{ki} \quad (2)$$

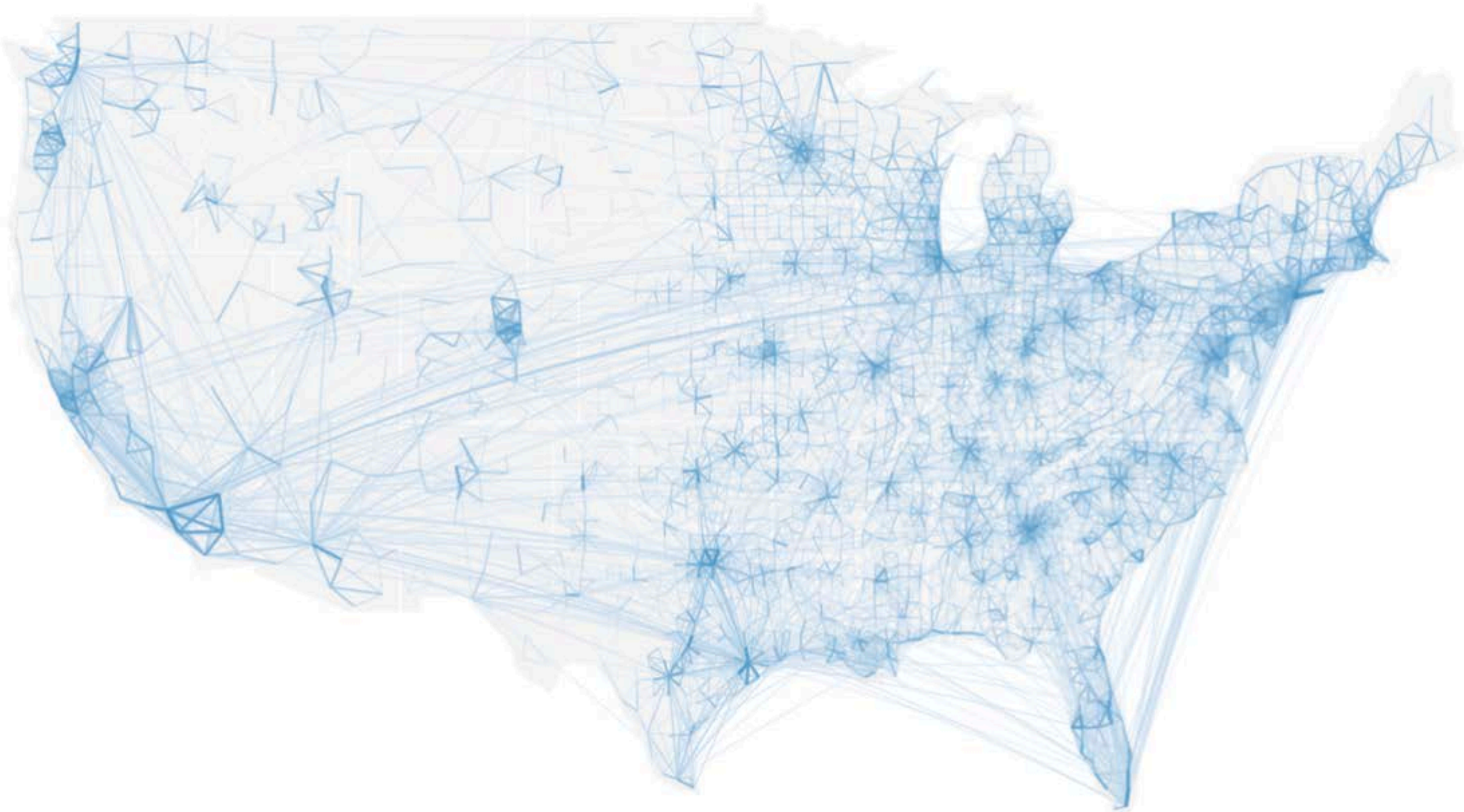
$$I_{ij}^r(t+dt_1) = I_{ij}^r(t) + \alpha\frac{E_{ij}(t)}{Z}dt_1 - \frac{I_{ij}^r(t)}{D}dt_1 \quad (3)$$

$$I_{ij}^u(t+dt_1) = I_{ij}^u(t) + (1-\alpha)\frac{E_{ij}(t)}{Z}dt_1 - \frac{I_{ij}^u(t)}{D}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)}\sum_{k\neq i}\frac{\bar{N}_{ik}\sum_l I_{kl}^u(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{I_{ij}^u(t)}{N_i^D(t) - \sum_l I_{li}^r(t)}\sum_{k\neq i}\bar{N}_{ki} \quad (4)$$

$$N_i^D(t) = N_{ii} + \sum_{k\neq i} I_{ki}^r(t) + \sum_{k\neq i}(N_{ik} - I_{ik}^r(t)) \quad (5)$$

