

# SARS-CoV-2 across scales

Stephen Kissler

March 17<sup>th</sup>, 2021

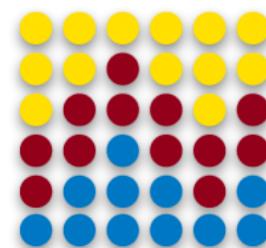
CU Boulder Applied Math Colloquium



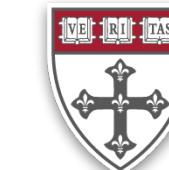
[skissler@hsph.harvard.edu](mailto:skissler@hsph.harvard.edu)



@StephenKissler

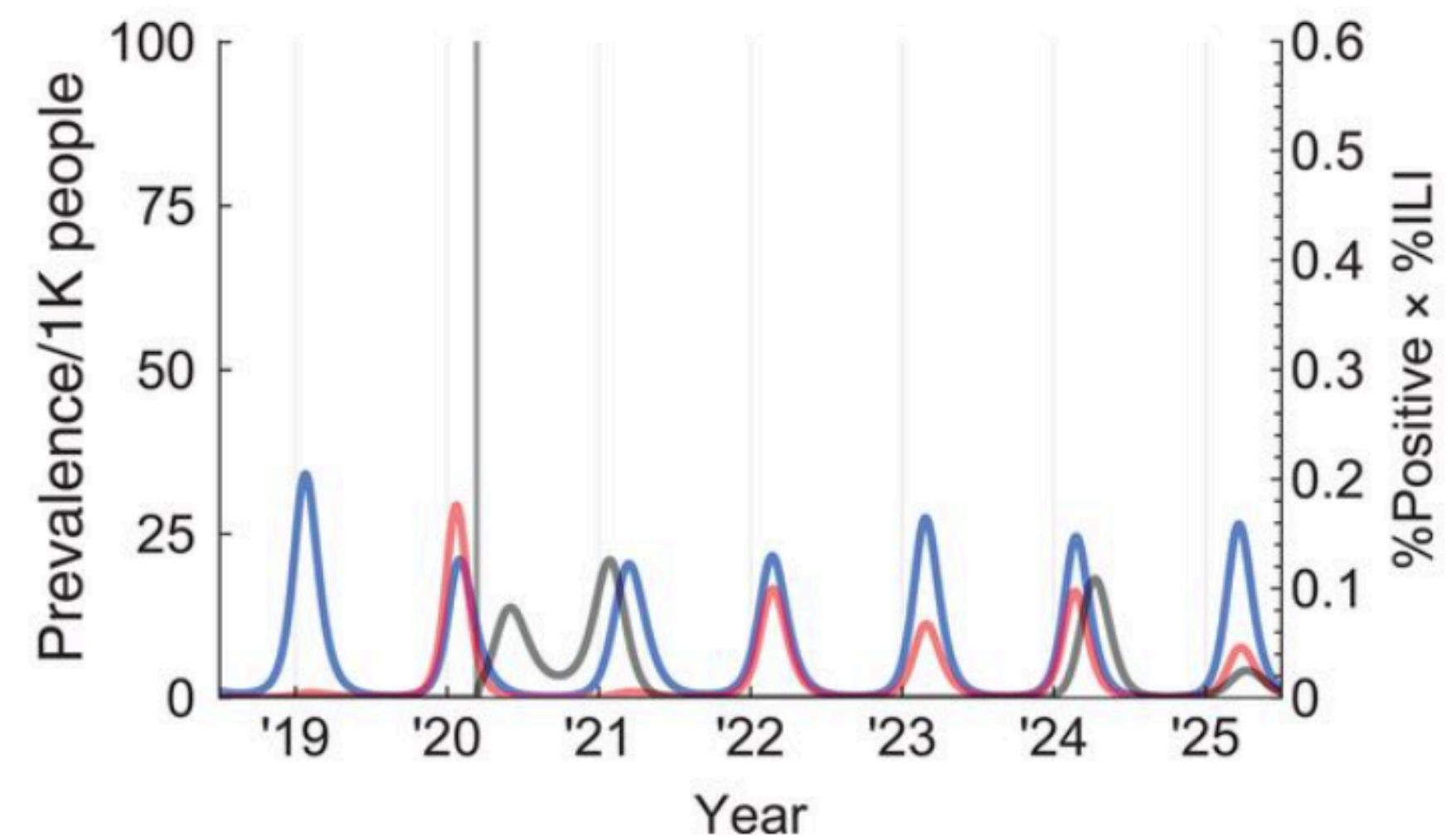


CENTER *for*  
COMMUNICABLE  
DISEASE DYNAMICS



**HARVARD T.H. CHAN**  
SCHOOL OF PUBLIC HEALTH

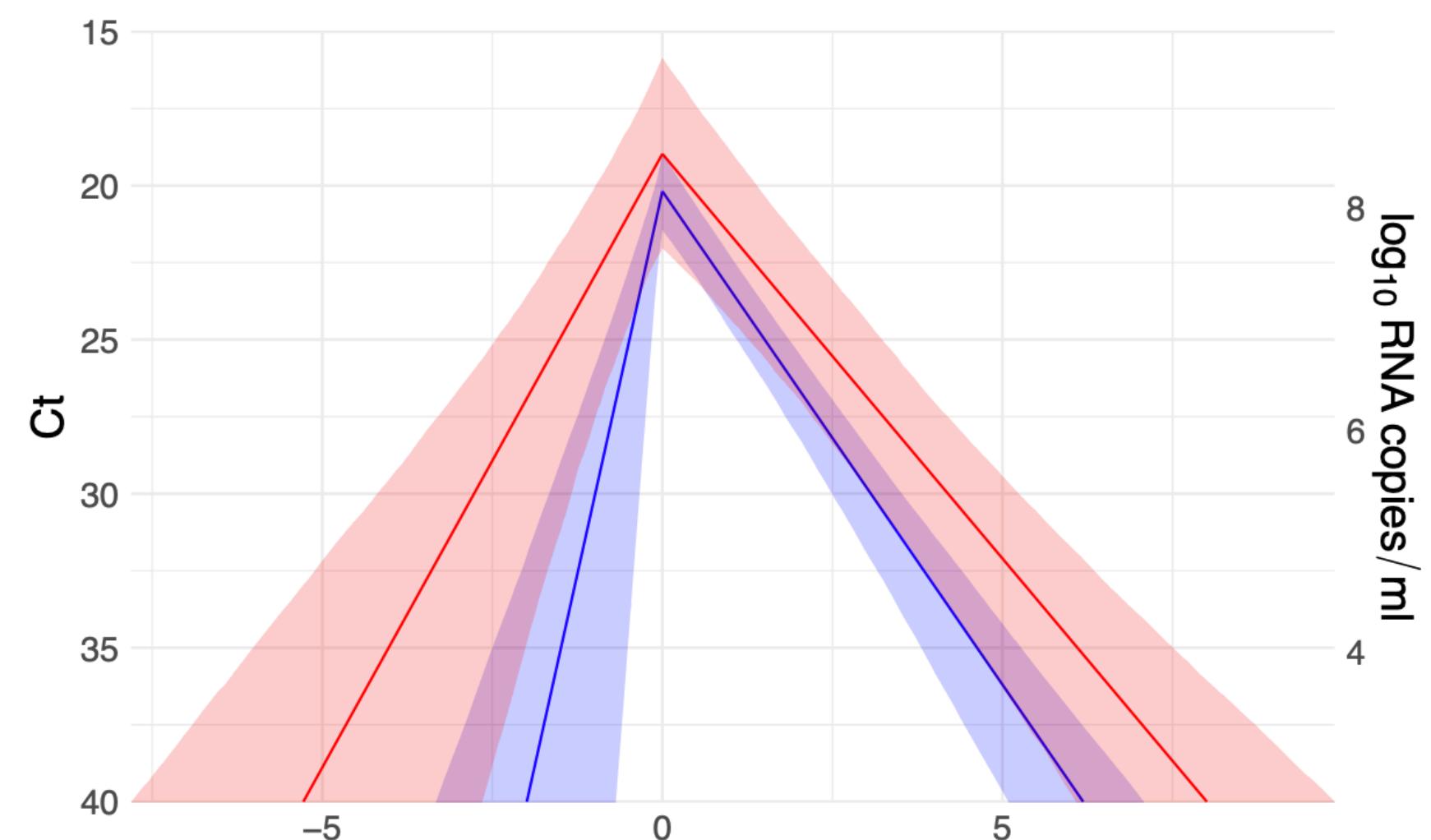
### I. Long-term global spread of SARS-CoV-2



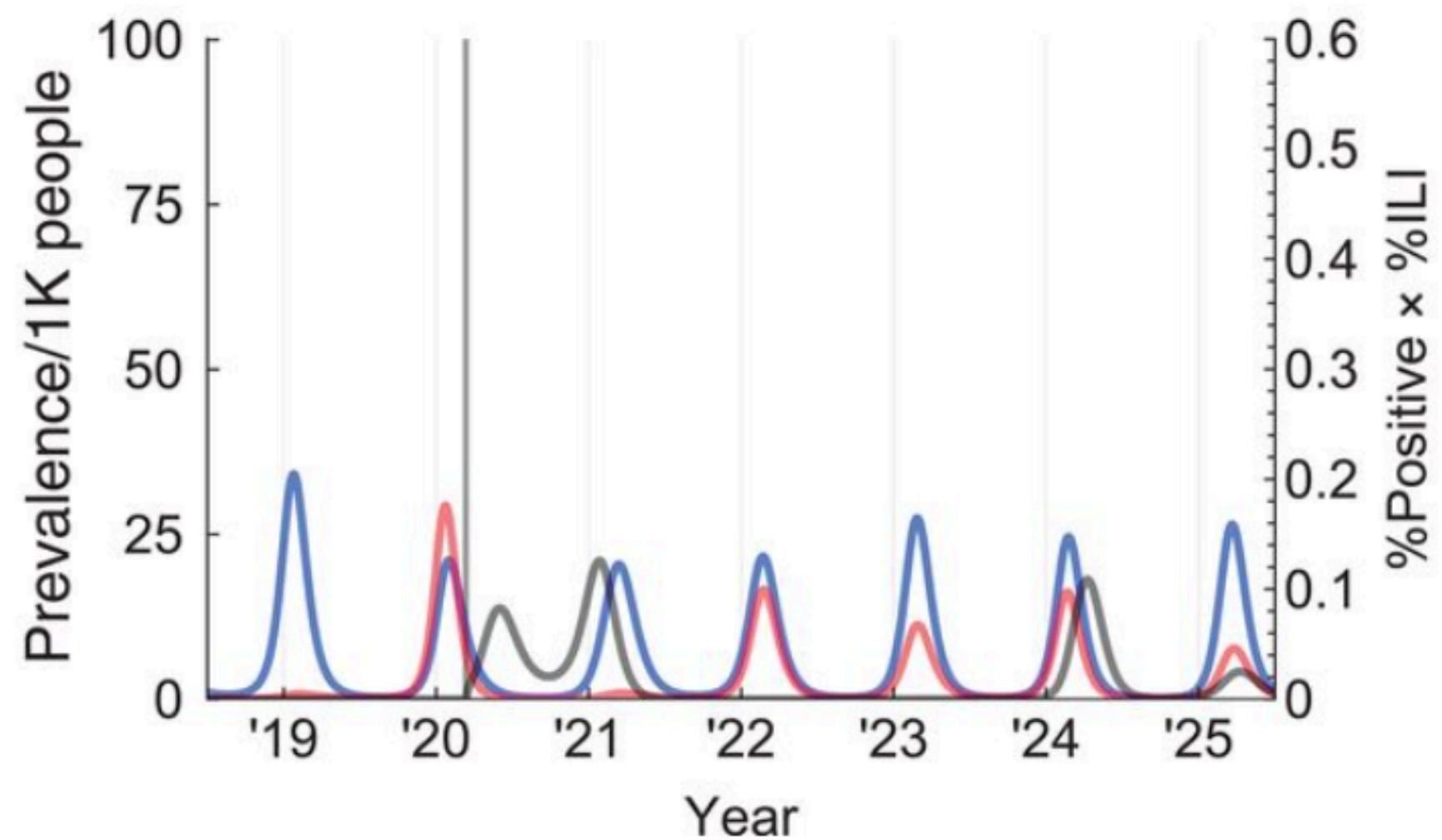
### II. Measuring SARS-CoV-2 prevalence in New York City



### III. Viral dynamics of SARS-CoV-2 variants



# I. Long-term global spread of SARS-CoV-2

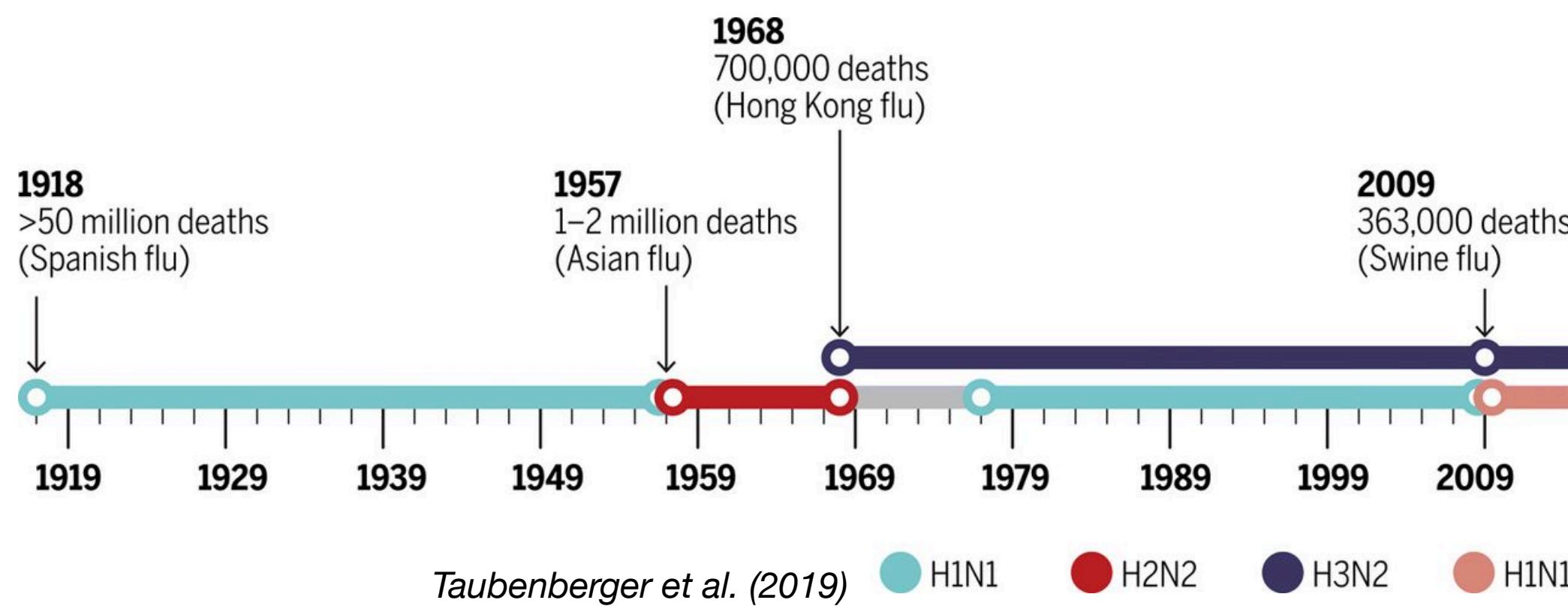
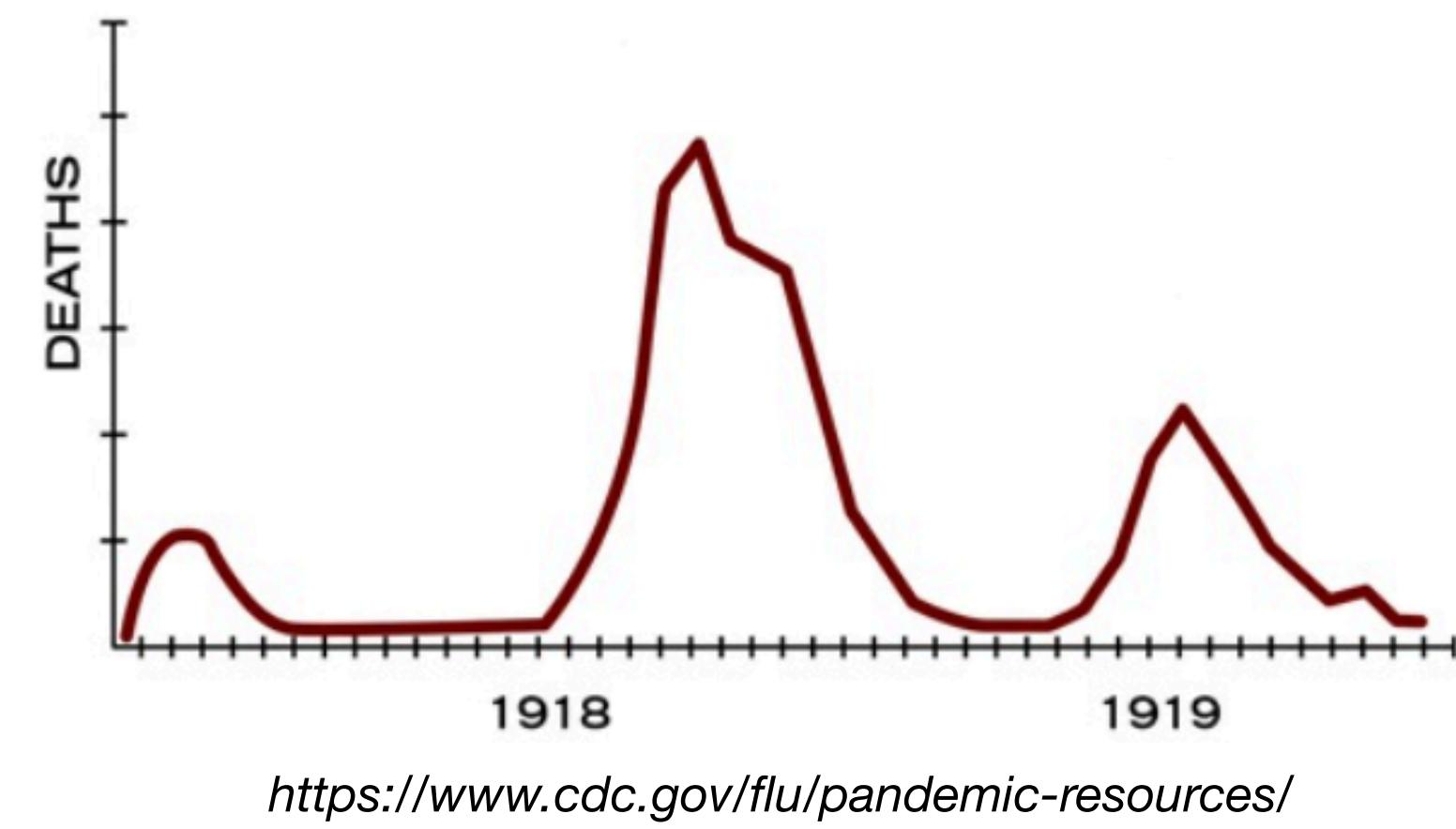


## II. Measuring SARS-CoV-2 prevalence in New York City

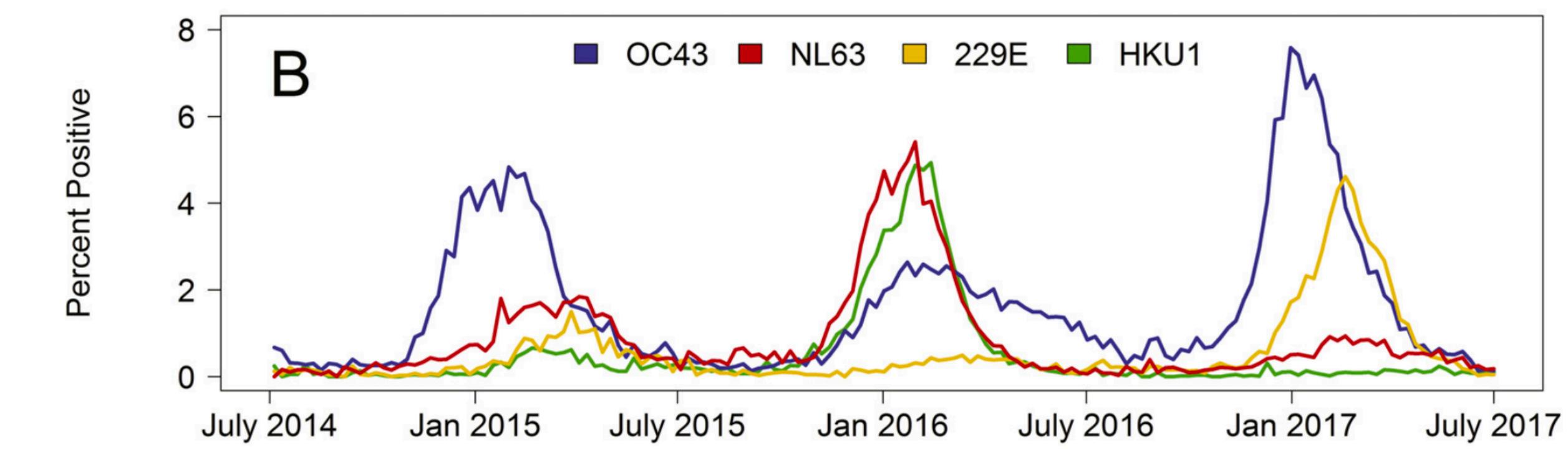
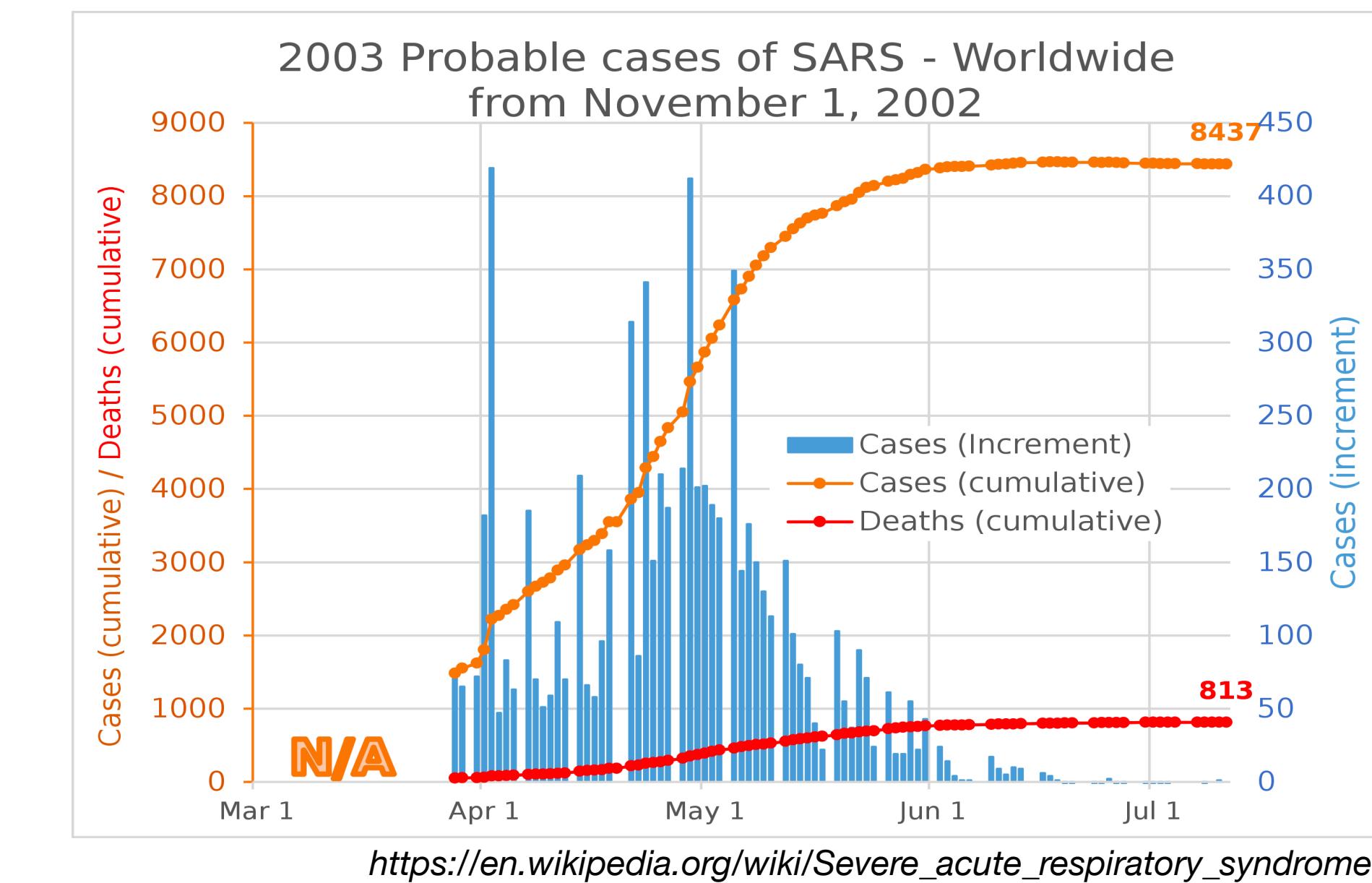
### III. Viral dynamics of SARS-CoV-2 variants