Pei and Shaman, 2020

Inter-county commuting data from US census survey



Pei et al., 2020

Initial Estimates for the US (through March 13, 2020)

Parameter	Median (95% CIs)
Transmission rate (β, days^{-1})	0.95 (0.84, 1.06)
Relative transmission rate (μ)	0.64 (0.56, 0.70)
Latency period (Z, days)	3.59 (3.28, 3.99)
Infectious period (D, days)	3.56 (3.21, 3.83)
Reporting rate (α)	0.080 (0.069, 0.093)
Basic reproductive number (R_e)	2.27 (1.87, 2.55)
Mobility factor (θ)	0.15 (0.12,0.17)

Pei and Shaman, 2020

Additional Features

$$S_{ij}(t+dt_1) = S_{ij}(t) - \frac{\beta S_{ij}(t)\sum_k I_{ki}^r(t)}{N_i^D(t)}dt_1 - \frac{\mu\beta S_{ij}(t)\sum_k I_{ik}^u(t)}{N_i^D(t)}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)} \sum_{k\neq i} \frac{\bar{N}_{ik}\sum_l S_{kl}(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{S_{ij}(t)}{N_i^D(t) - \sum_l I_{li}^r(t)} \sum_{k\neq i} \bar{N}_{ki} \quad (1)$$

$$E_{ij}(t+dt_1) = E_{ij}(t) + \frac{\beta S_{ij}(t)\sum_k I_{ki}^r(t)}{N_i^D(t)} + \frac{\mu\beta S_{ij}(t)\sum_k I_{ik}^u(t)}{N_i^D(t)}dt_1 - \frac{E_{ij}(t)}{Z}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)} \sum_{k\neq i} \frac{\bar{N}_{ik}\sum_l E_{kl}(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{E_{ij}(t)}{N_i^D(t) - \sum_l I_{li}^r(t)} \sum_{k\neq i} \bar{N}_{ki} \quad (2)$$

$$I_{ij}^r(t+dt_1) = I_{ij}^r(t) + \alpha \frac{E_{ij}(t)}{Z}dt_1 - \frac{I_{ij}^r(t)}{D}dt_1 \quad (3)$$

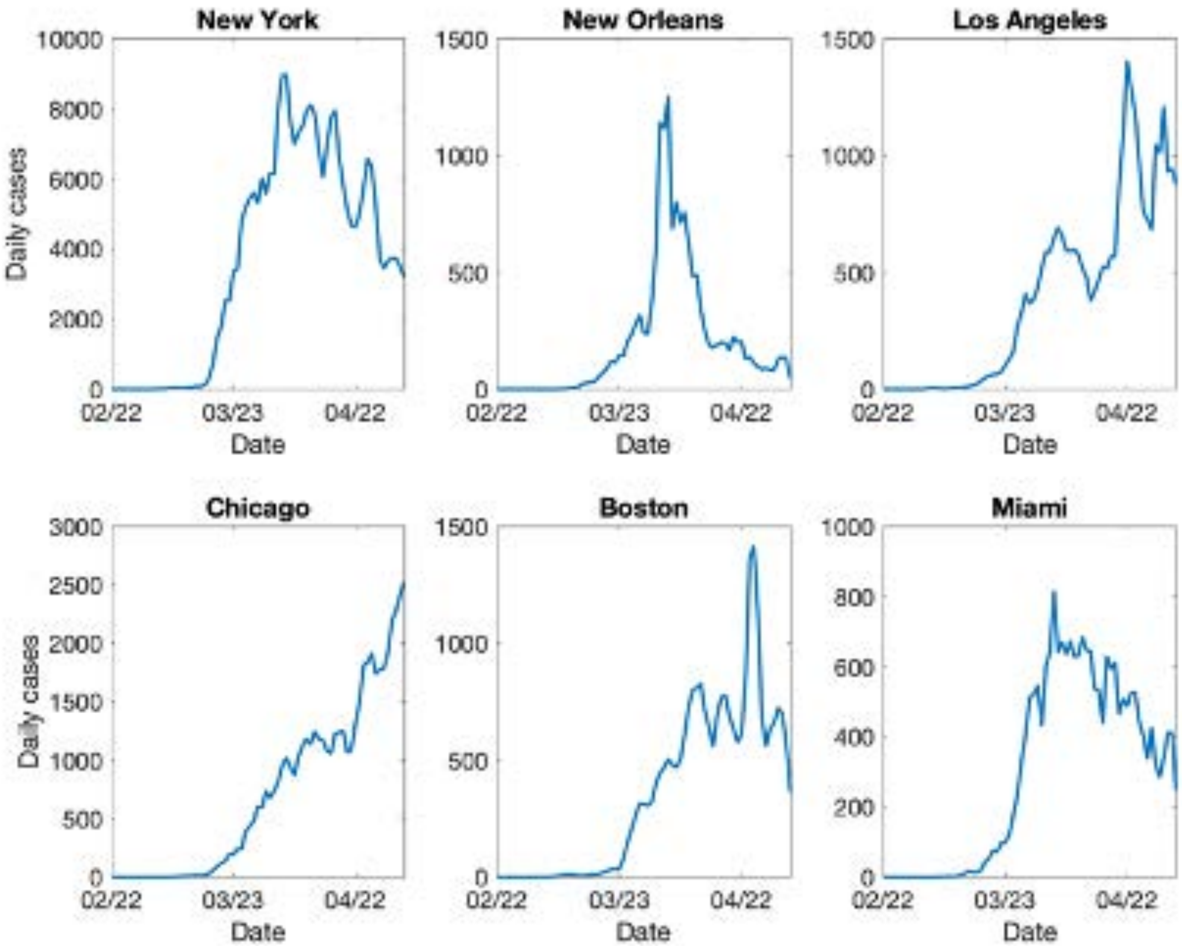
$$I_{ij}^u(t+dt_1) = I_{ij}^u(t) + (1-\alpha)\frac{E_{ij}(t)}{Z}dt_1 - \frac{I_{ij}^u(t)}{D}dt_1 + \theta dt_1 \frac{N_{ij} - I_{ij}^r(t)}{N_i^D(t)} \sum_{k\neq i} \frac{\bar{N}_{ik}\sum_l I_{kl}^u(t)}{N_k^D(t) - \sum_l I_{lk}^r(t)} - \theta dt_1 \frac{I_{ij}^u(t)}{N_i^D(t) - \sum_l I_{li}^r(t)} \sum_{k\neq i} \bar{N}_{ki} \quad (4)$$

$$N_i^D(t) = N_{ii} + \sum_{k\neq i} I_{ki}^r(t) + \sum_{k\neq i}(N_{ik} - I_{ik}^r(t)) \quad (5)$$

- Assimilate Cases and Deaths
- Allow certain parameters to vary through time
- Allow certain parameters to vary by county

Pei and Shaman, 2020

Inference, Fitting and Projection

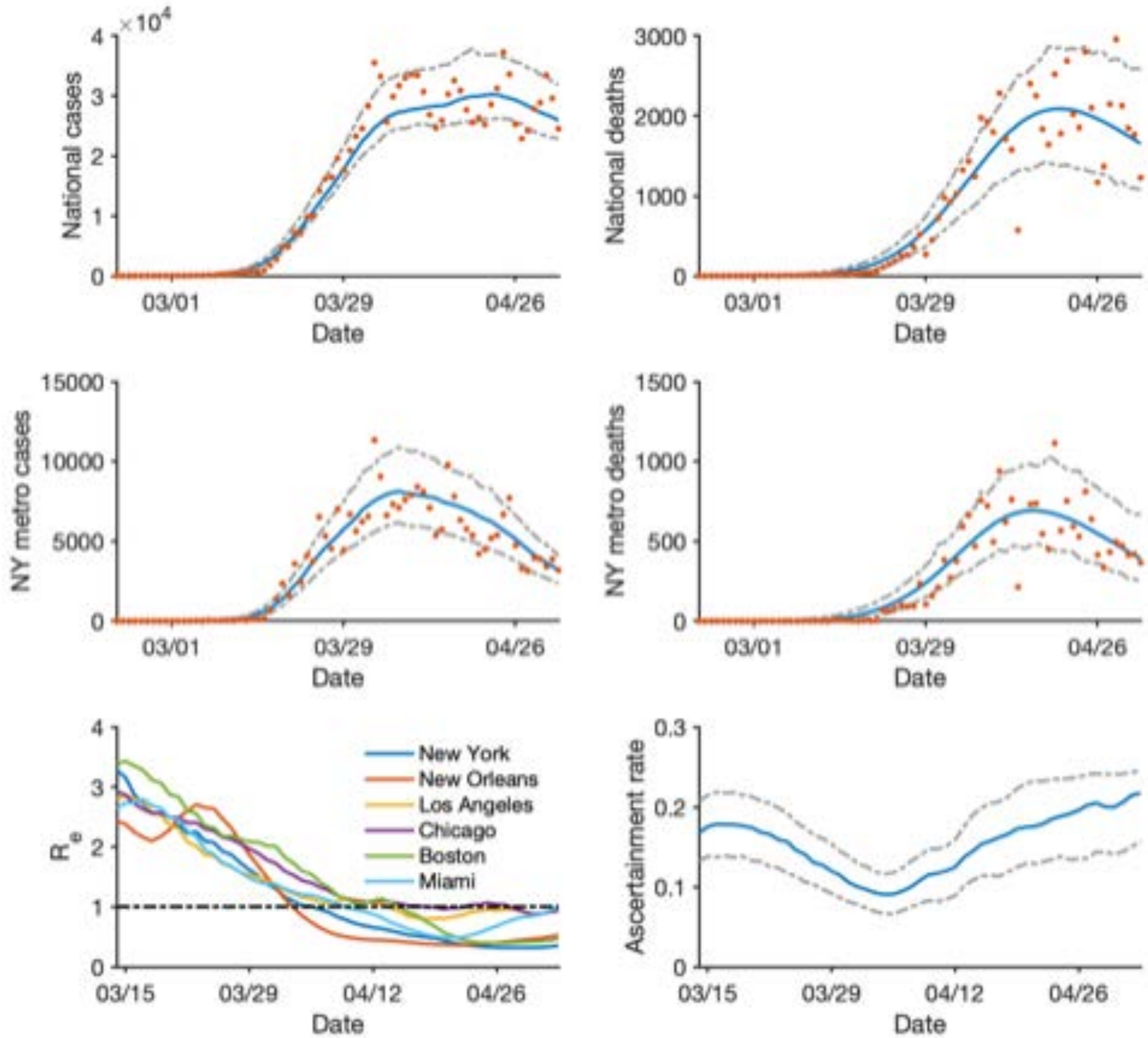


- Estimate β in all counties with more than 400 cumulative cases as of May 3, 2020
- Vary movement between counties using Safe Graph location-based mobility data
- Spotlight activity in six metropolitan areas. These counties are:

1.New York: Kings County NY, Queens County NY, New York County NY, Bronx County NY, Richmond County NY, Westchester County NY, Bergen County NJ, Hudson County NJ, Passaic County NJ, Putnam County NY, Rockland County NY
2.New Orleans: Jefferson Parish LA, Orleans Parish LA, St. John the Baptist Parish LA, St. Tammany Parish LA
3.Los Angeles: Los Angeles County CA, Orange County CA
4.Chicago: Cook County IL, DuPage County IL, Kane County IL, McHenry County IL, Will County IL
5.Boston: Norfolk County MA, Plymouth County MA, Suffolk County MA
6.Miami: Miami-Dade County FL, Broward County FL, Palm Beach County FL