# Two respiratory pandemic paradigms

## Influenza

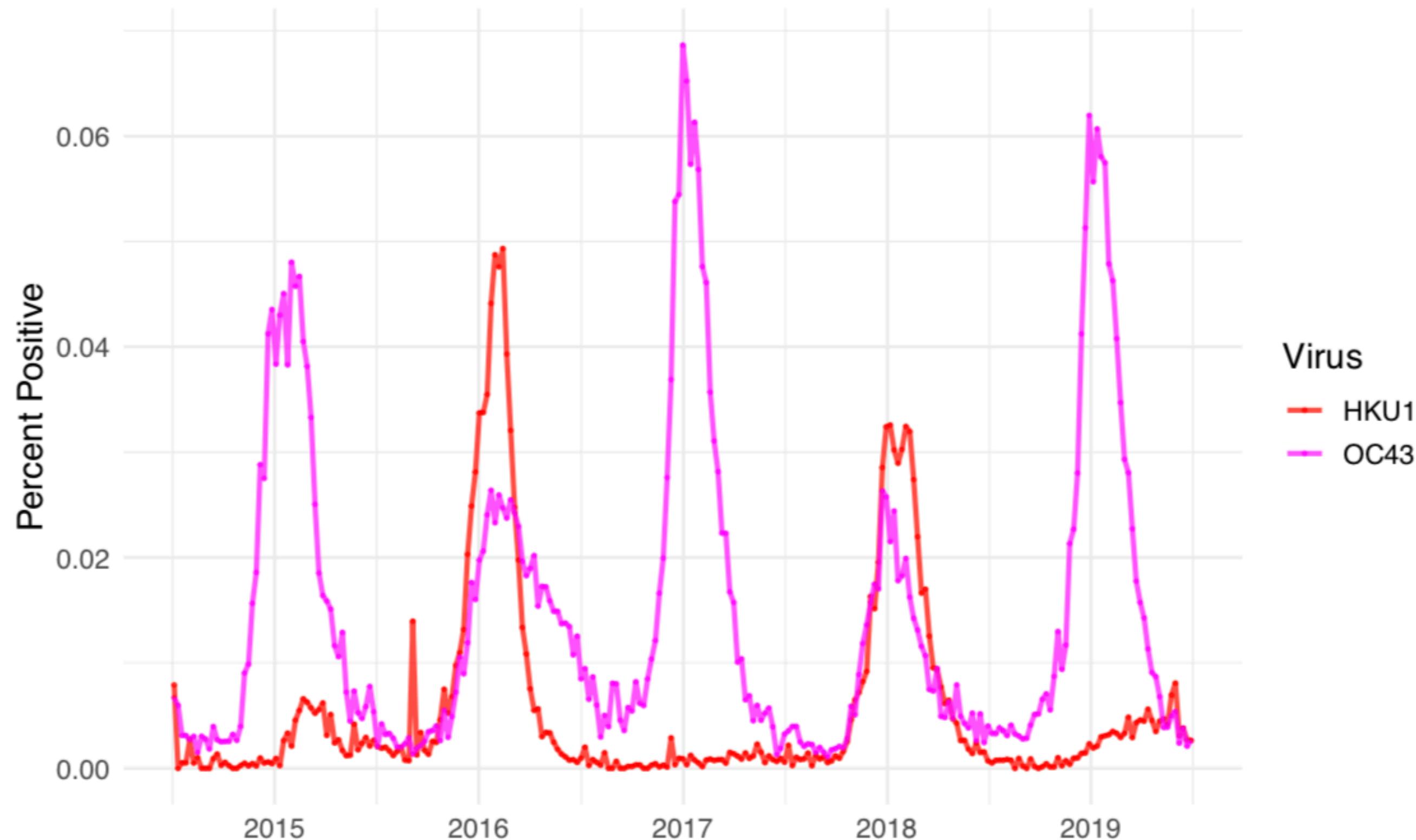


## Coronavirus

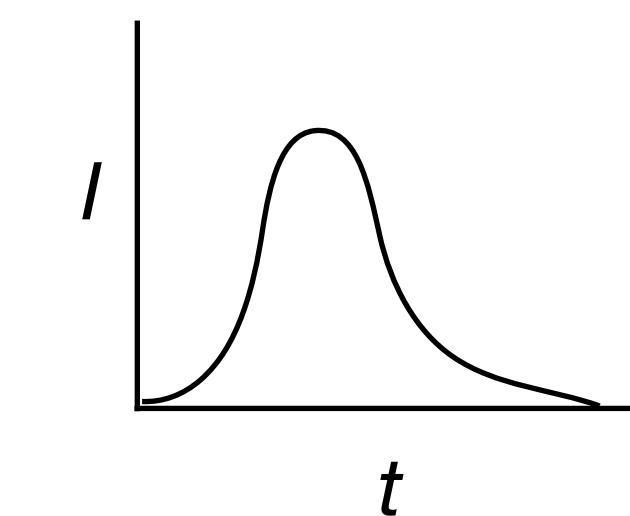
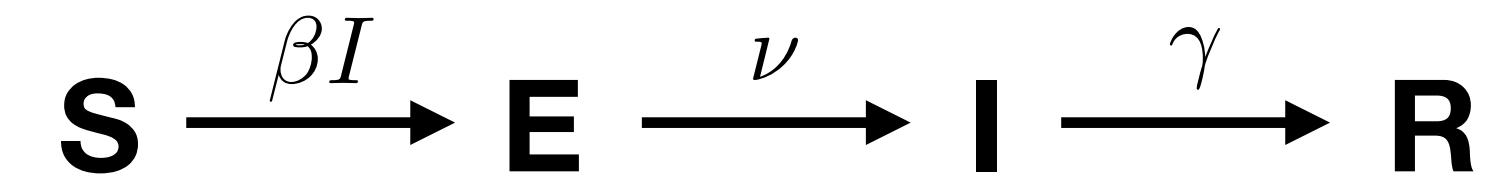
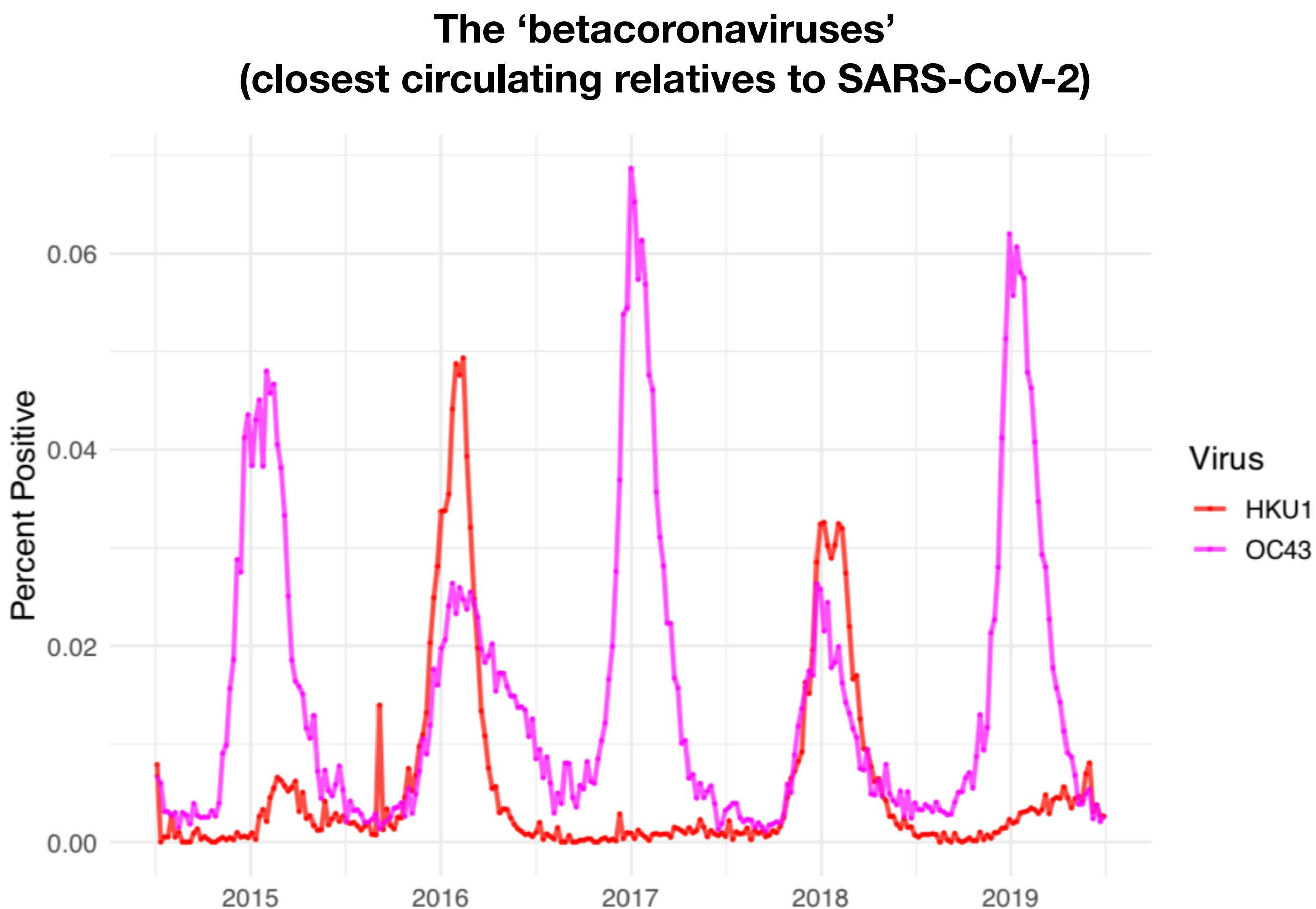


# Filling in gaps

The ‘betacoronaviruses’  
(closest circulating relatives to SARS-CoV-2)



# Filling in gaps



$$\frac{dS}{dt} = -\beta IS$$

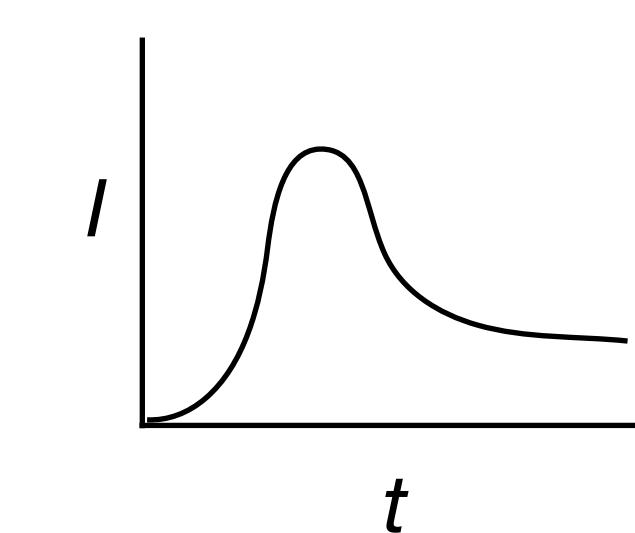
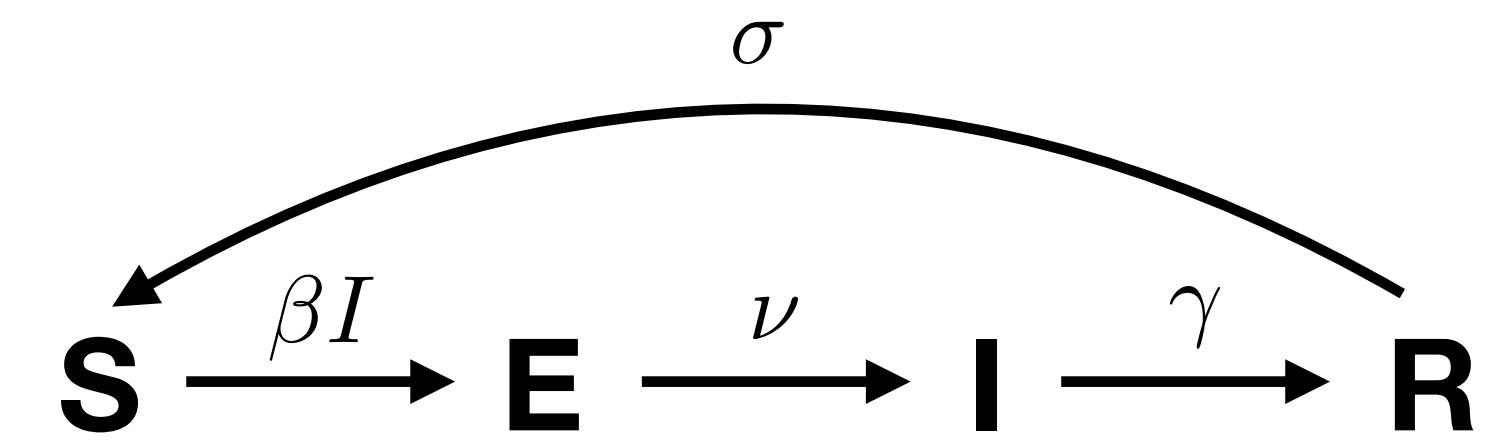
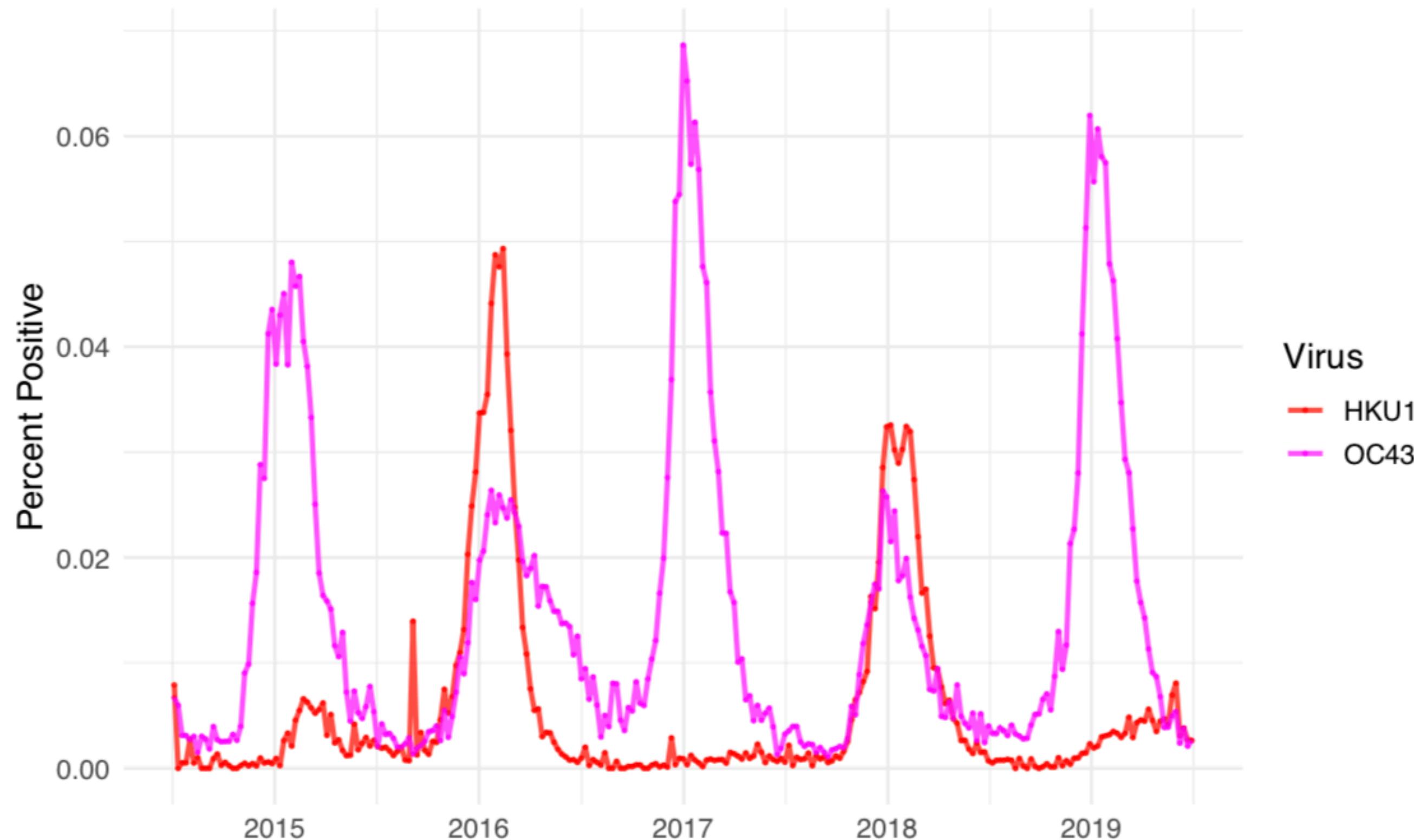
$$\frac{dE}{dt} = \beta IS - \nu E$$

$$\frac{dI}{dt} = \nu E - \gamma I$$

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

# Filling in gaps

The ‘betacoronaviruses’  
(closest circulating relatives to SARS-CoV-2)



$$\frac{dS}{dt} = -\beta IS + \sigma R$$

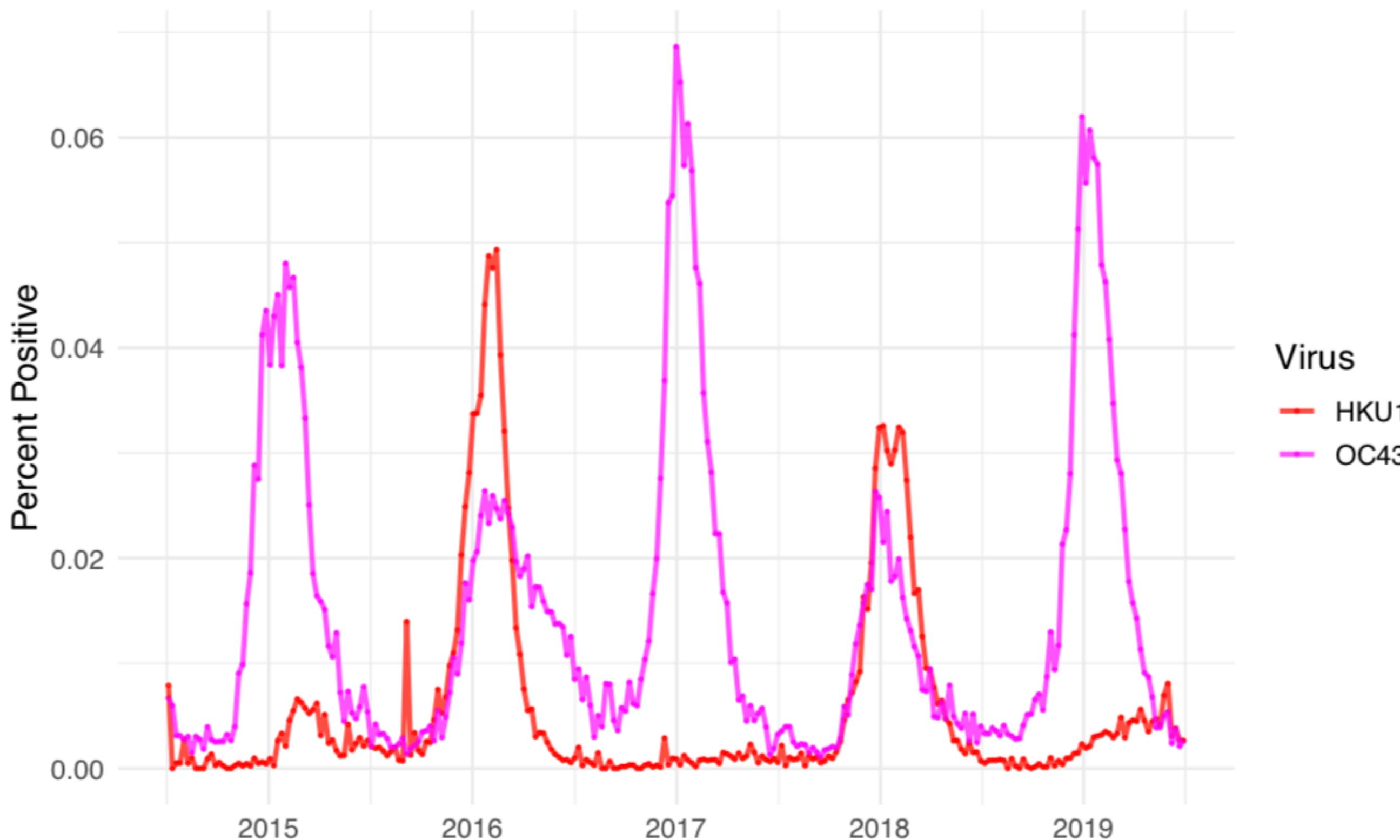
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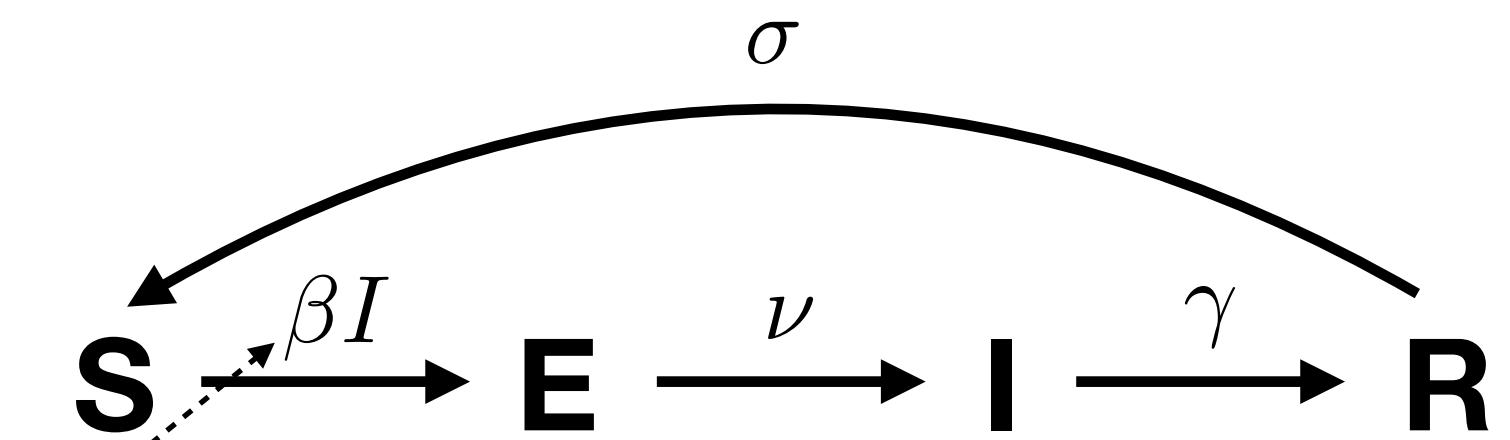
$$\frac{dR}{dt} = \gamma I - \sigma R$$