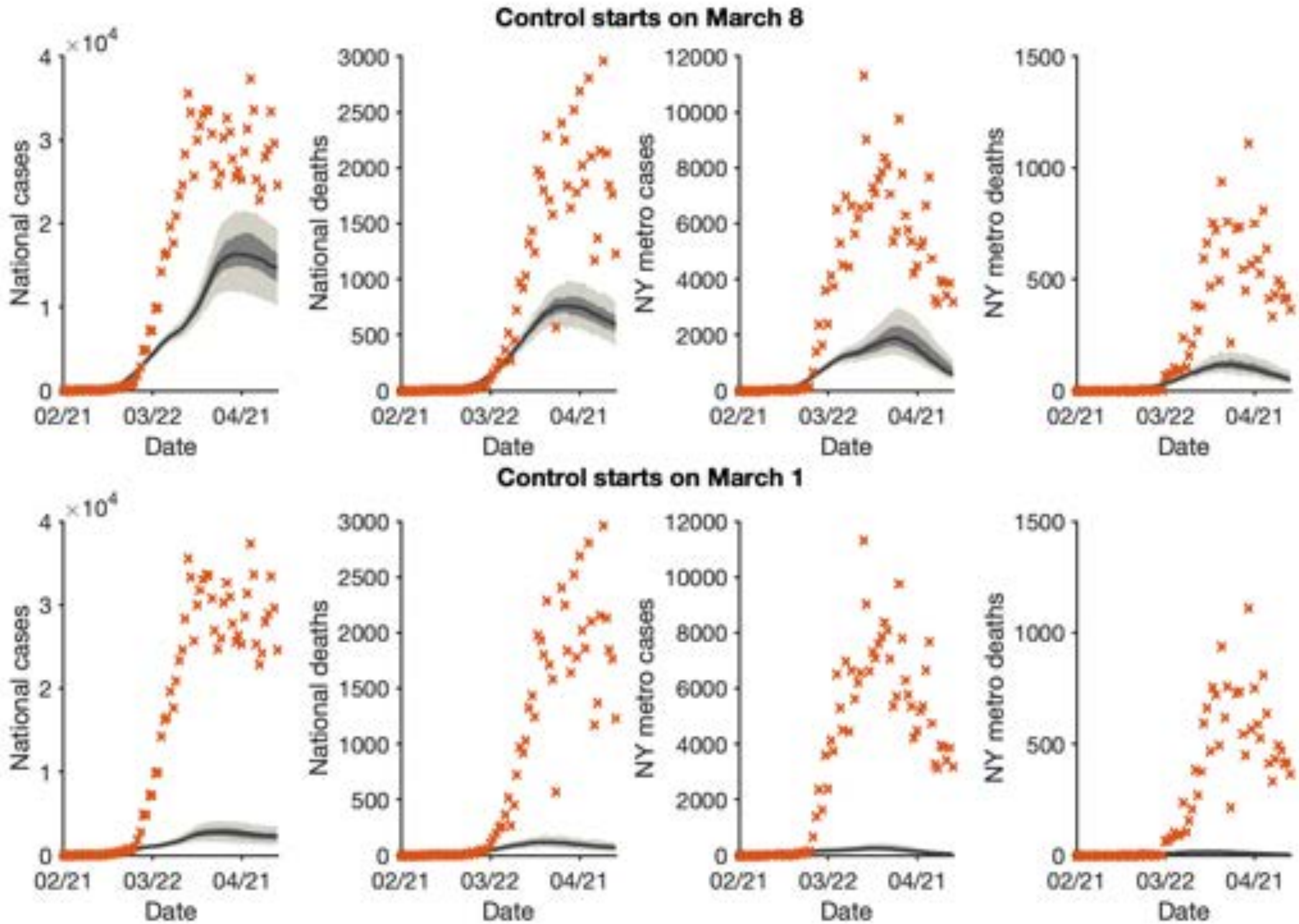
Pei et al., 2020

Fitting and Inference



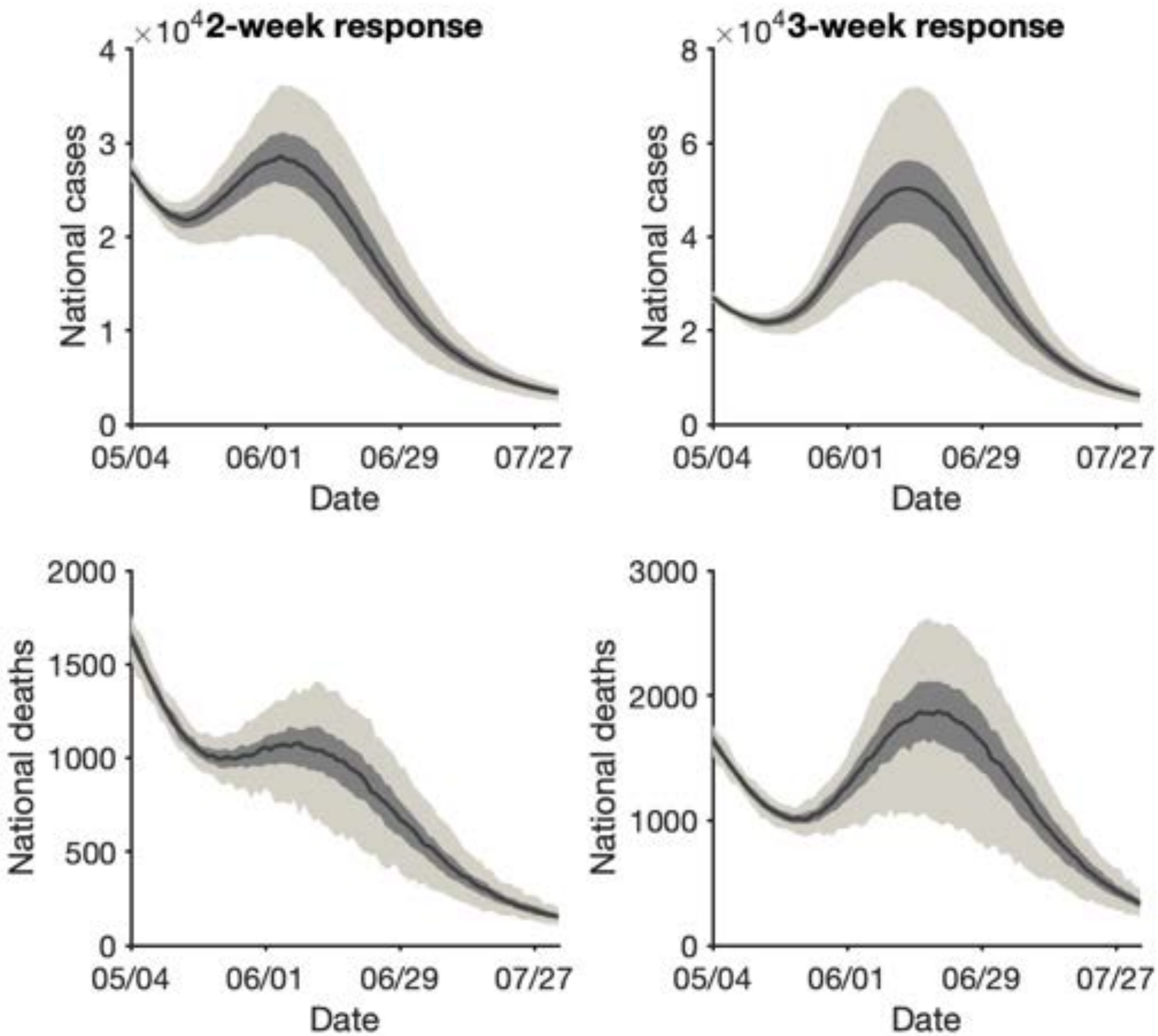
Pei et al., 2020

Counterfactuals



• Pei et al., 2020

Going Forward



- Rebound outbreaks confront a similar problem
- A one-week further delay to the resumption of control measures results in tens of thousands of extra deaths