# Filling in gaps

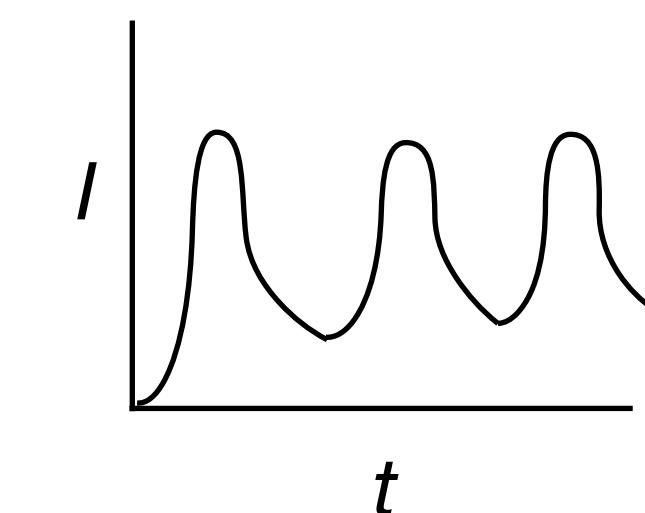
The ‘betacoronaviruses’  
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Virus  
— HKU1  
— OC43



Let  $\beta$  depend on  $t$

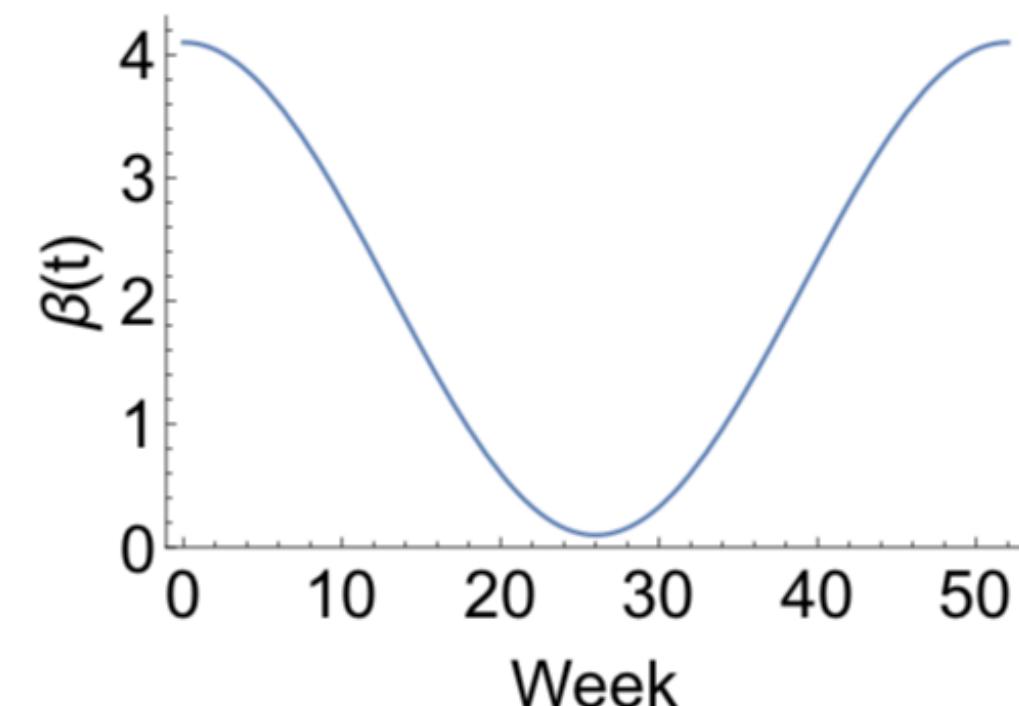


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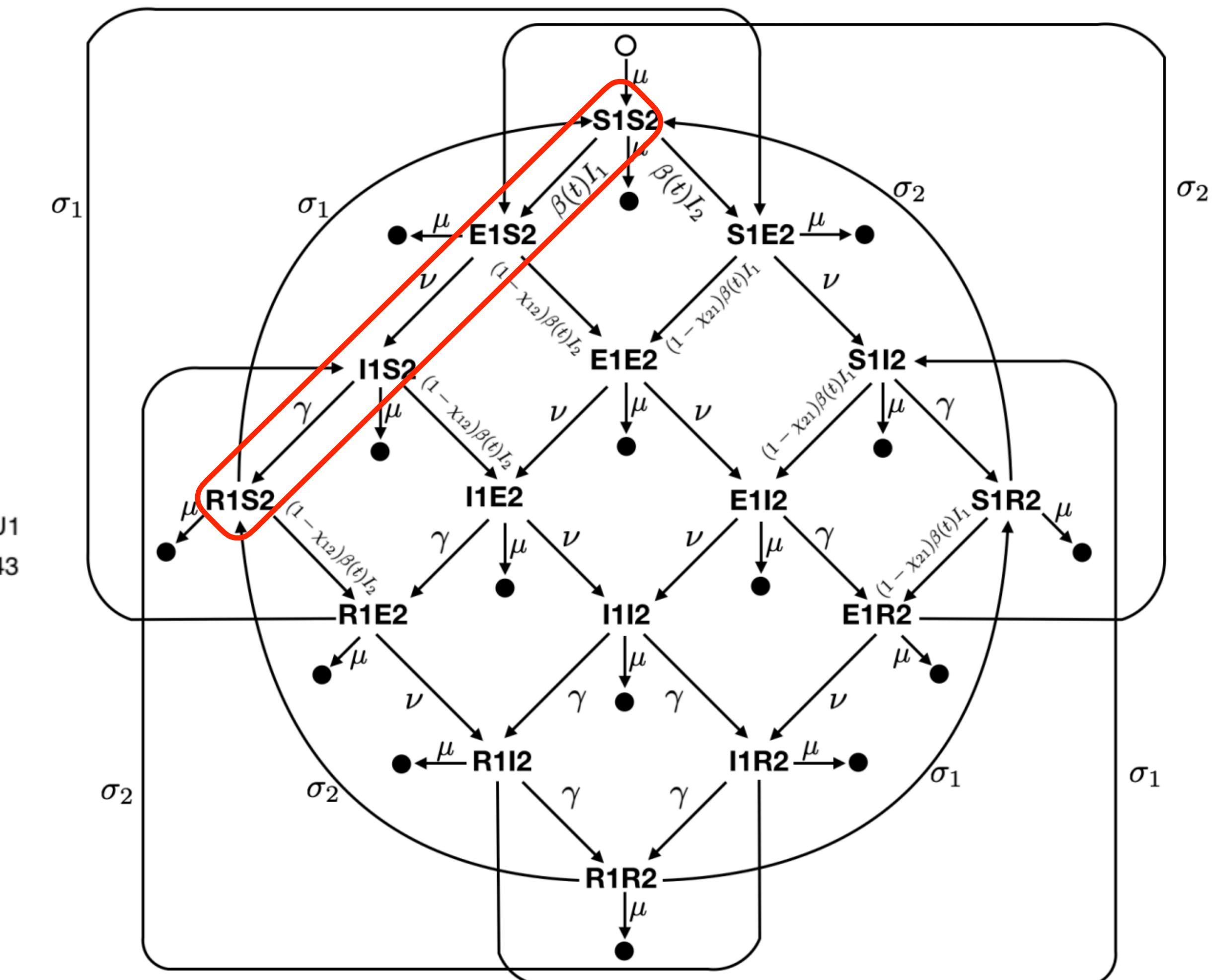
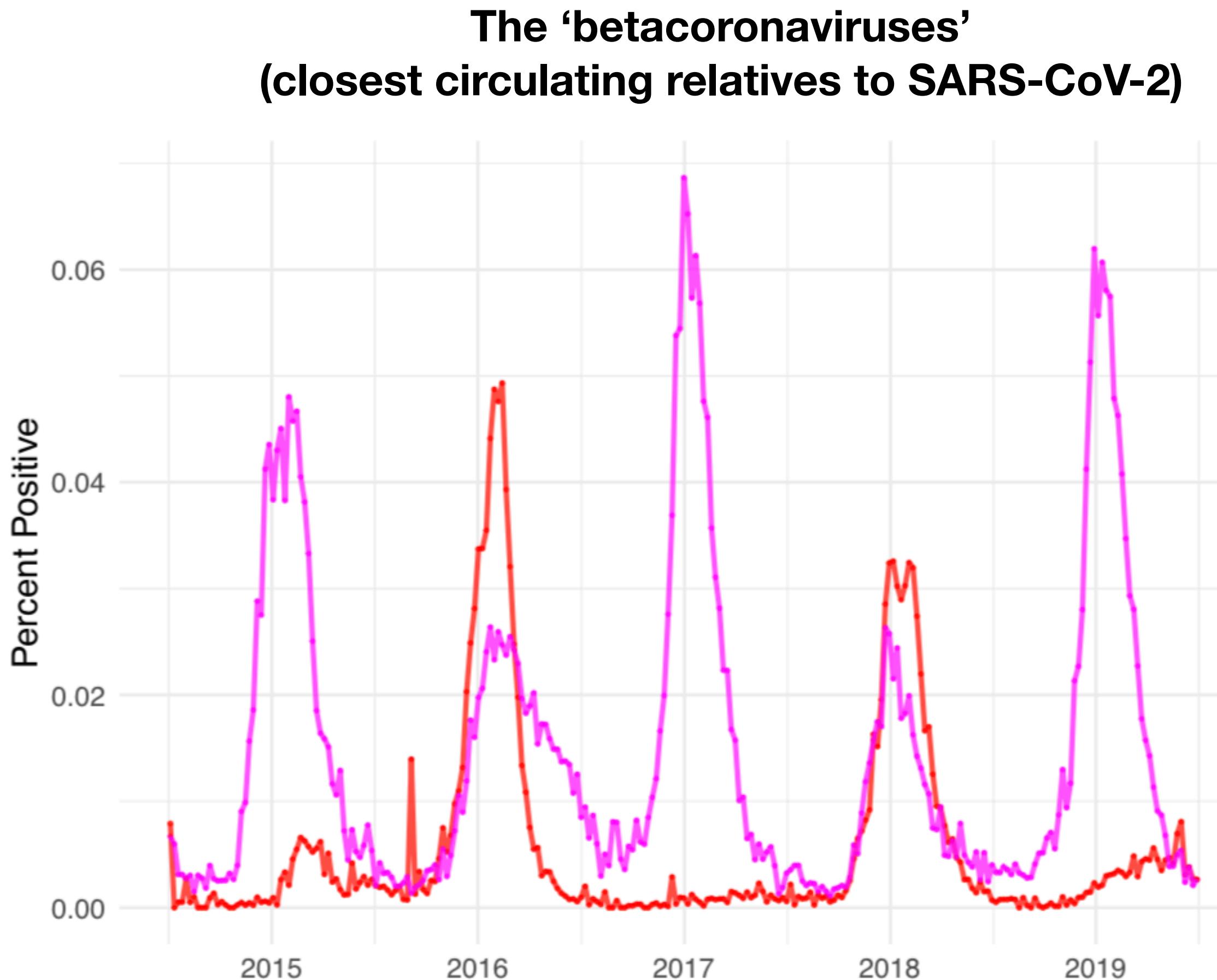
$$\frac{dI}{dt} = \nu E - \gamma I$$

$$\frac{dR}{dt} = \gamma I - \sigma R$$



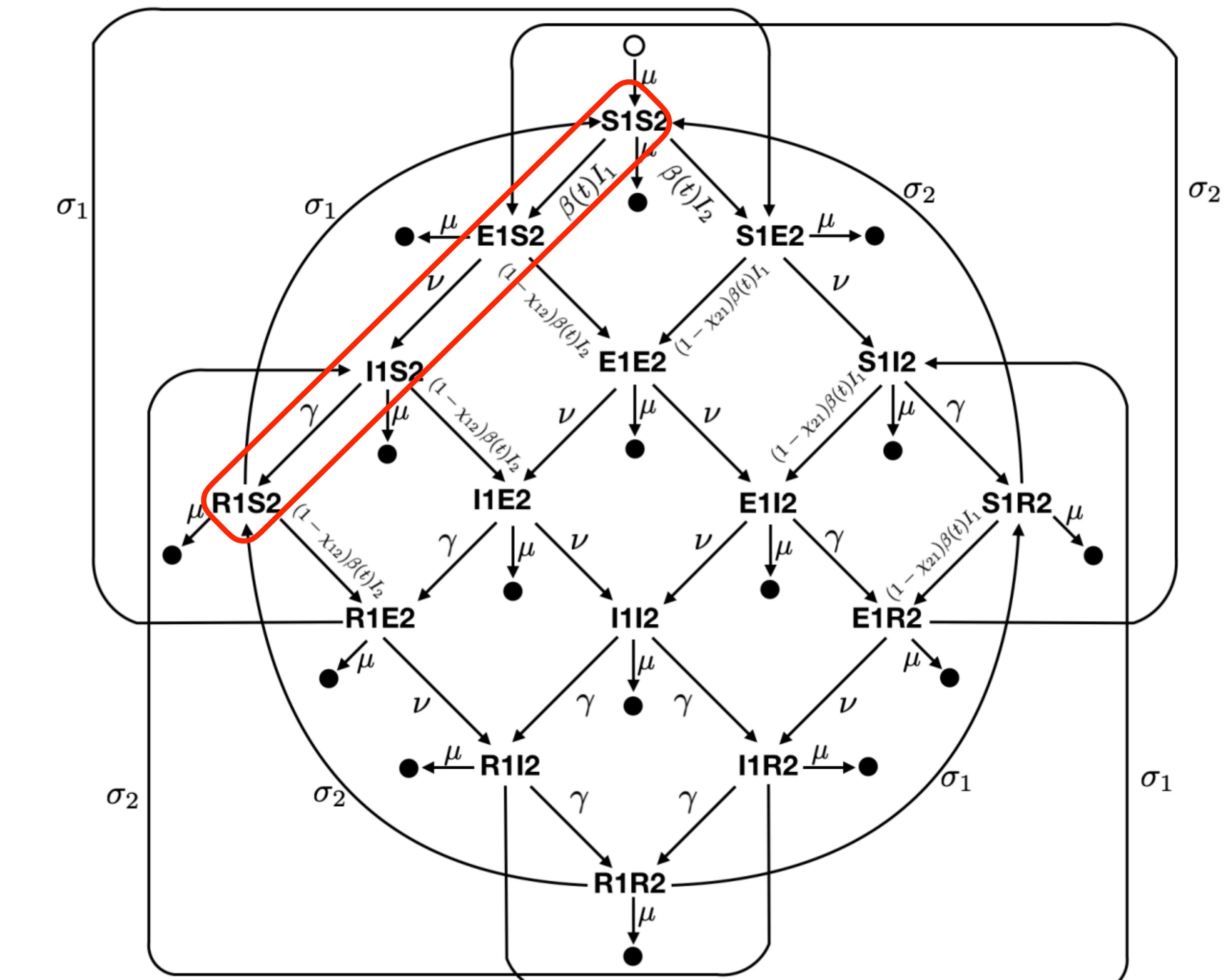
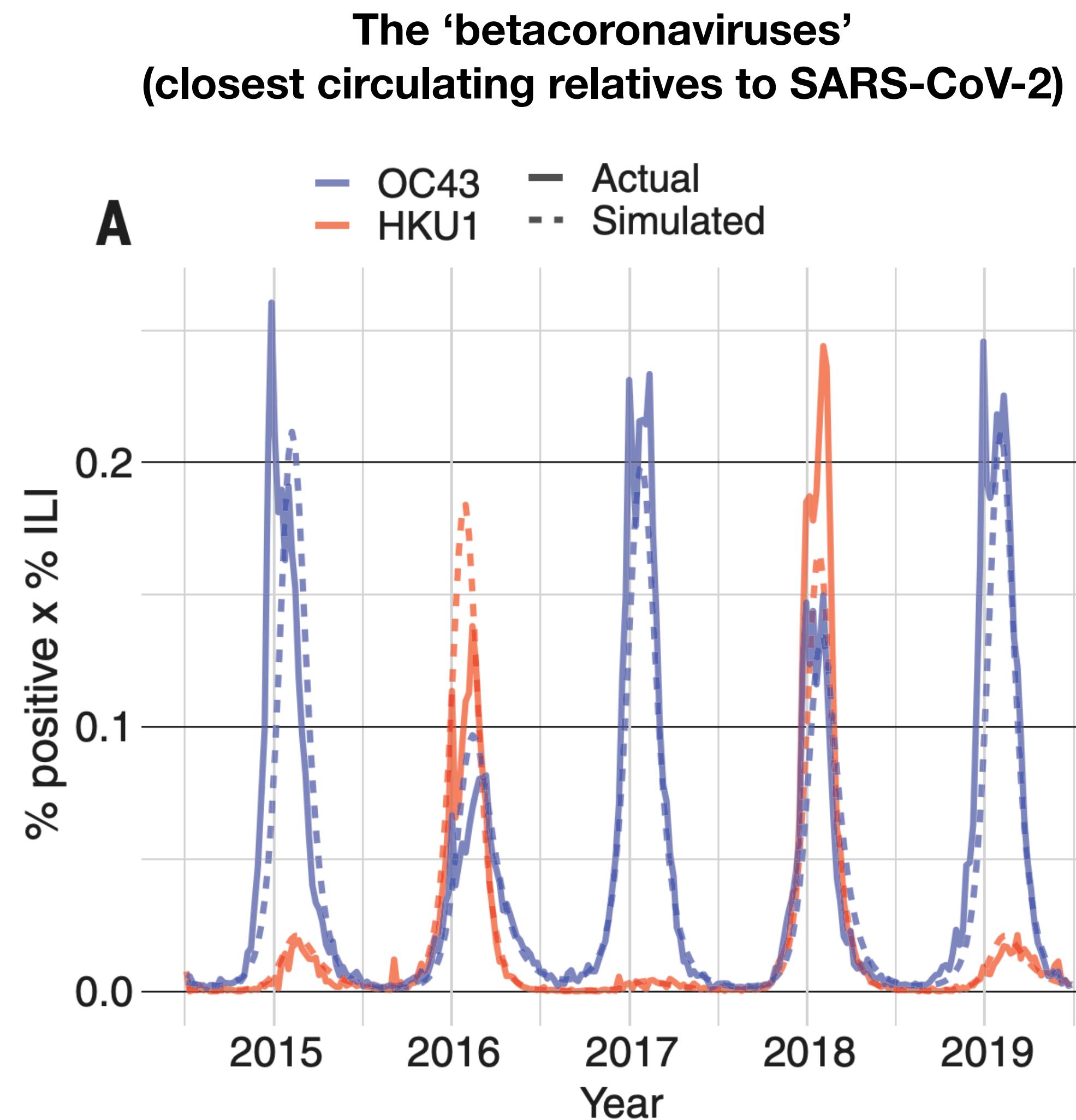
# Filling in gaps