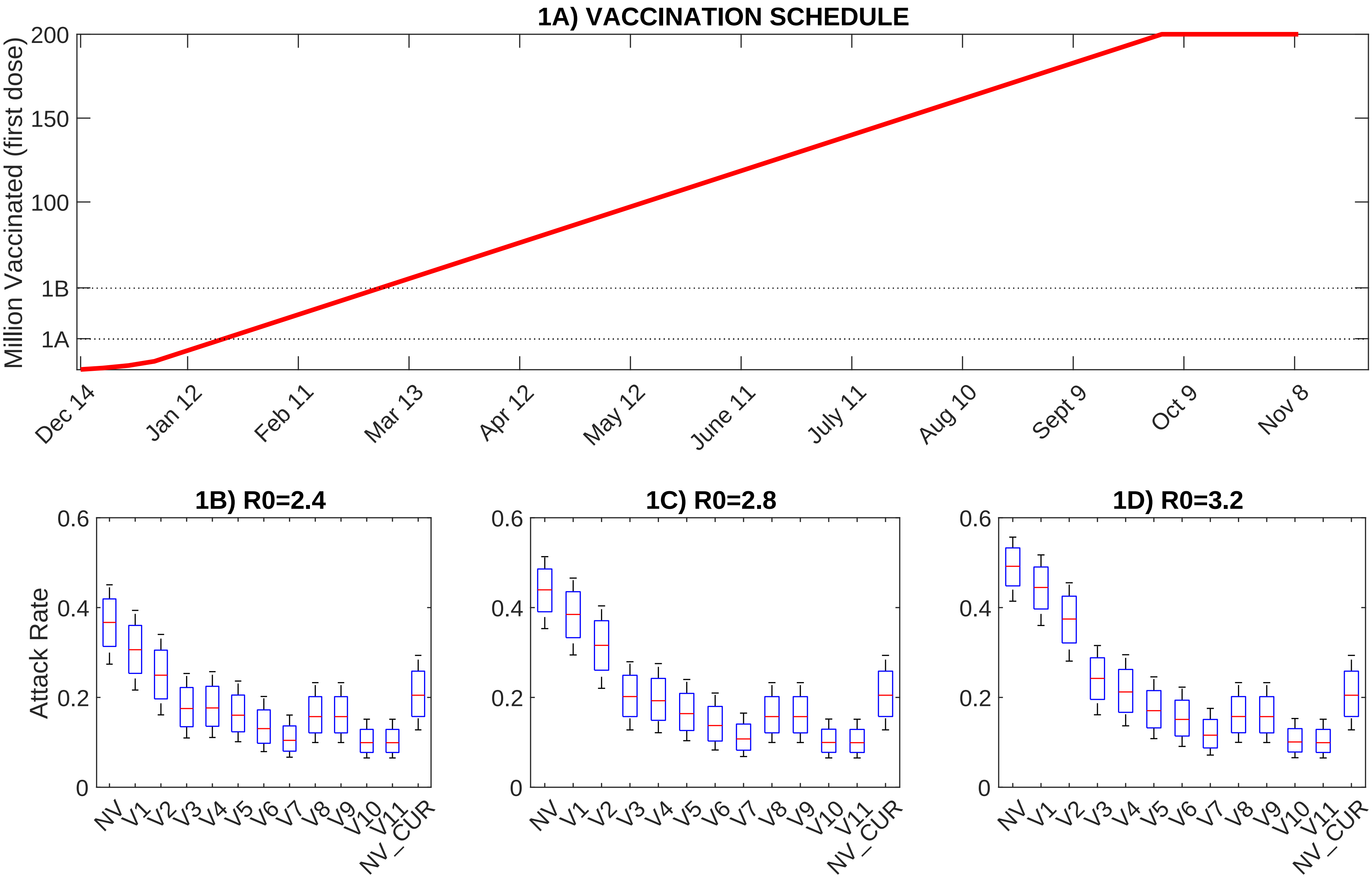
- Pei et al., 2020

Vaccination

NV	NPIs fully **relaxed on December 4th; no vaccination**
V1	NPIs fully **relaxed on December 4th**; vaccination
V2	NPIs maintained at currently estimated levels then **fully relaxed after PHASE1 (HC+LTCF)** vaccination
V3	NPIs maintained at currently estimated levels then **fully relaxed after PHASE2 (EW)** vaccination
V4	NPIs maintained at currently estimated levels then **gradually relaxed after PHASE1 (HC+LTCF)** vaccination
V5	NPIs maintained at currently estimated levels then **gradually relaxed after PHASE2 (EW)** vaccination
V6	NPIs **strengthened to R_0=1.4**, then gradually relaxed after **PHASE1 (HC+LTCF)** vaccination
V7	NPIs **strengthened to R_0=1.4**, then gradually relaxed after **PHASE2 (EW)** vaccination
V8	NPIs **maintained** at currently estimated levels then fully **relaxed upon vaccination of 140** million people
V9	NPIs **maintained** at currently estimated levels then gradually **relaxed upon vaccination of 140** million people
V10	NPIs **strengthened to R_0=1.4** then fully **relaxed upon vaccination of 140** million people
V11	NPIs **strengthened to R_0=1.4** then gradually **relaxed upon vaccination of 140** million people