A two-strain model



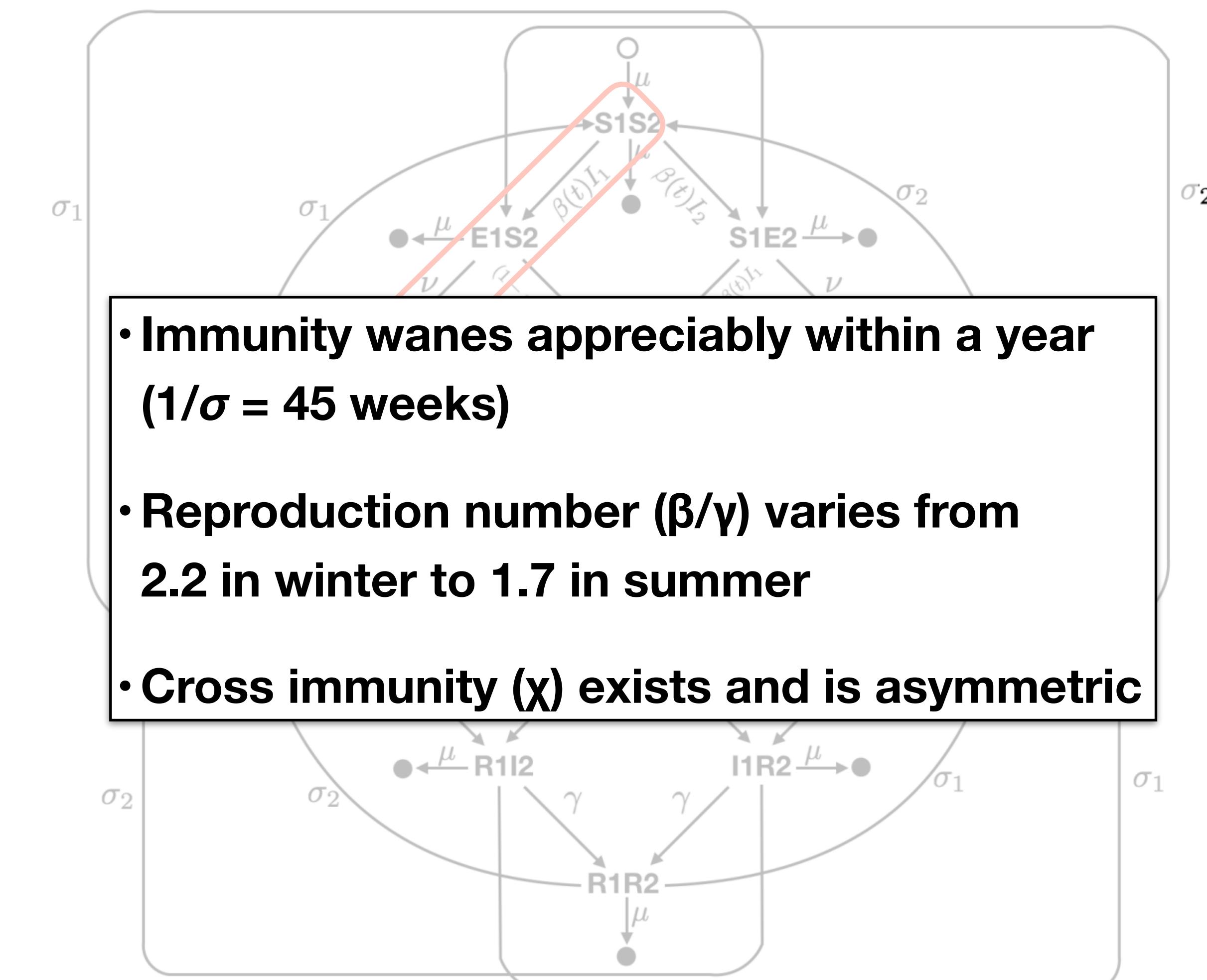
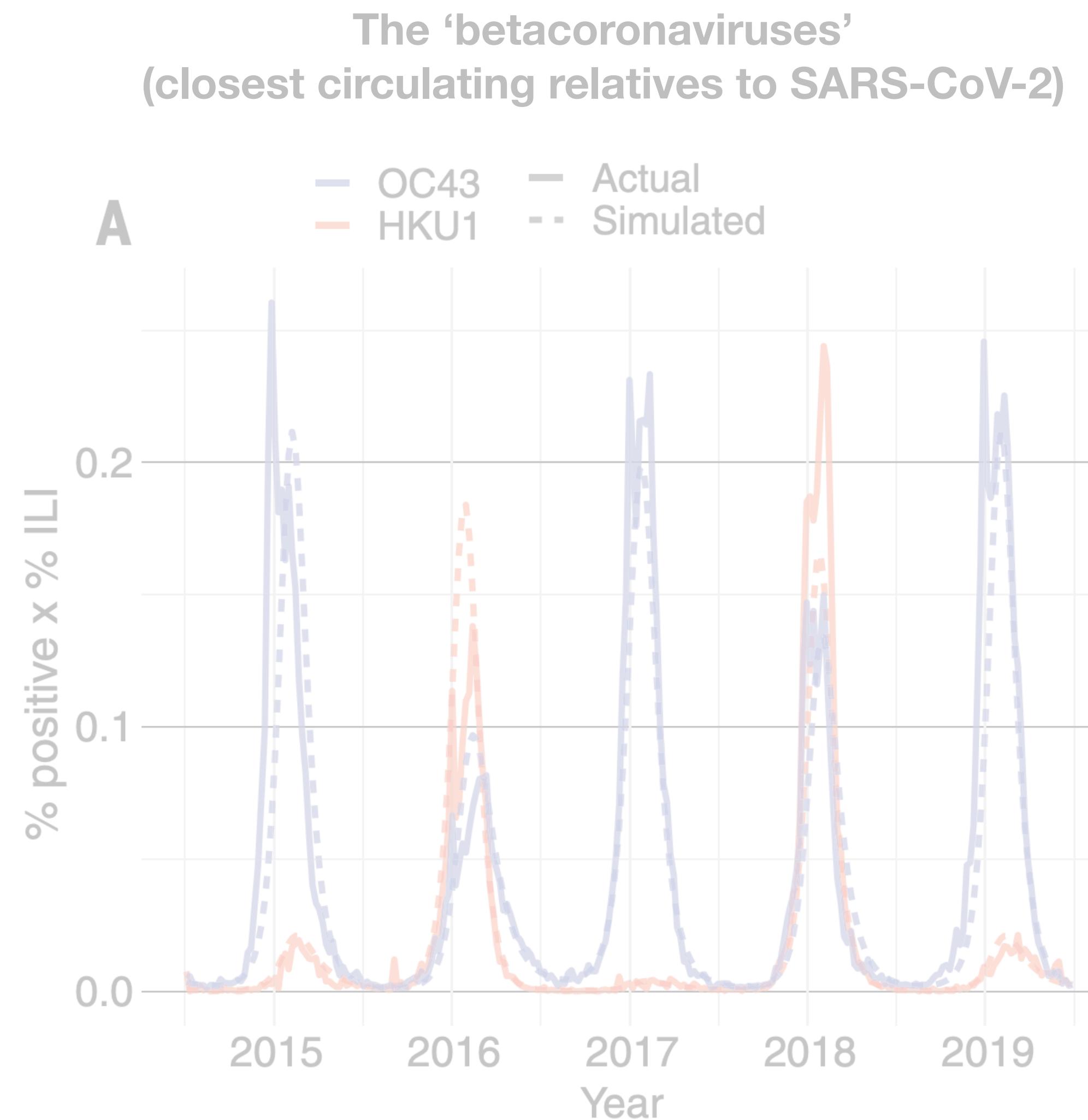
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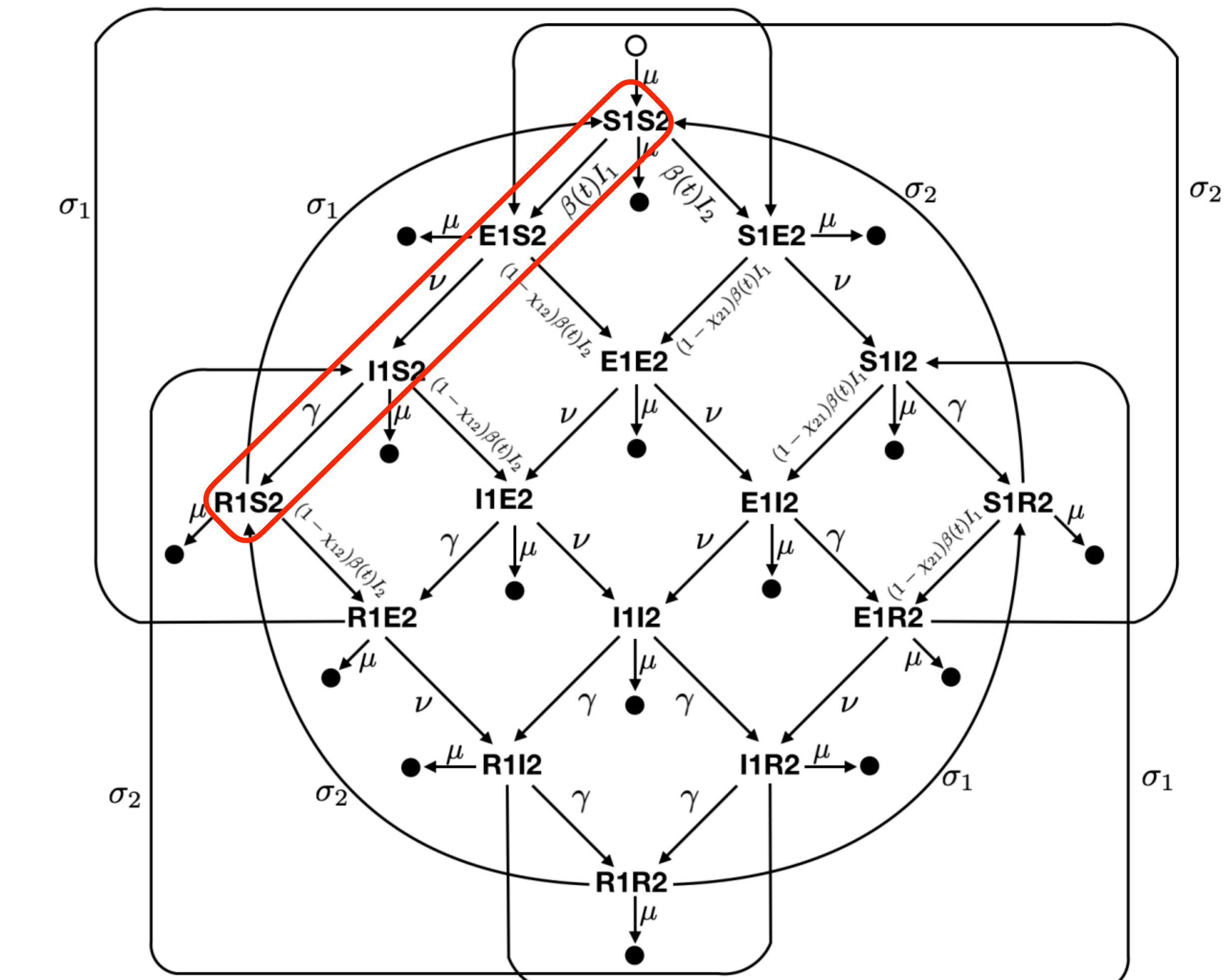
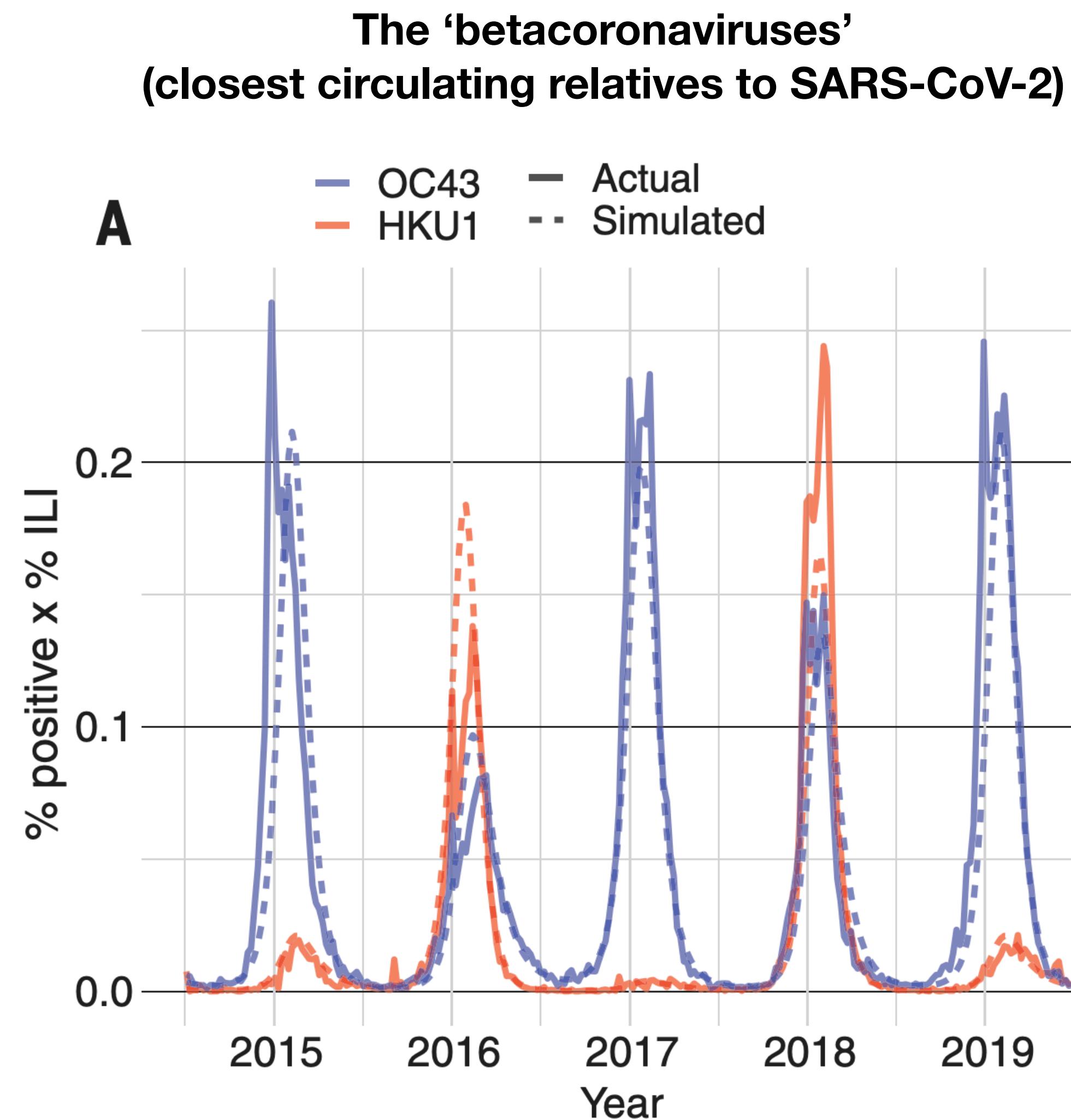
# Filling in gaps

A two-strain model



# Filling in gaps

A two-strain model



Then incorporate a third strain...

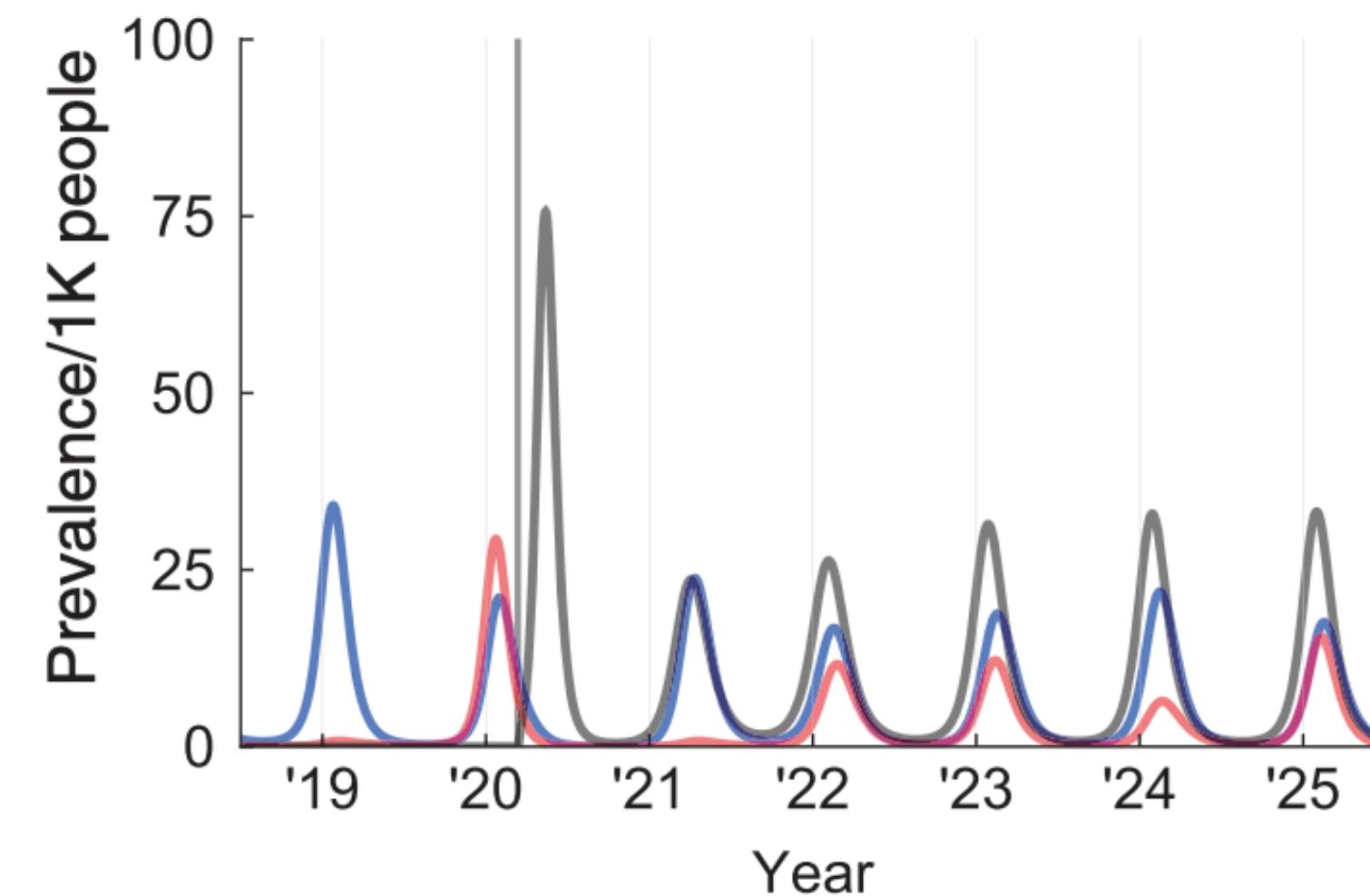
# Some projections

Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period

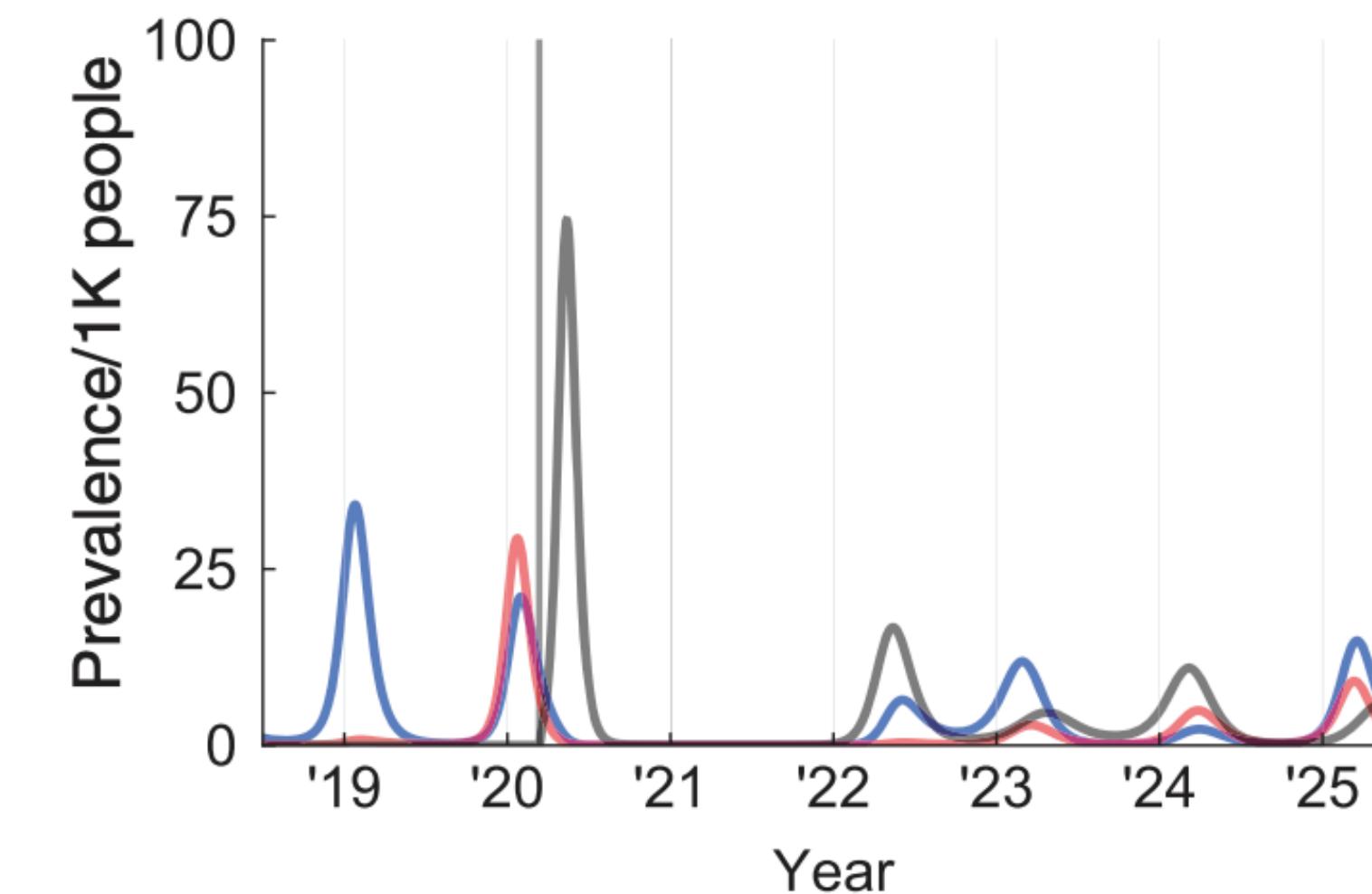
Science 22 May 2020;  
Vol. 368, Issue 6493, pp. 860-868  
DOI: 10.1126/science.abb5793

Stephen M. Kissler<sup>1,\*</sup>, Christine Tedijanto<sup>2,\*</sup>, Edward Goldstein<sup>2</sup>, Yonatan H. Grad<sup>1,†,‡</sup>, Marc Lipsitch<sup>2,†,‡</sup>

## Short (~45-month) immunity

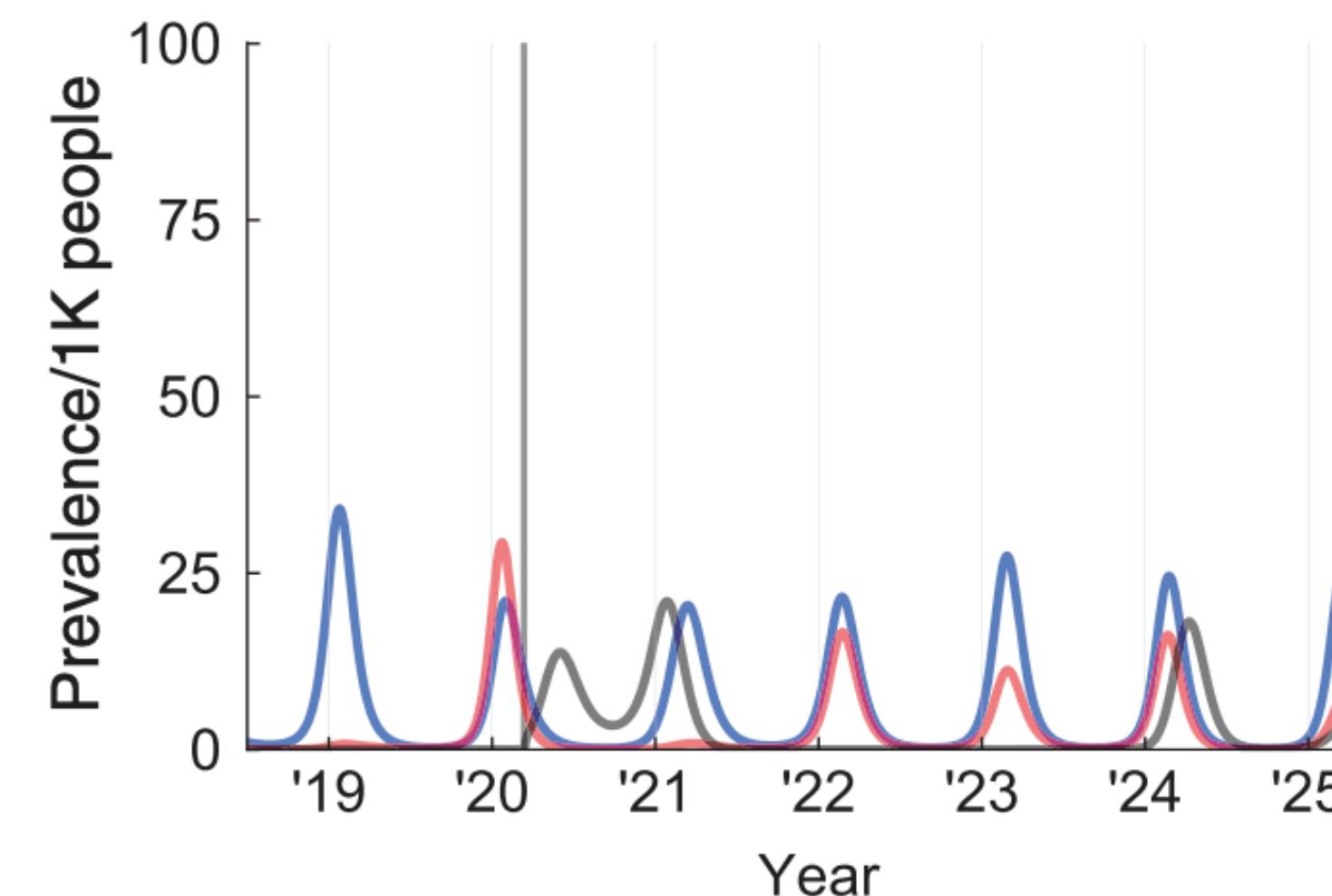


## Long (~2-year) immunity

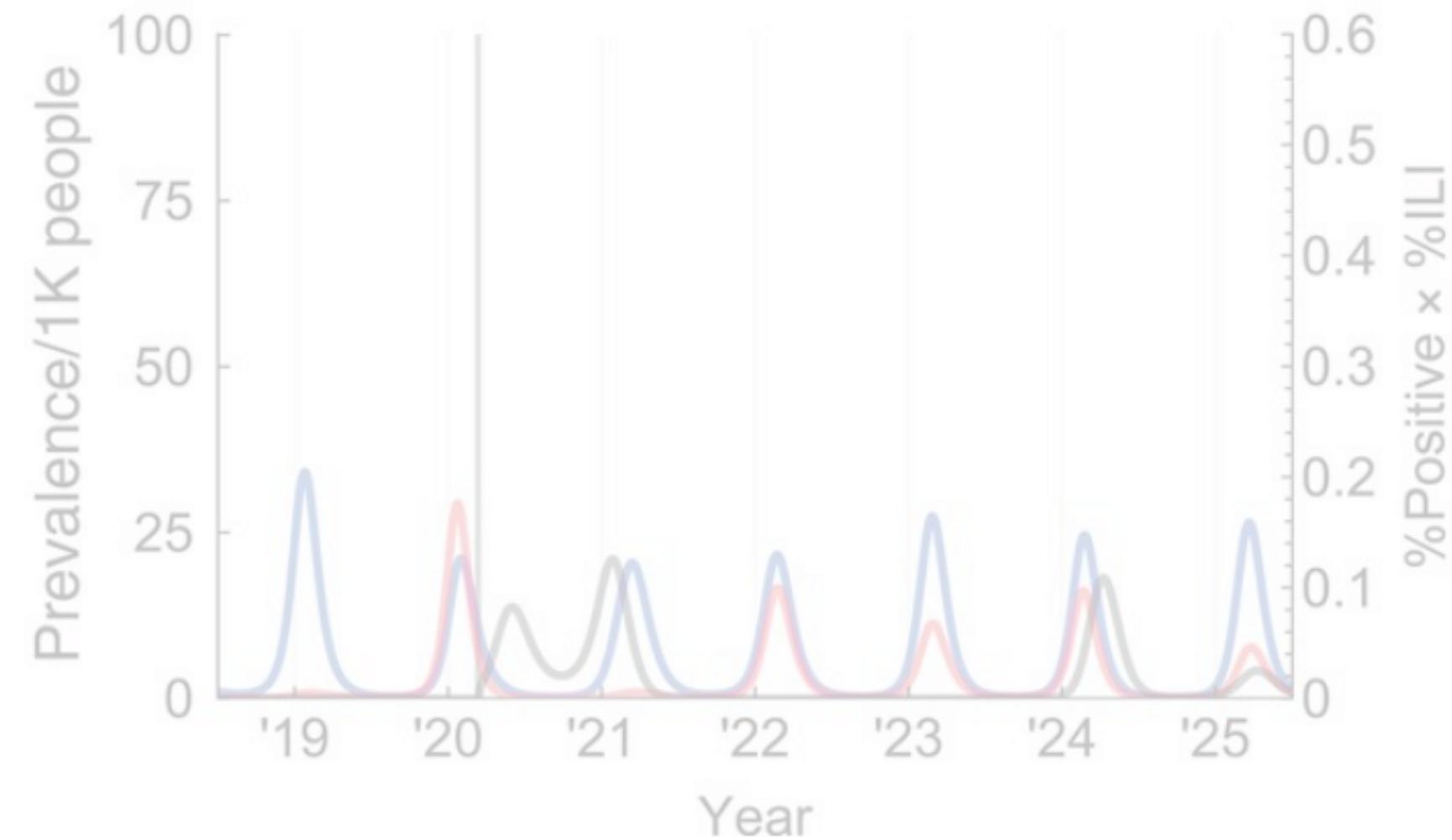


OC43  
HKU1  
SARS-CoV-2

## Cross-immunity



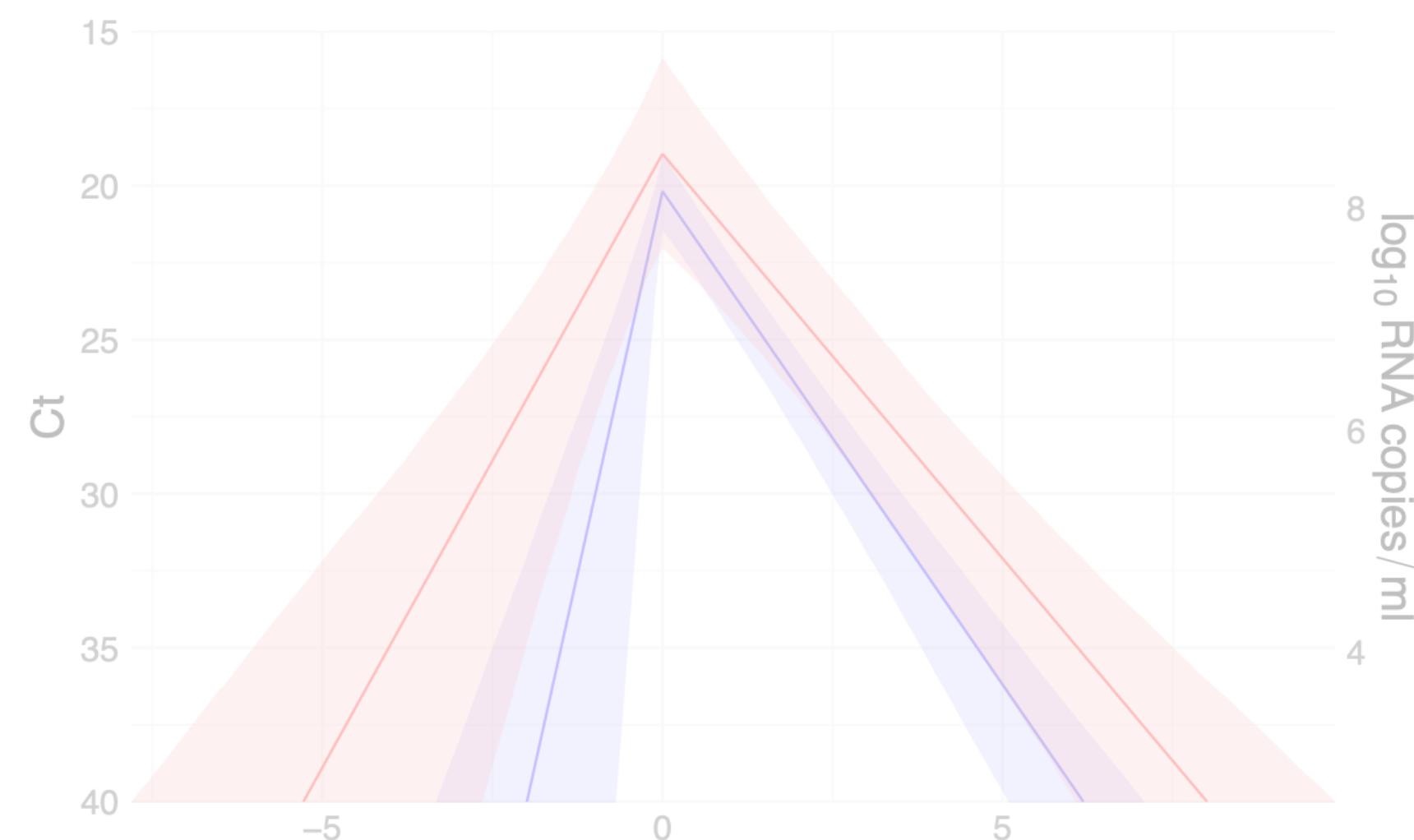
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# Disparities in COVID-19 cases, hospitalizations, and deaths in NYC

Research Letter

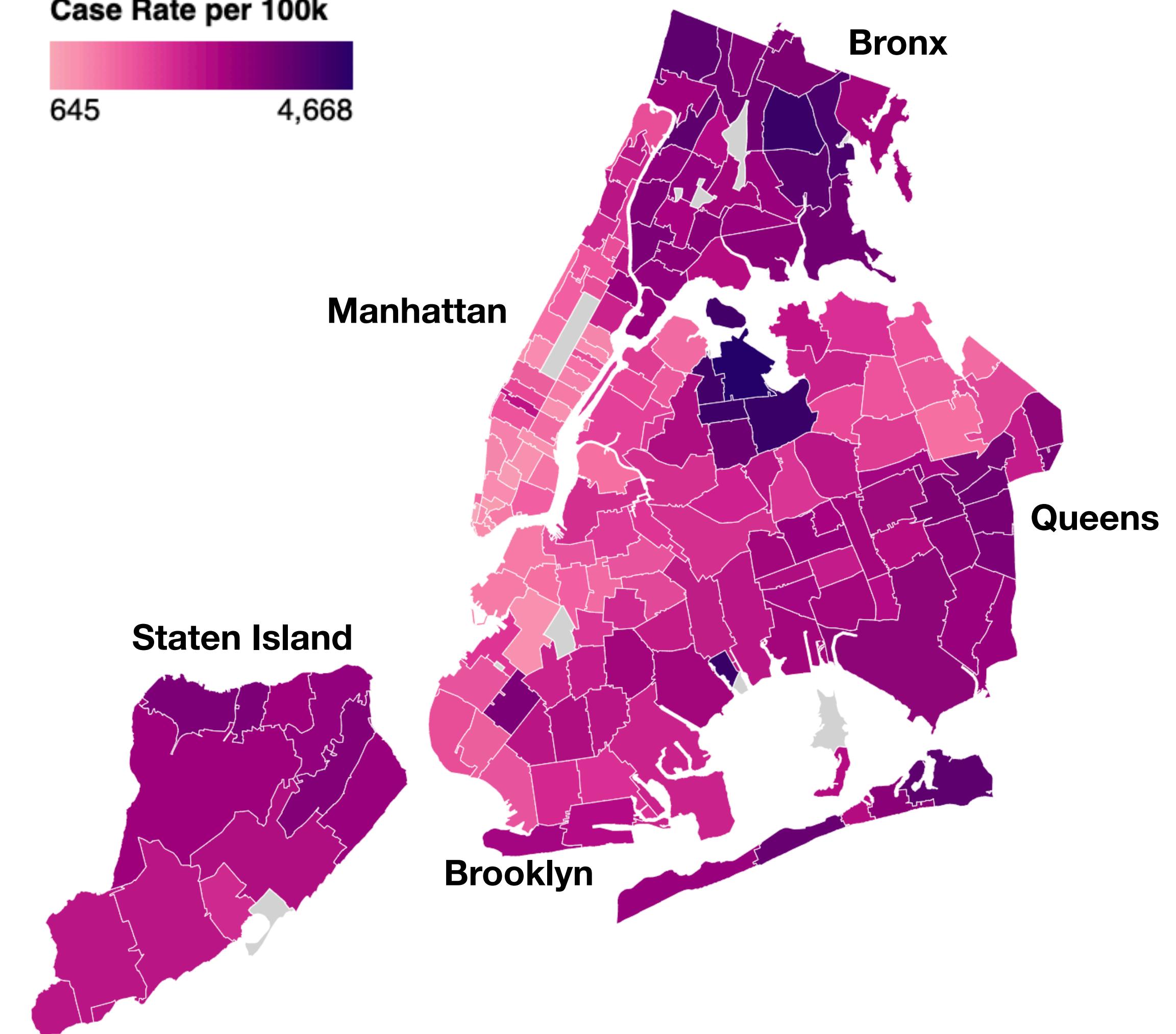
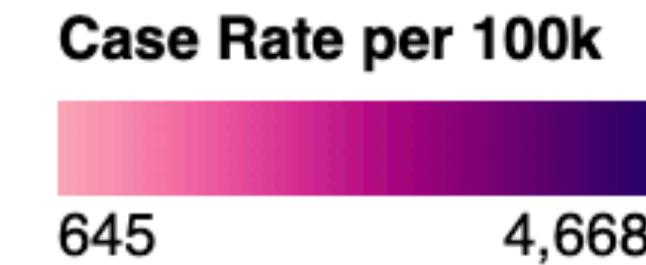
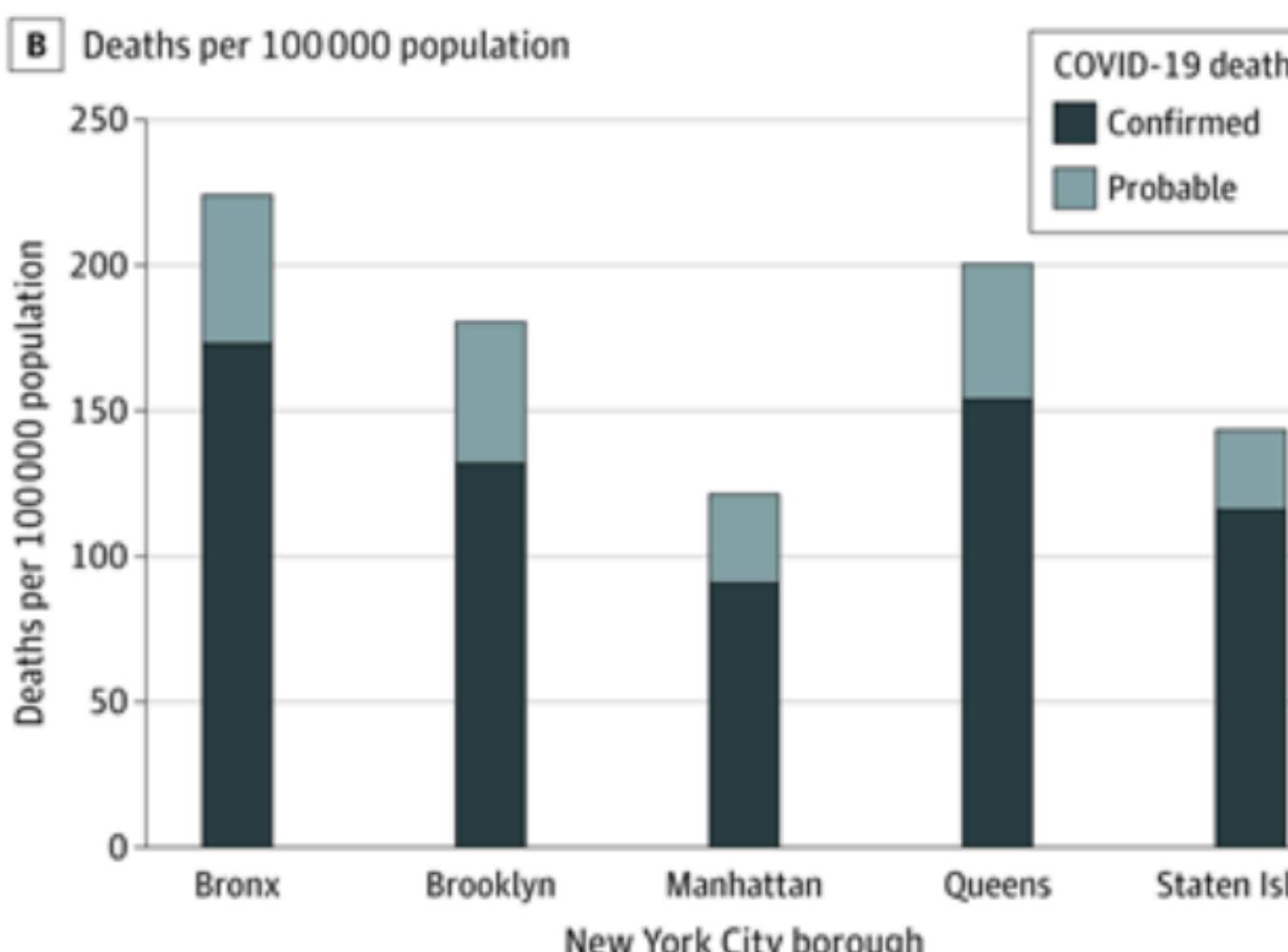
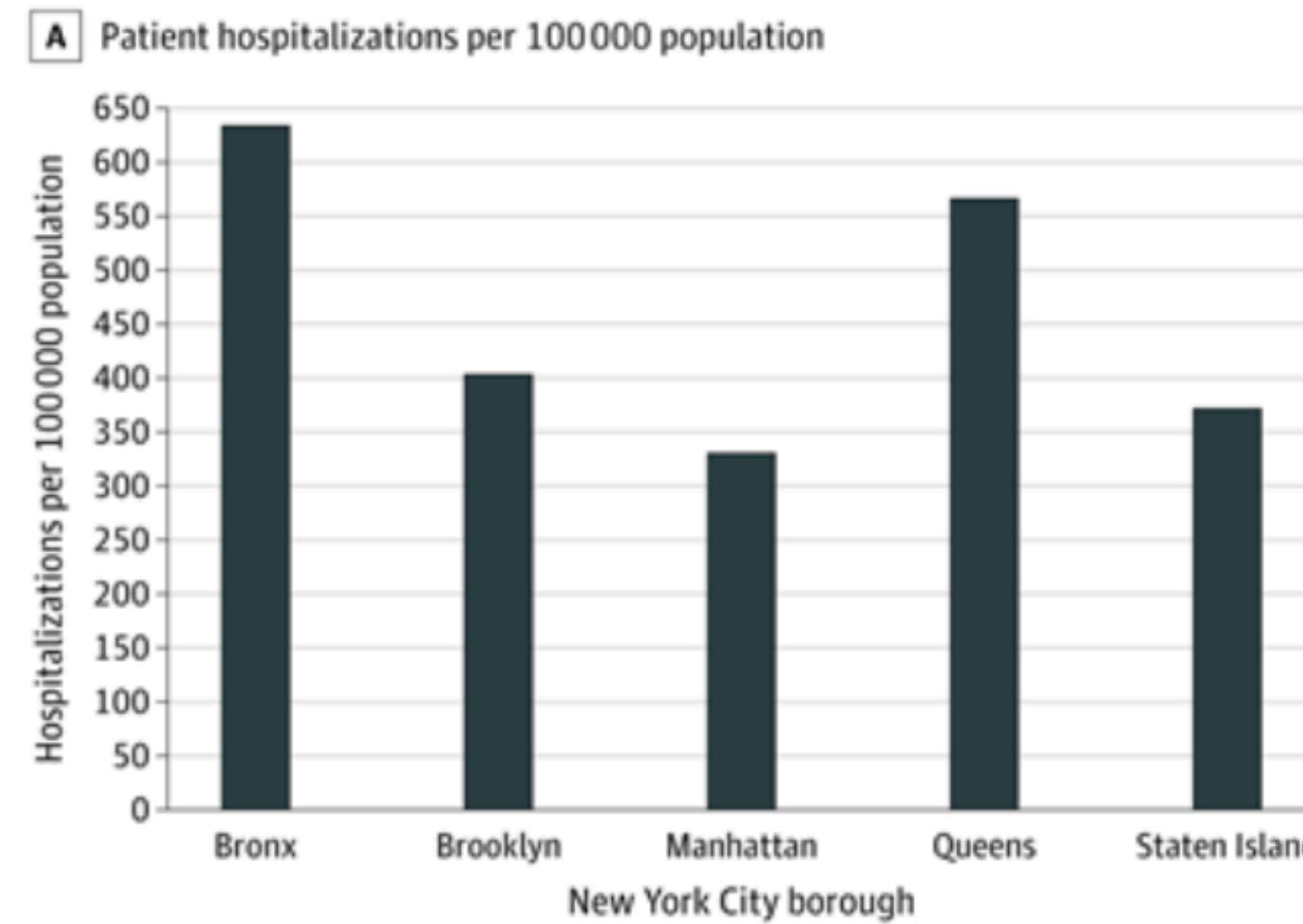
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April 29, 2020

## Variation in COVID-19 Hospitalizations and Deaths Across New York City Boroughs

Rishi K. Wadhera, MD, MPP, MPhil<sup>1</sup>; Priya Wadhera, MD, MS<sup>2</sup>; Prakriti Gaba, MD<sup>3</sup>; et al