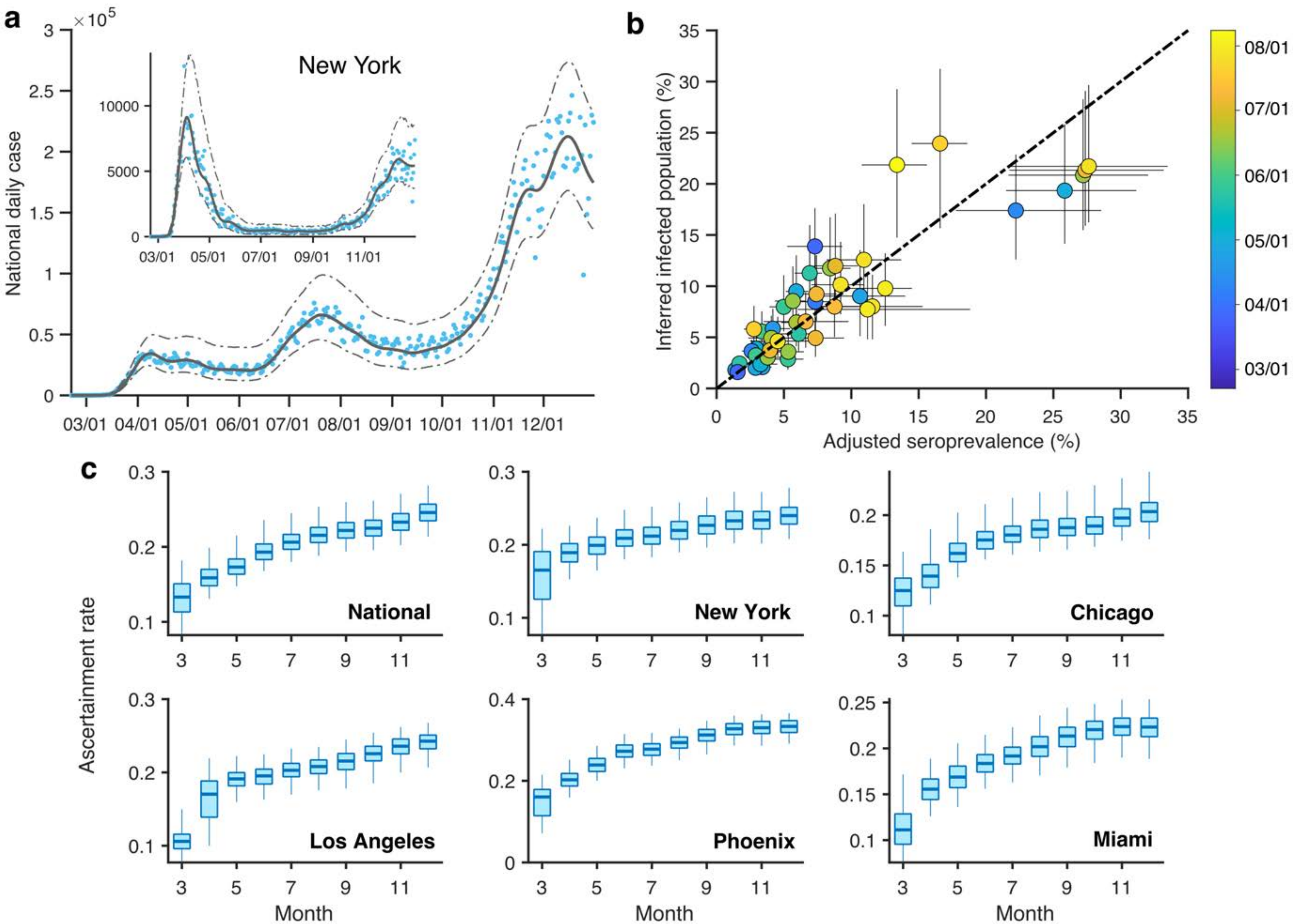
- Galanti et al., 2020

Vaccination



- Galanti et al., 2021

2020 - Epidemiological Characteristics