NYC  
Health

<https://www1.nyc.gov/site/doh/covid/covid-19-data.page>

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Research Letter

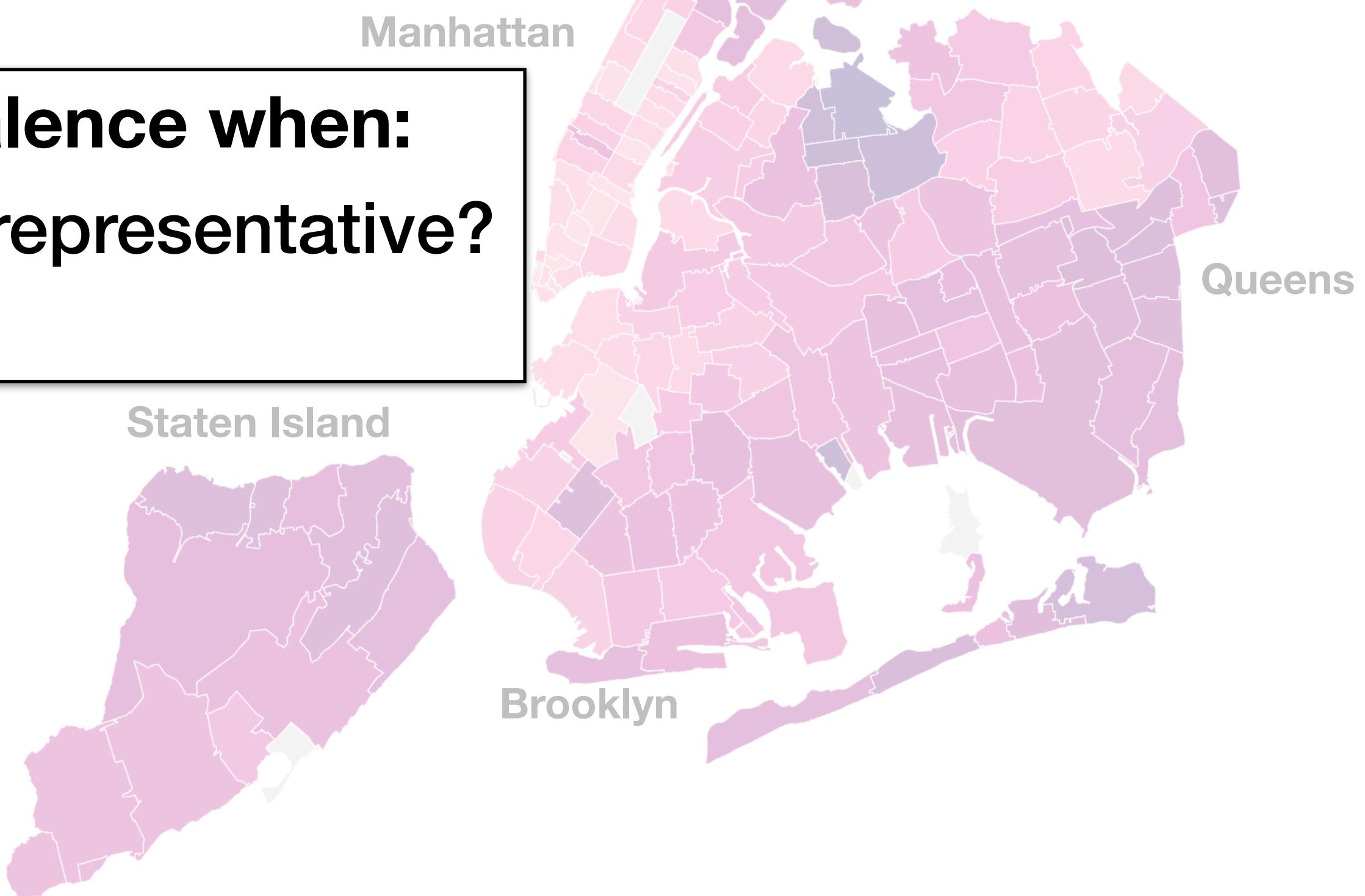
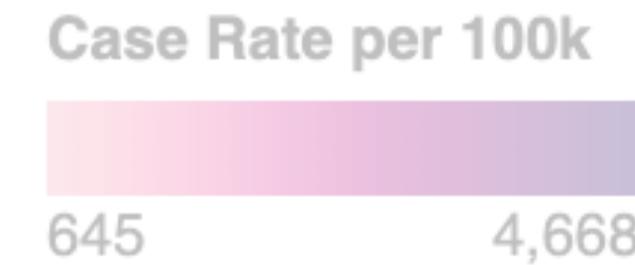
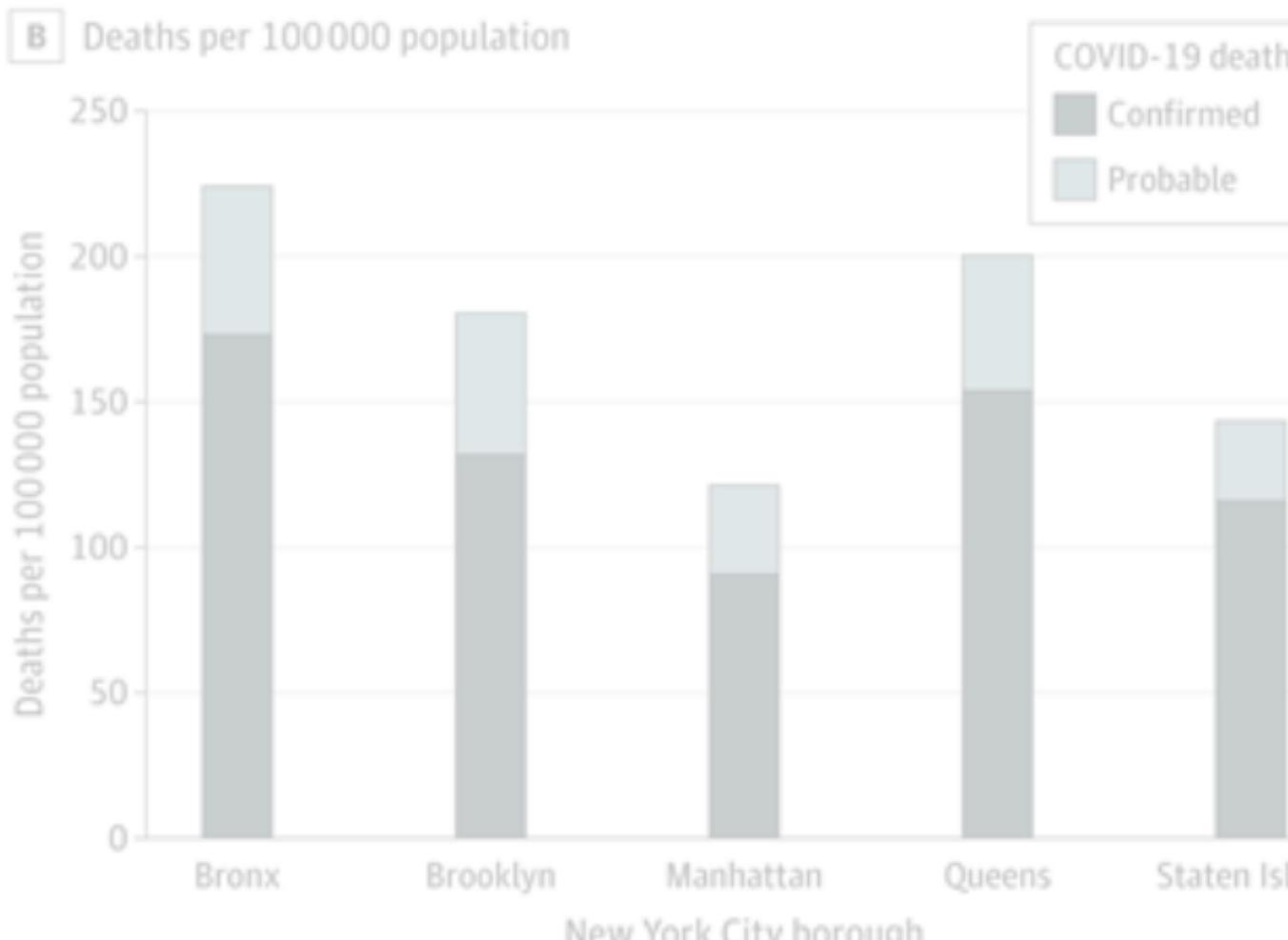
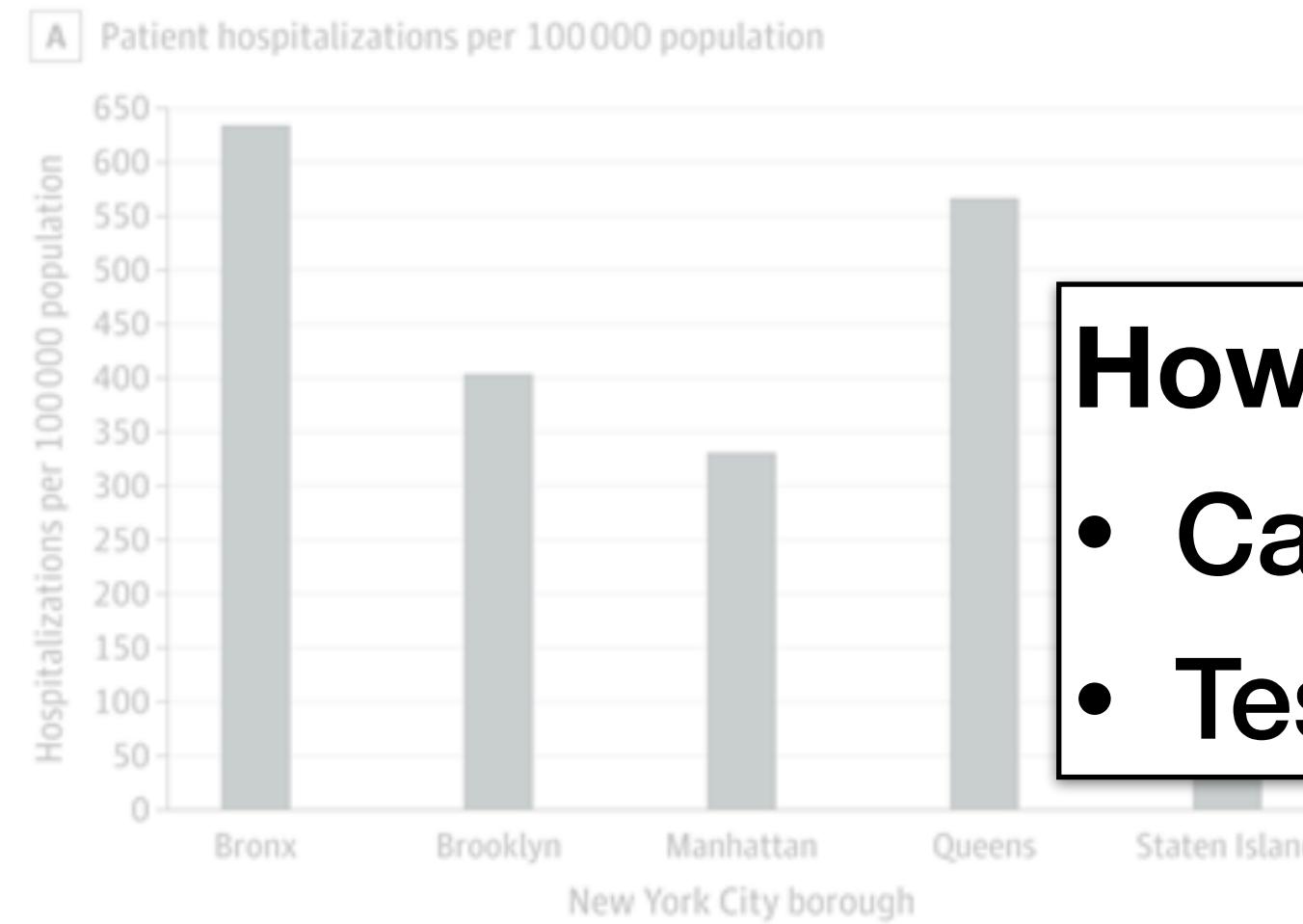
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# Universal screening of women hospitalized for delivery



The NEW ENGLAND  
JOURNAL of MEDICINE

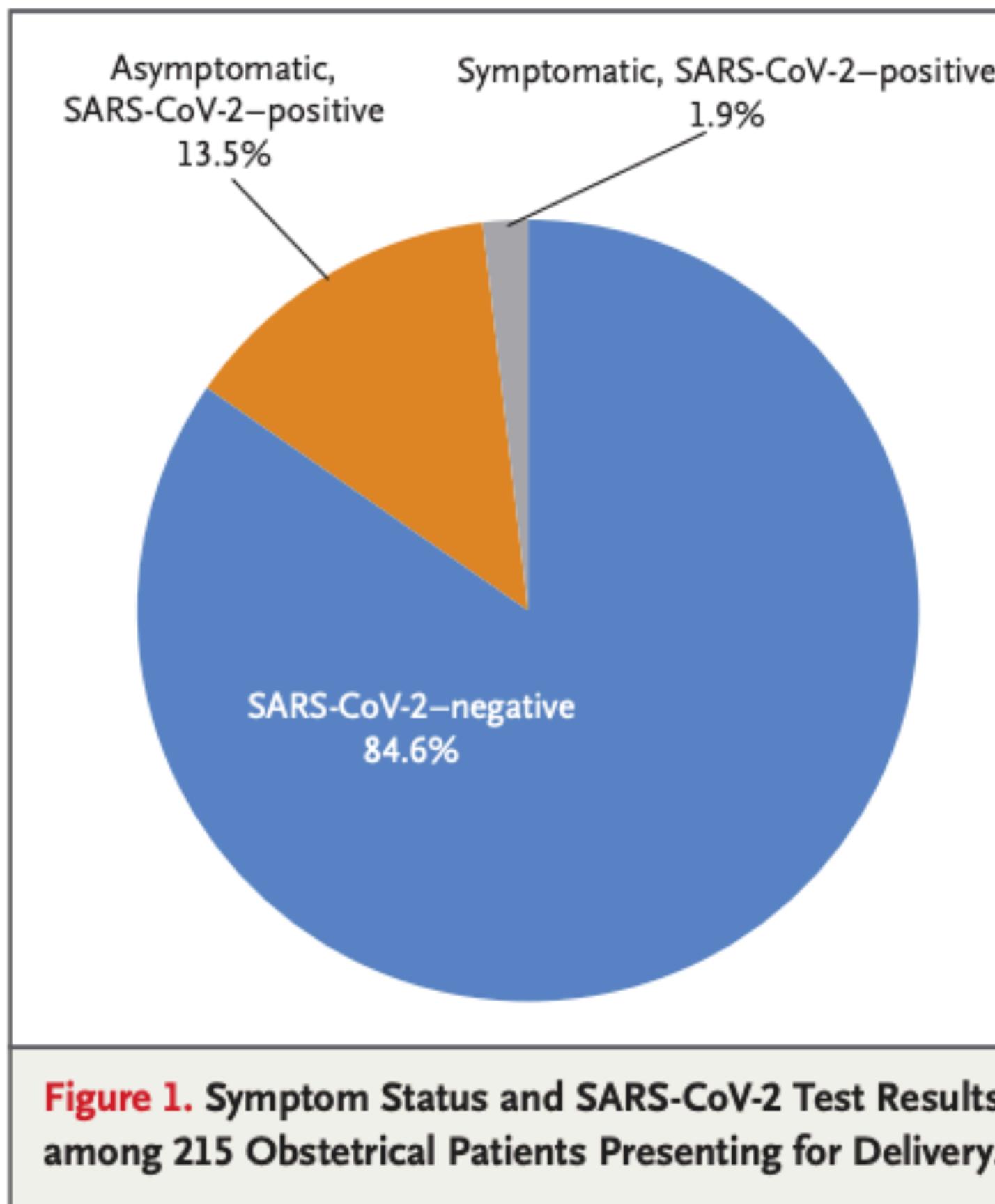
CORRESPONDENCE

May 28, 2020

N Engl J Med 2020; 382:2163-2164

DOI: 10.1056/NEJMc2009316

## Universal Screening for SARS-CoV-2 in Women Admitted for Delivery



Desmond Sutton, M.D.  
Karin Fuchs, M.D., M.H.A.  
Mary D'Alton, M.D.  
Dena Goffman, M.D.

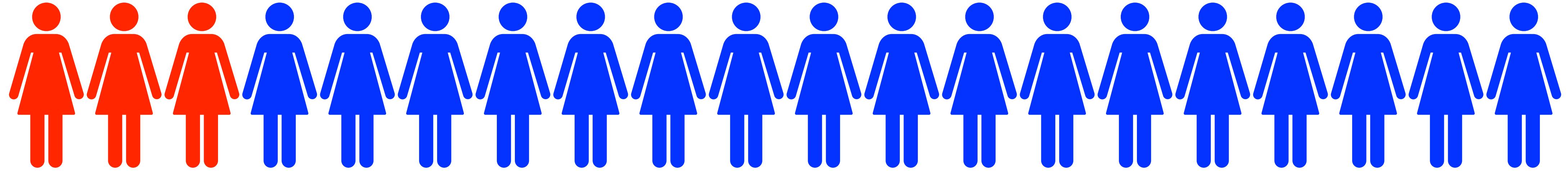
Columbia University Irving Medical Center  
New York, NY  
dg2018@cumc.columbia.edu

# Estimating population prevalence with an imperfect test

Estimating SARS-CoV-2 seroprevalence and epidemiological parameters with uncertainty from serological surveys



Daniel B Larremore , Bailey K Fosdick, Kate M Bubar, Sam Zhang,  
Stephen M Kissler, C Jessica E Metcalf, Caroline Buckee, Yonatan H Grad

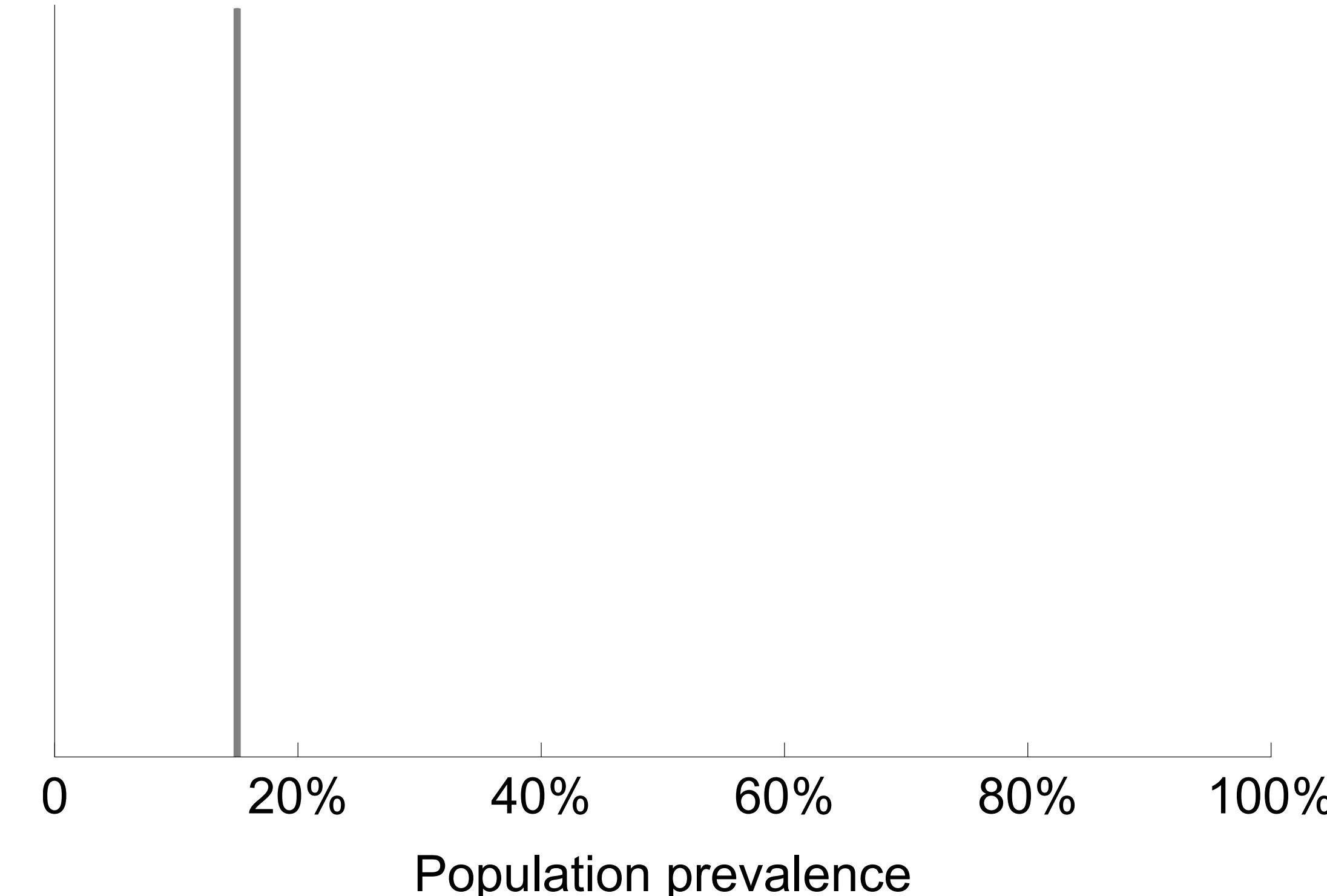
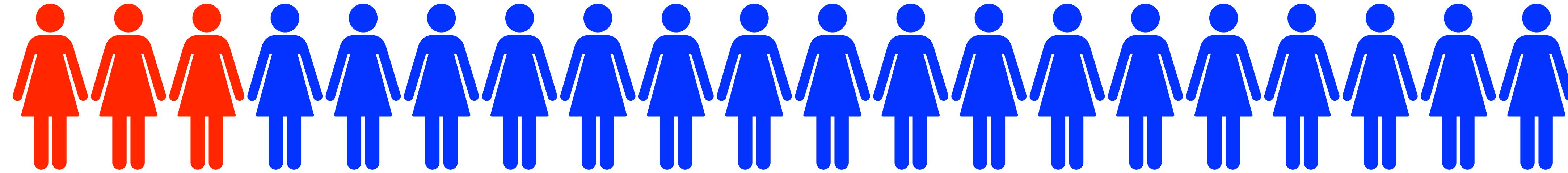


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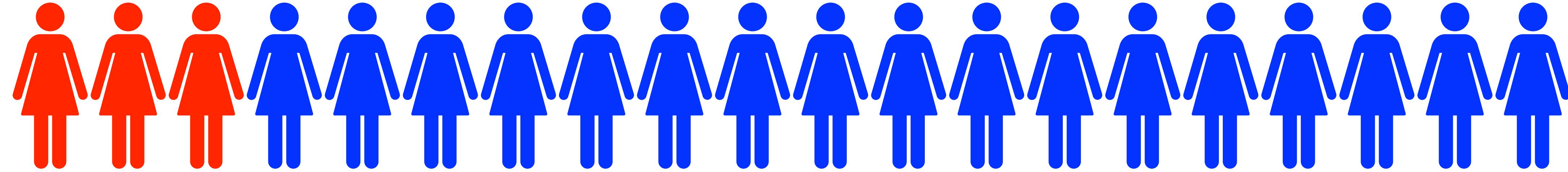
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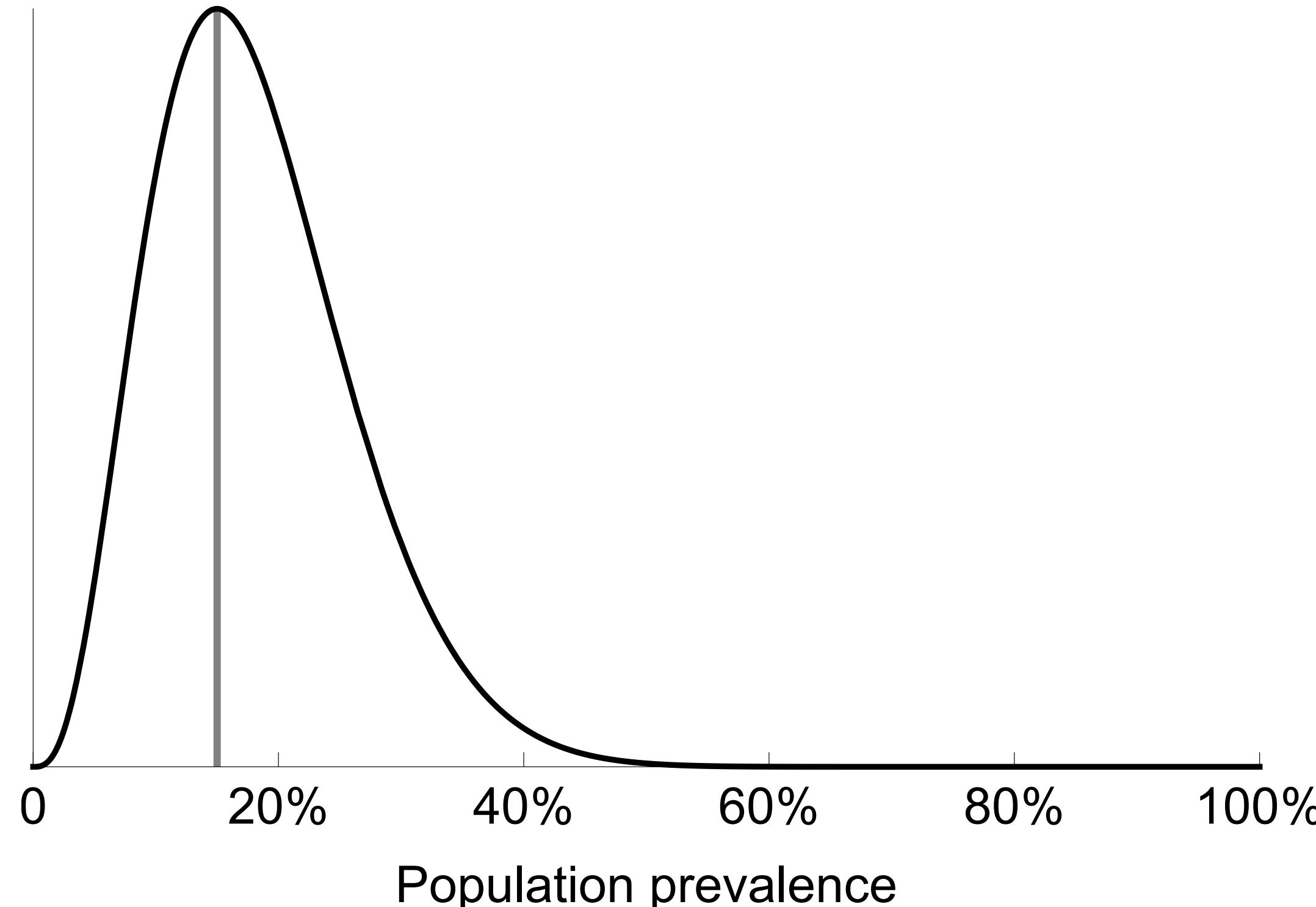


f t e s

Daniel B Larremore , Bailey K Fosdick, Kate M Bubar, Sam Zhang,  
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$$\Pr(n_+ \mid \theta) = \binom{n}{n_+} \theta^{n_+} (1 - \theta)^{n - n_+}$$



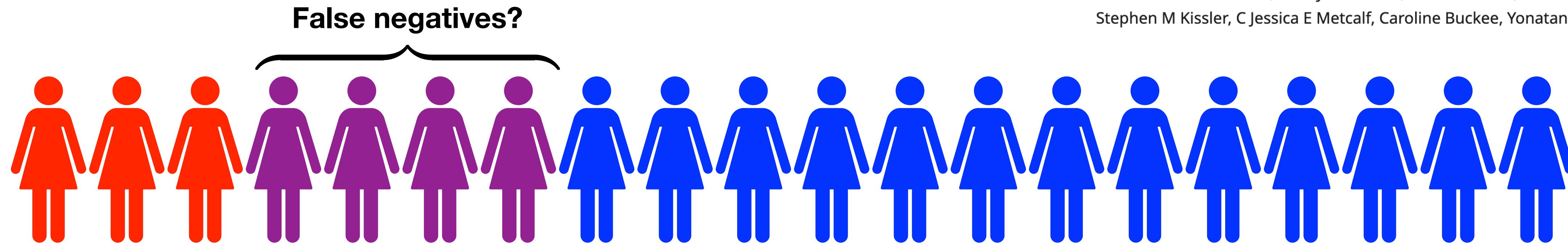
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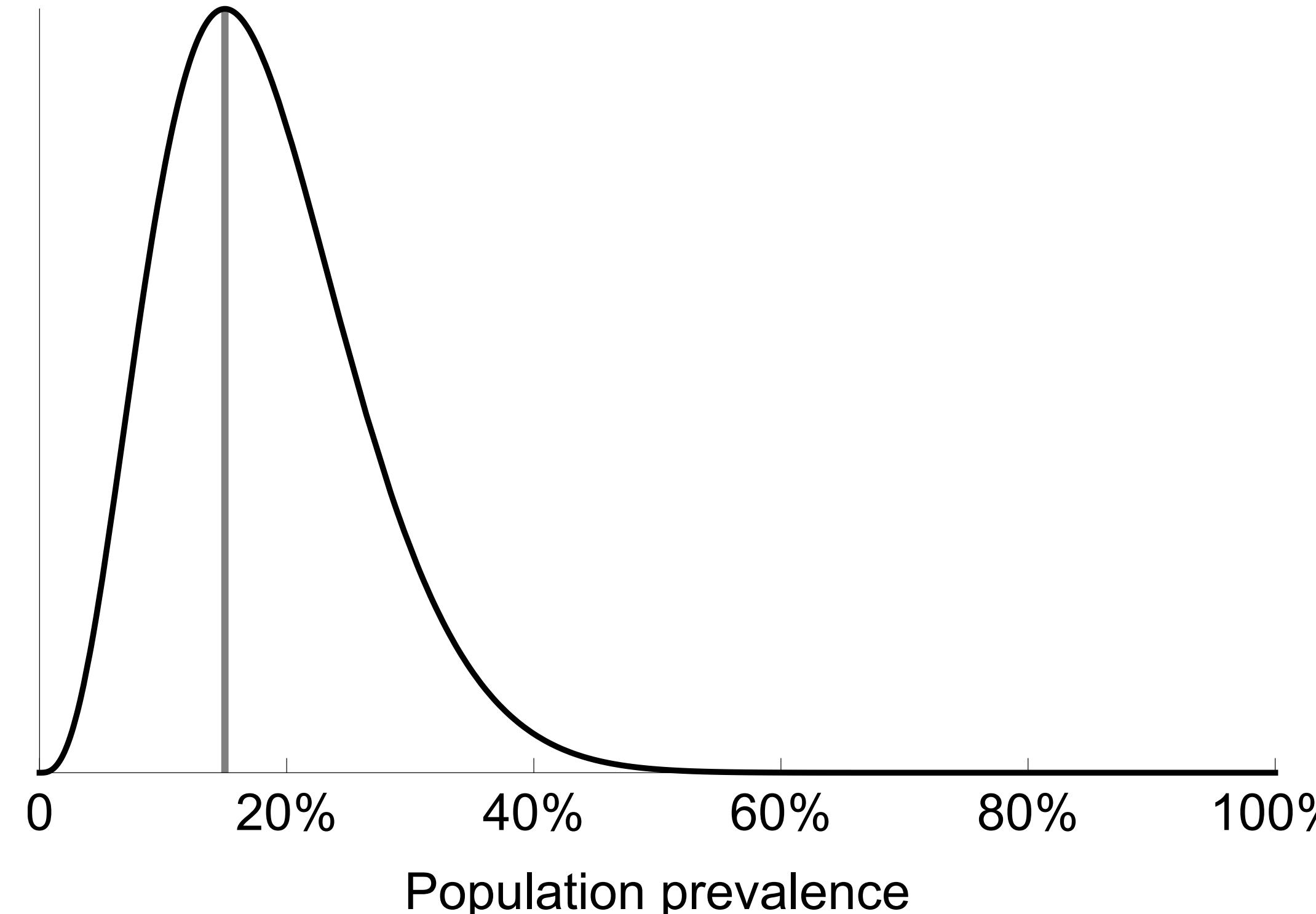
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false positive rate      false negative rate

$$\Pr(n_+ | \theta, u, v) = \binom{n}{n_+} [u + \theta(1 - u - v)]^{n_+} \\ [1 - u - \theta(1 - u - v)]^{n-n_+}$$



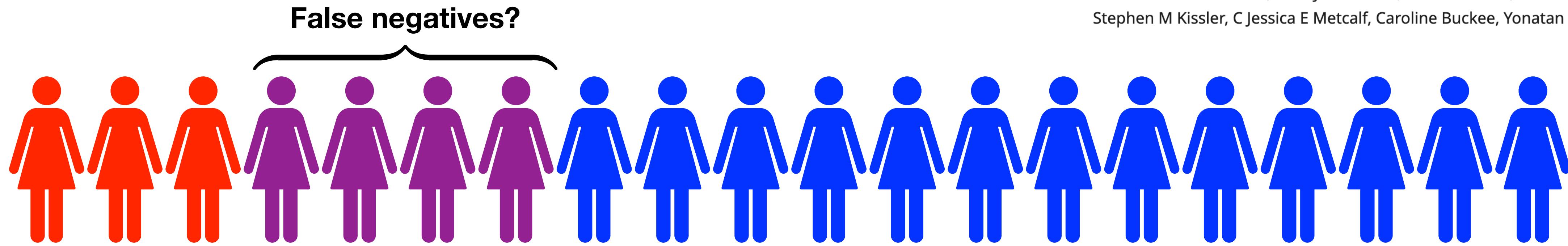
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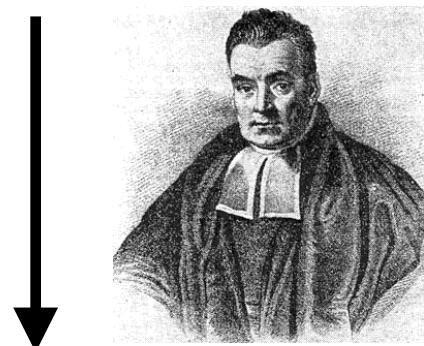
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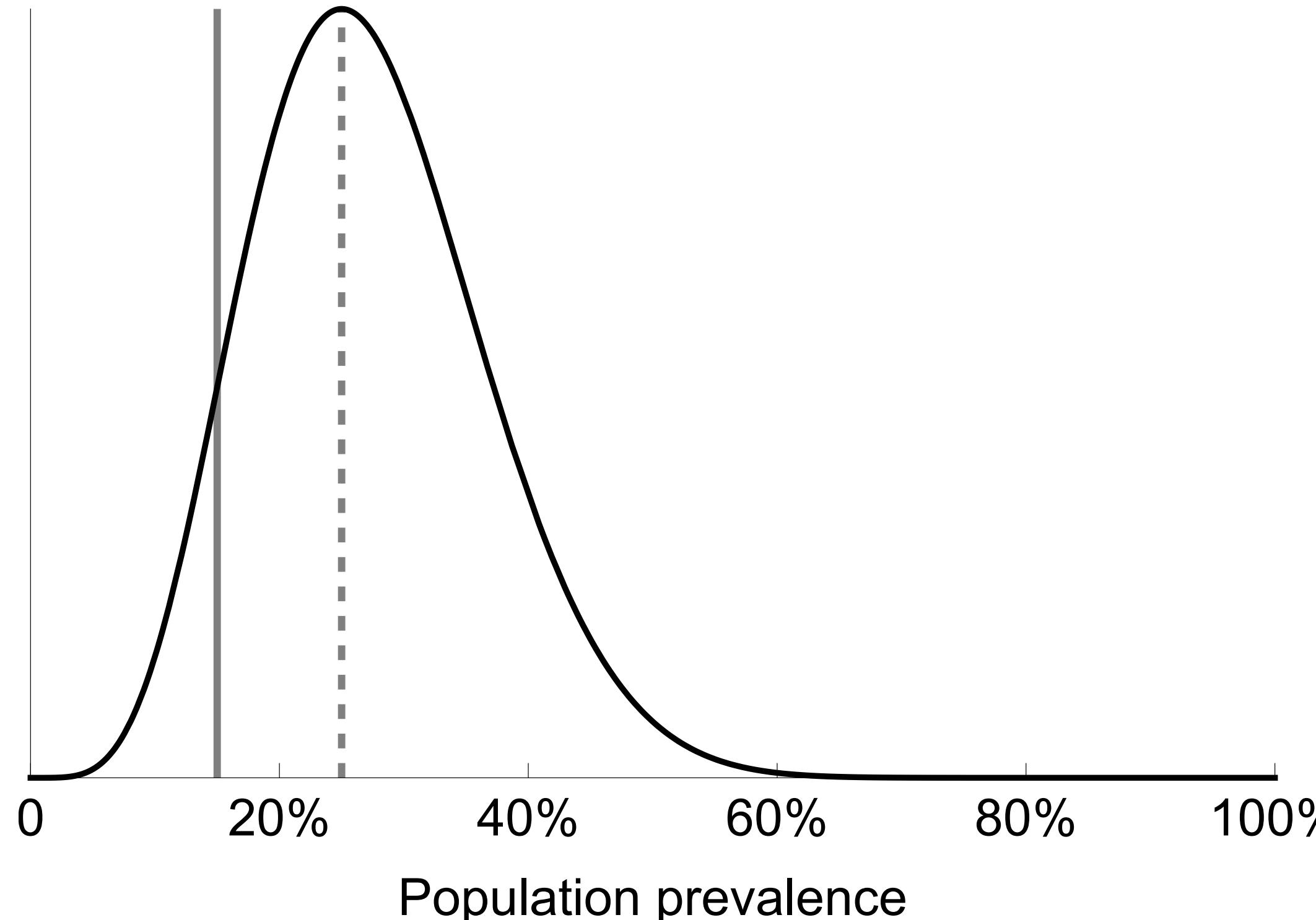


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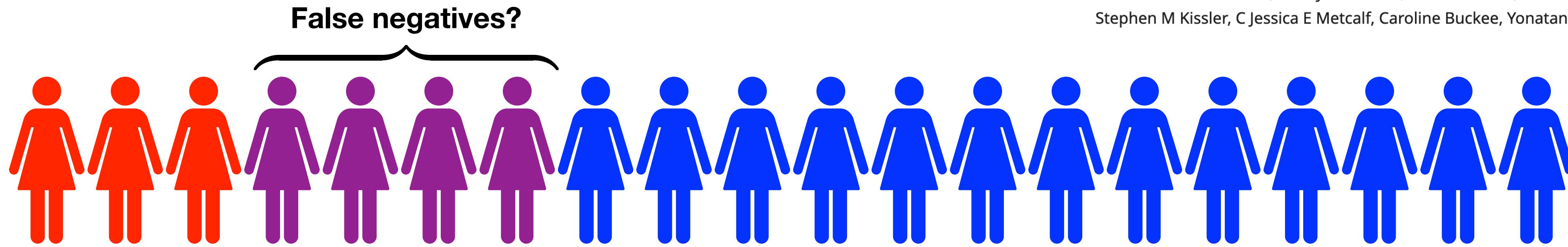
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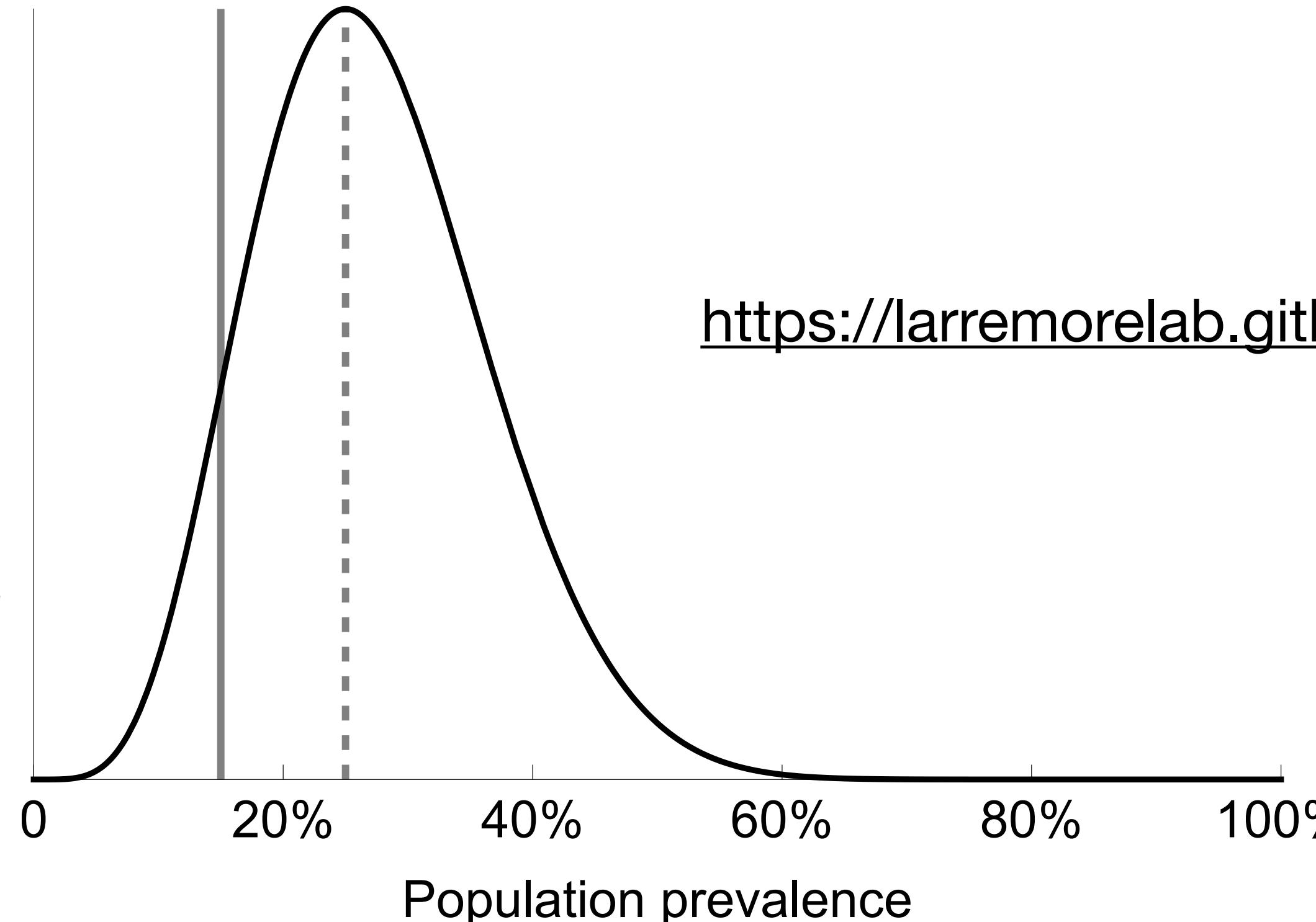
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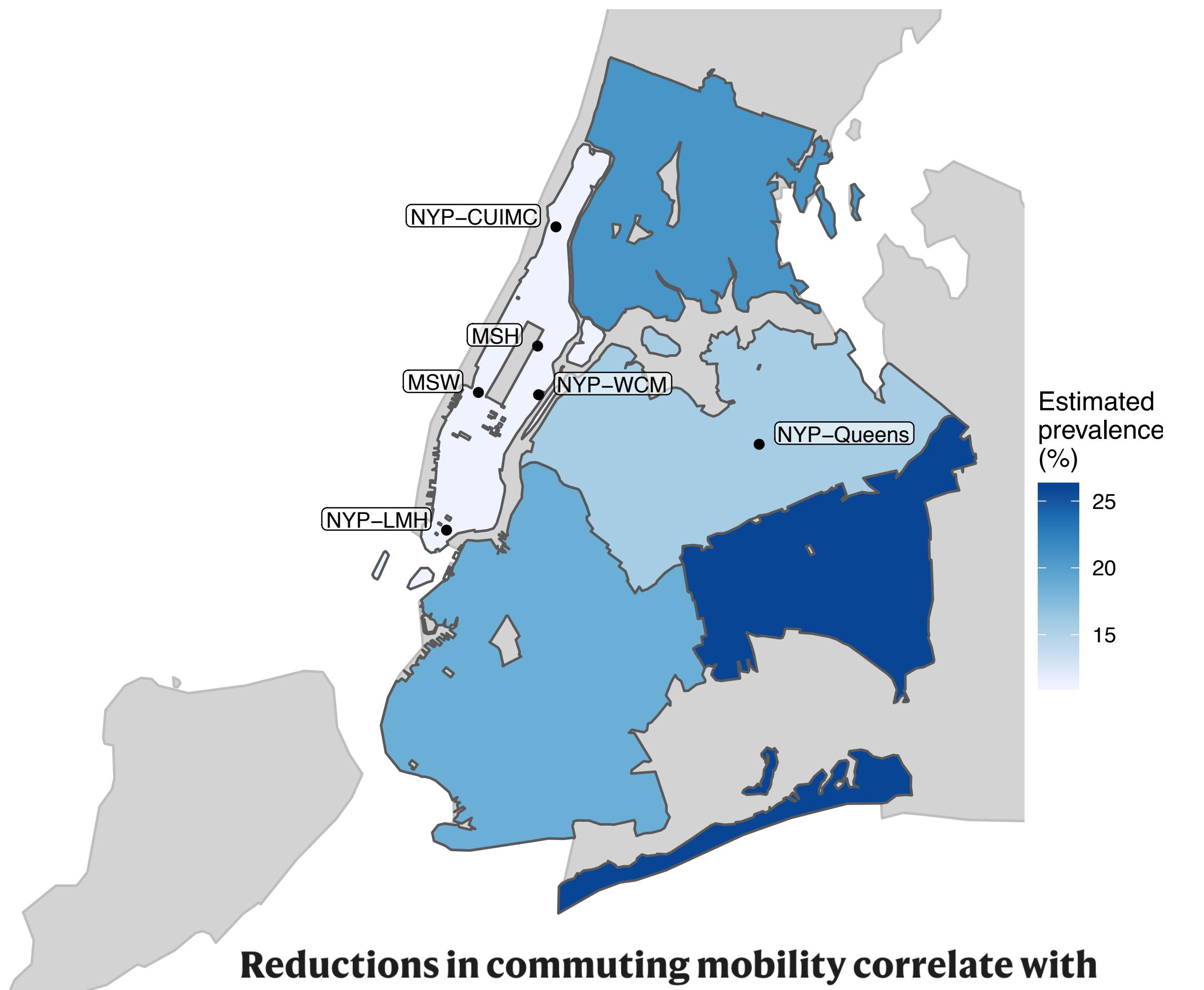
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# Prevalence by borough

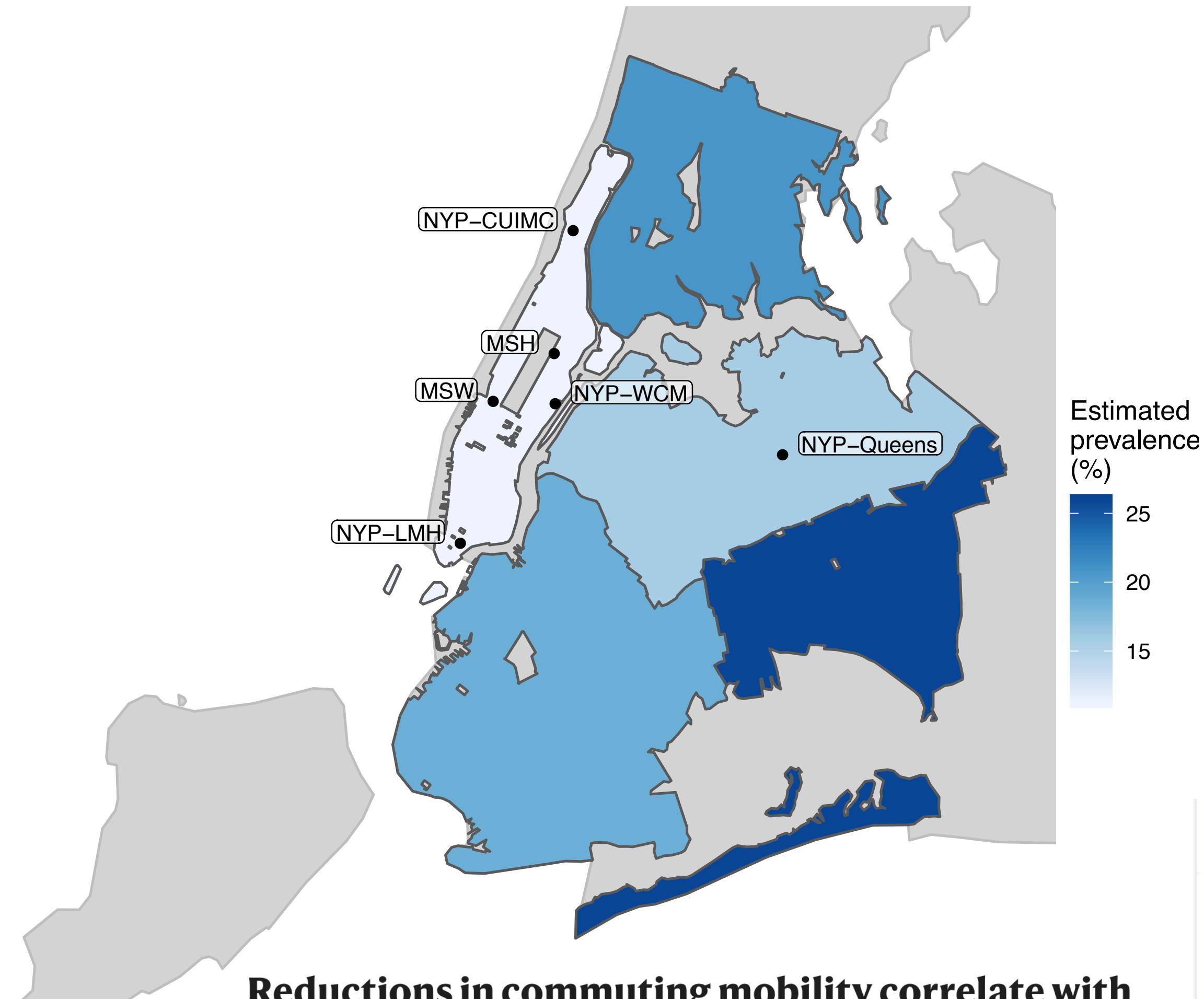


**Reductions in commuting mobility correlate with geographic differences in SARS-CoV-2 prevalence in New York City**

Stephen M. Kissler, Nishant Kishore, Malavika Prabhu, Dena Goffman, Yaakov Beilin, Ruth Landau, Cynthia Gyamfi-Bannerman, Brian T. Bateman, Jon Snyder, Armin S. Razavi, Daniel Katz, Jonathan Gal, Angela Bianco, Joanne Stone, Daniel Larremore, Caroline O. Buckee & Yonatan H. Grad [✉](mailto:Yonatan.H.Grad@nyu.edu)