- Pei et al., 2021

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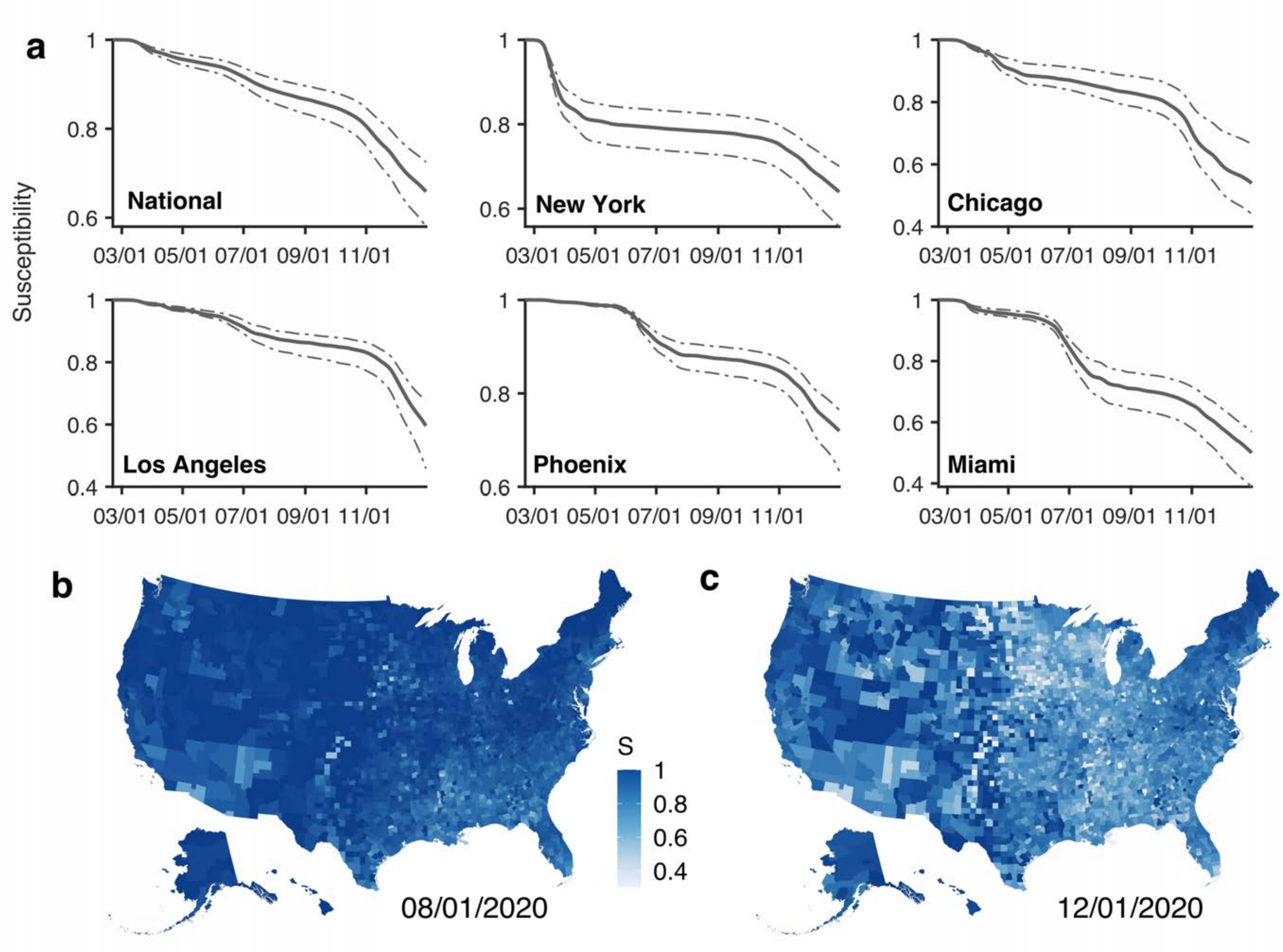

- Pei et al., 2021