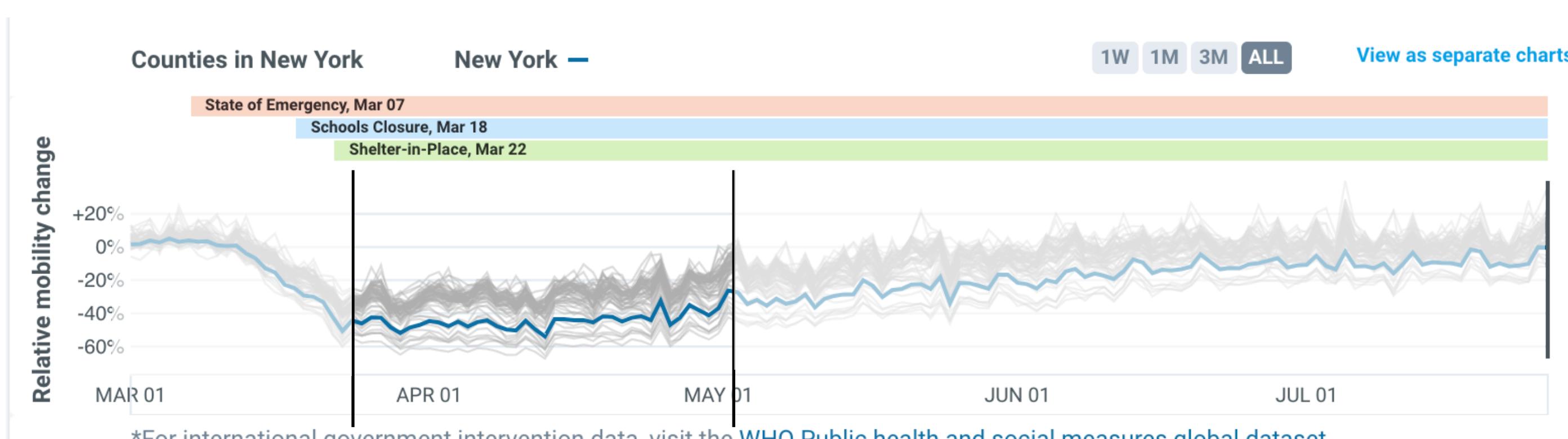
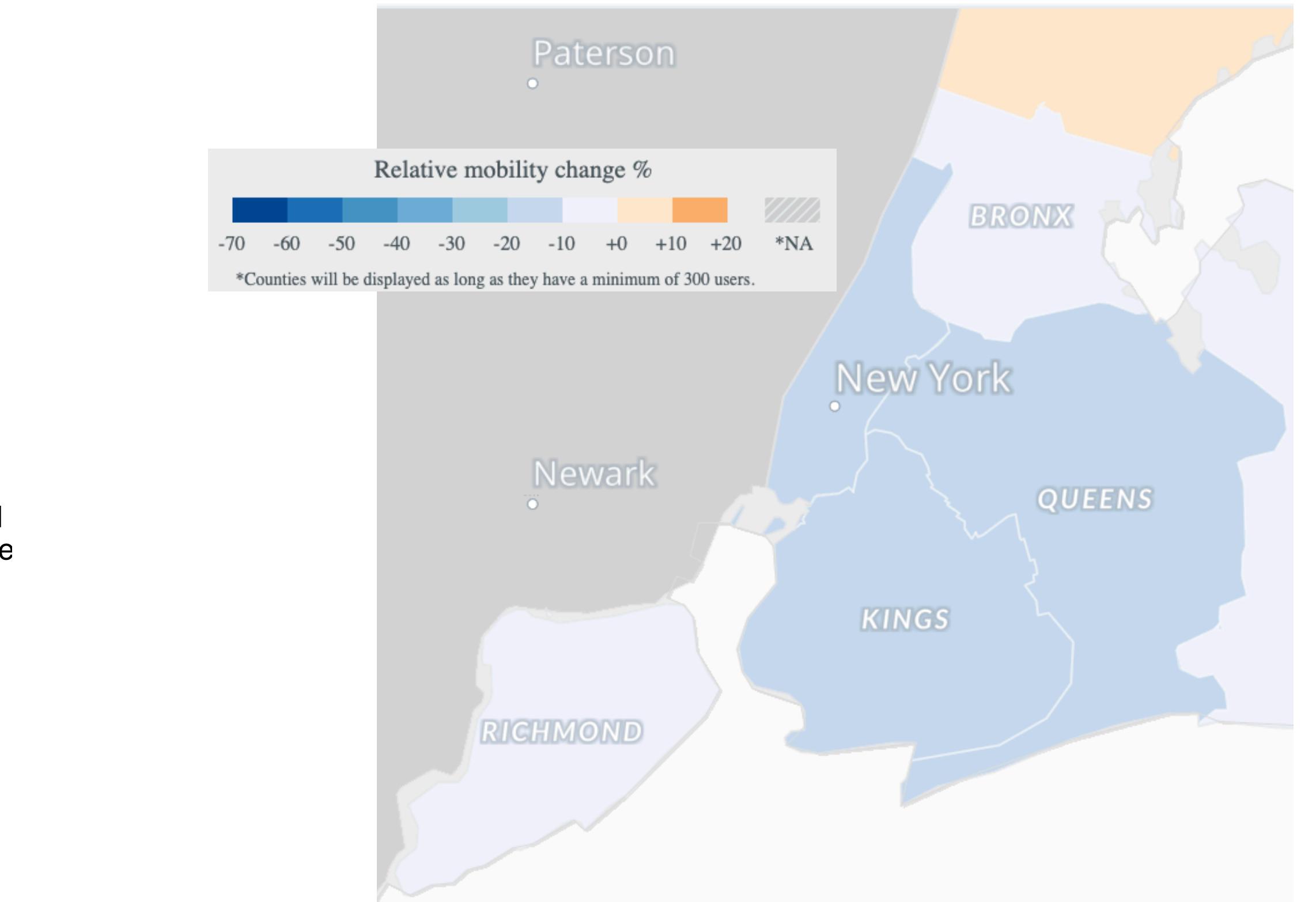
# Prevalence by borough

FACEBOOK Data for Good



**Reductions in commuting mobility correlate with geographic differences in SARS-CoV-2 prevalence in New York City**

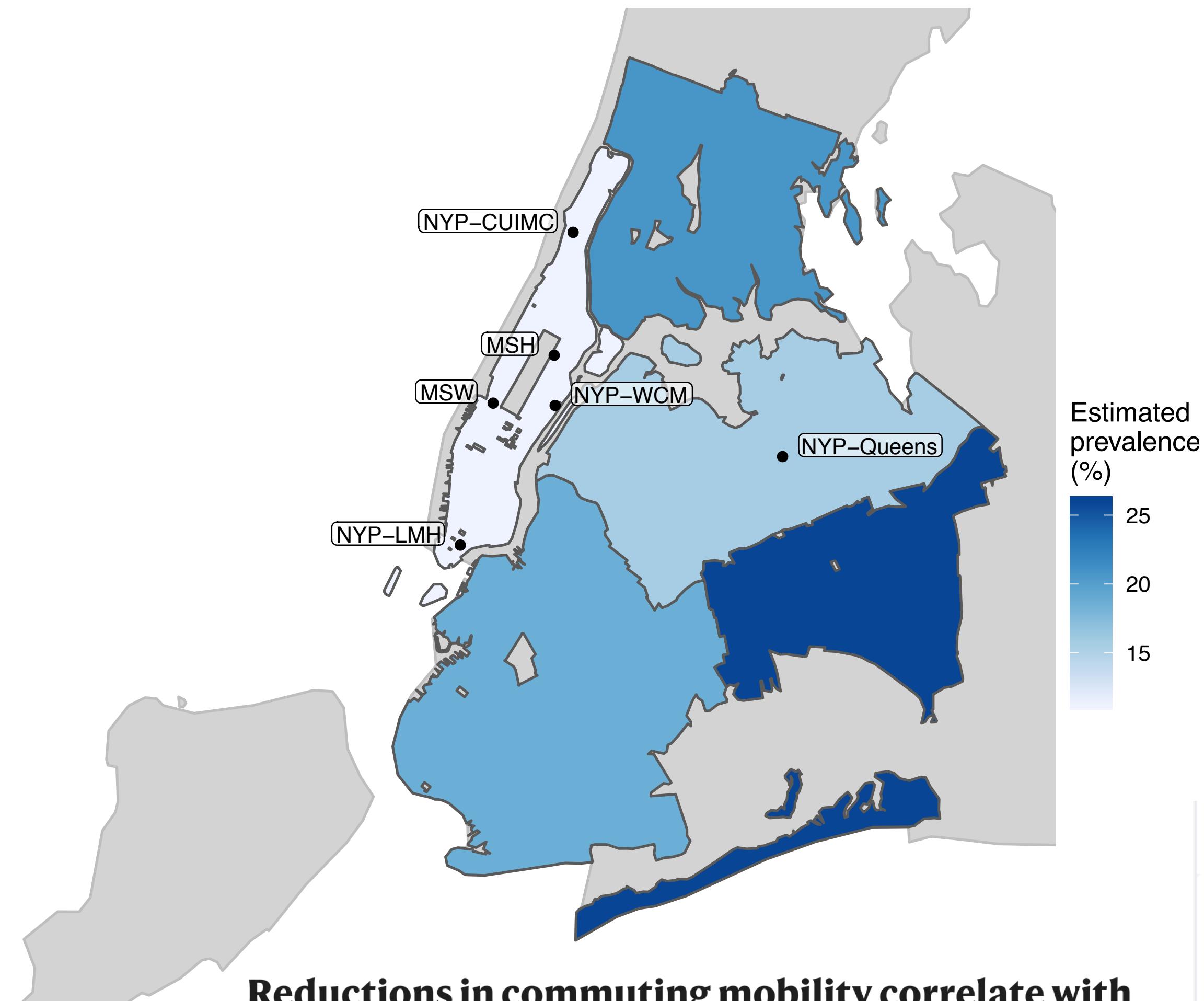
Stephen M. Kissler, Nishant Kishore, Malavika Prabhu, Dena Goffman, Yaakov Beilin, Ruth Landau, Cynthia Gyamfi-Bannerman, Brian T. Bateman, Jon Snyder, Armin S. Razavi, Daniel Katz, Jonathan Gal, Angela Bianco, Joanne Stone, Daniel Larremore, Caroline O. Buckee & Yonatan H. Grad



\*For international government intervention data, visit the [WHO Public health and social measures global dataset](#).

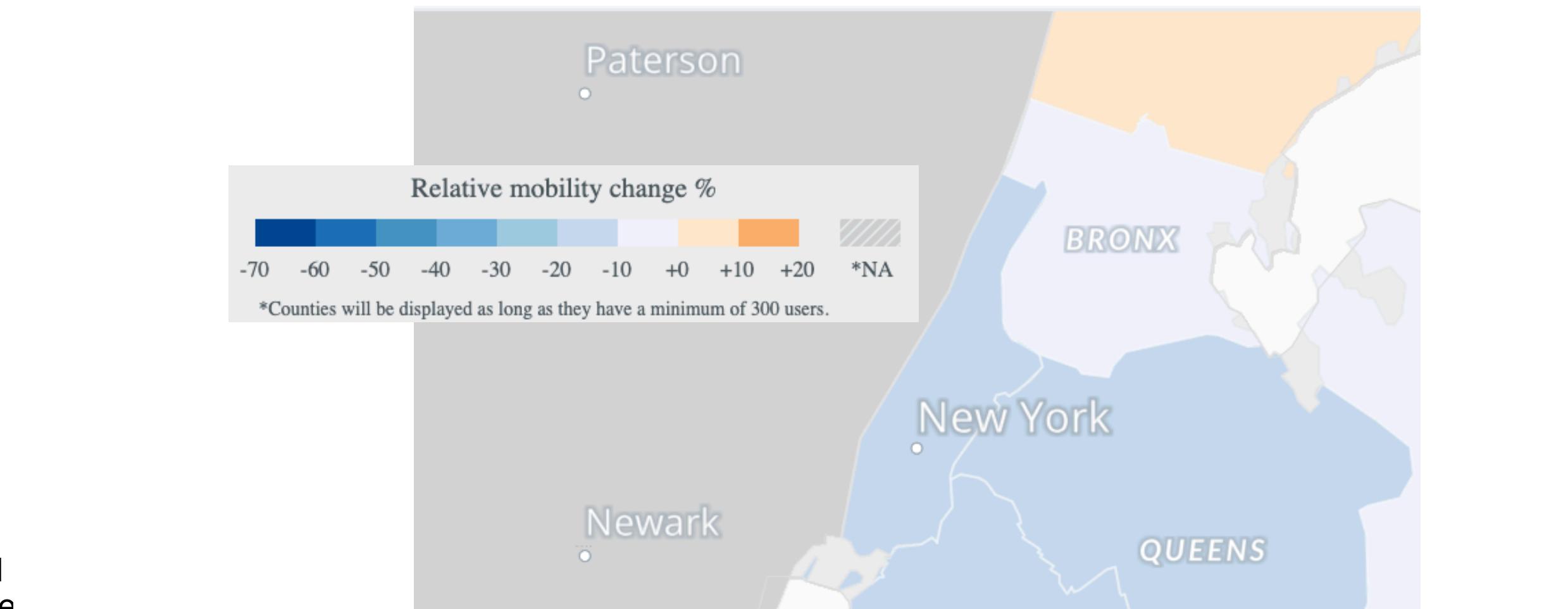
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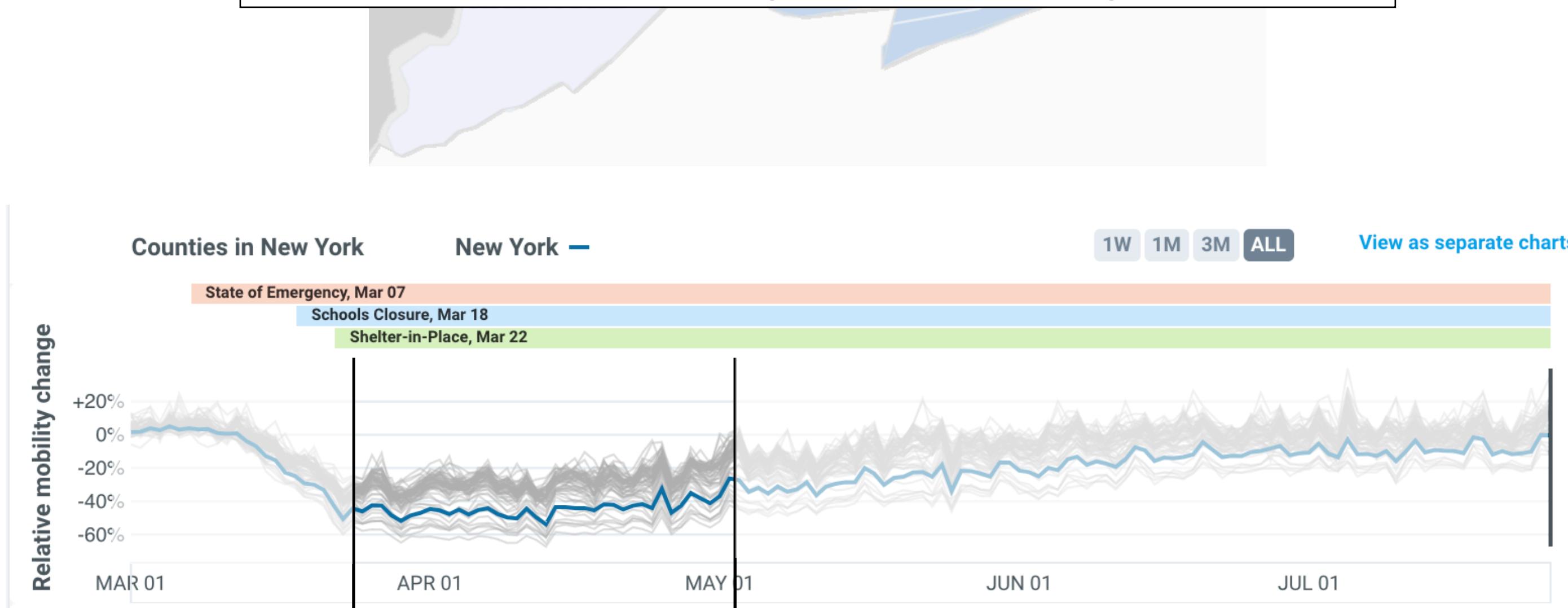


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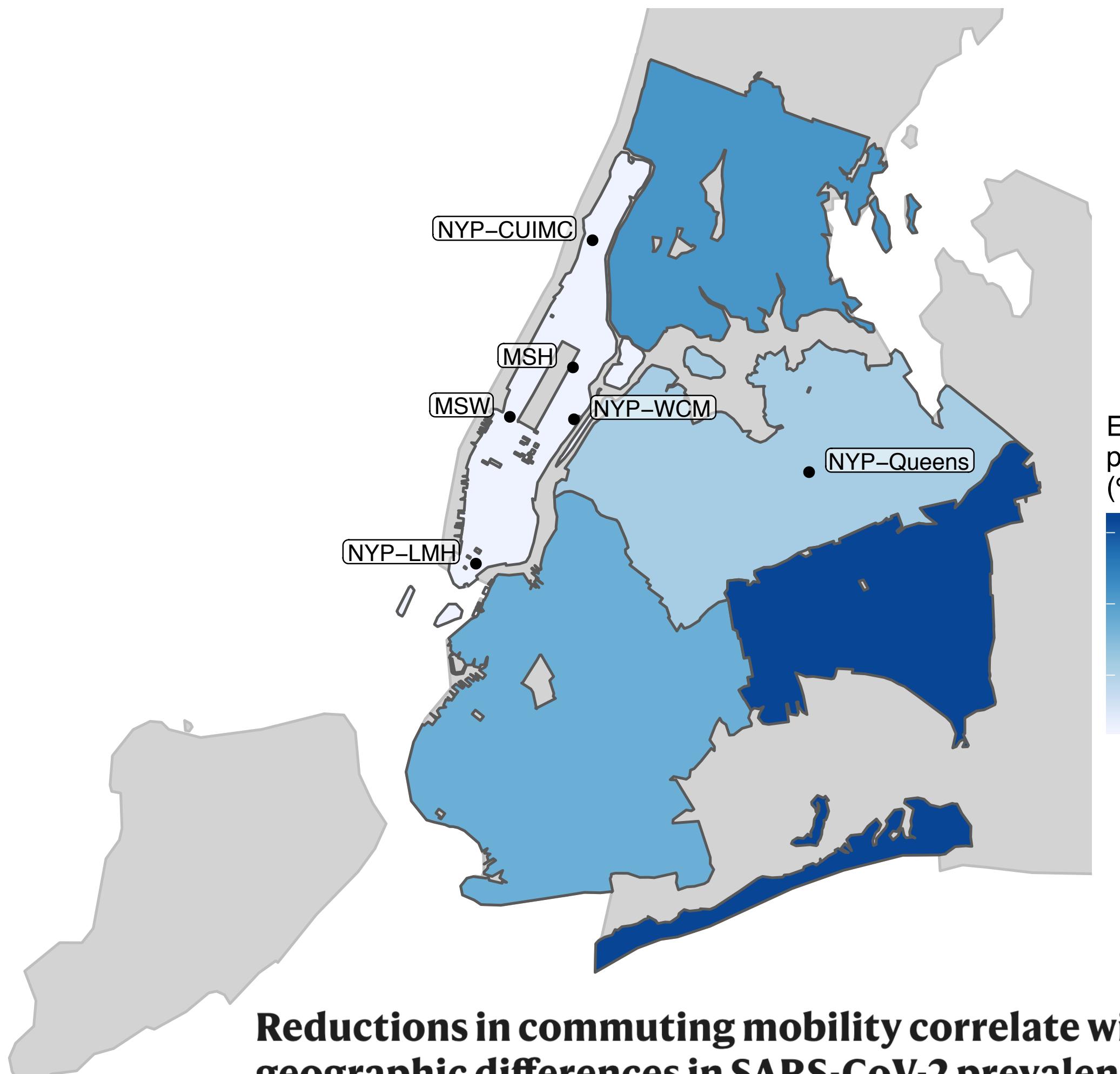


**Measure decline in “commuting-style movements”:  
movements out of borough in the morning +  
movements into borough in the evening**



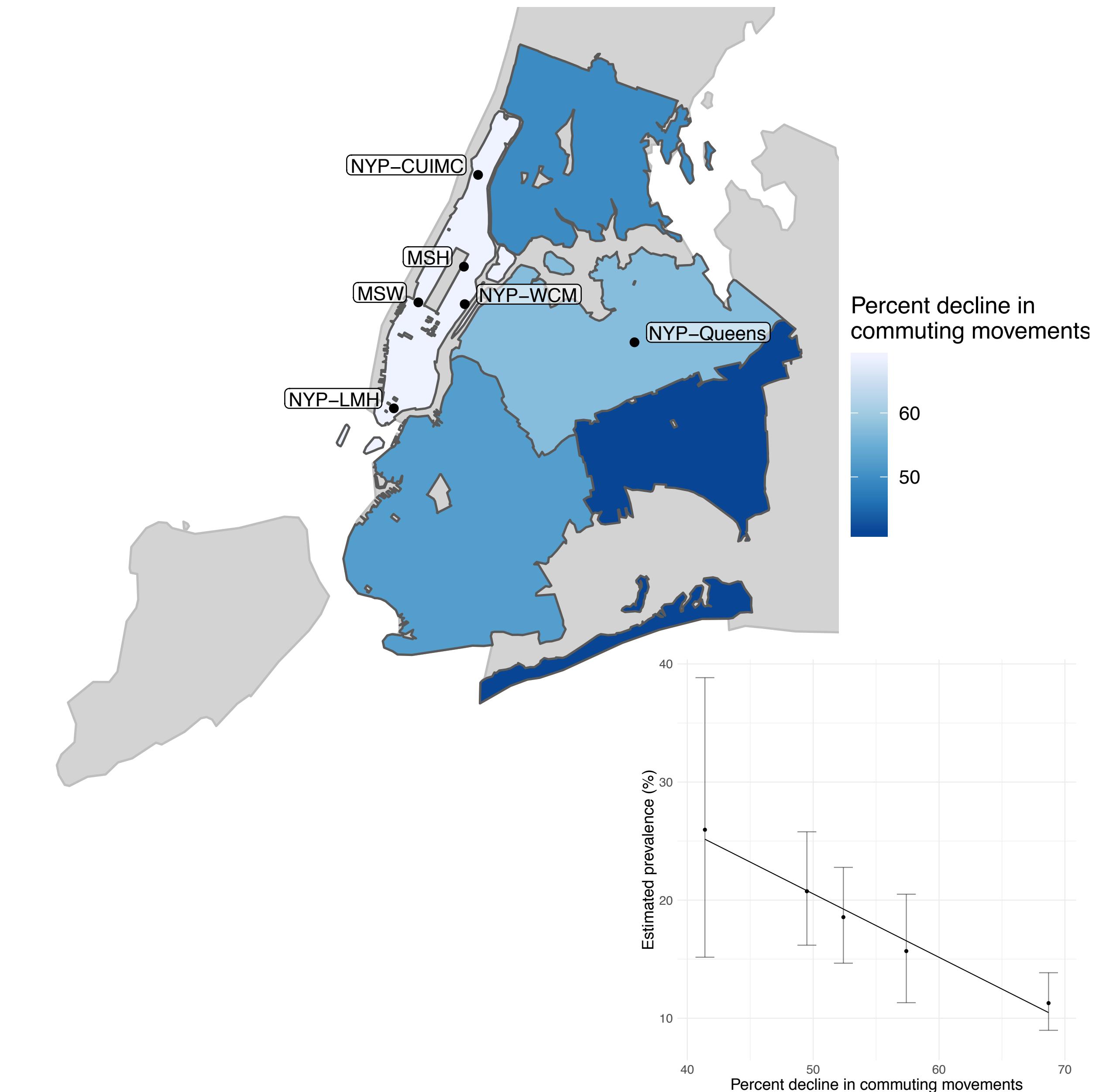
\*For international government intervention data, visit the [WHO Public health and social measures global dataset](#).

# Prevalence by borough correlates with reductions in commuting

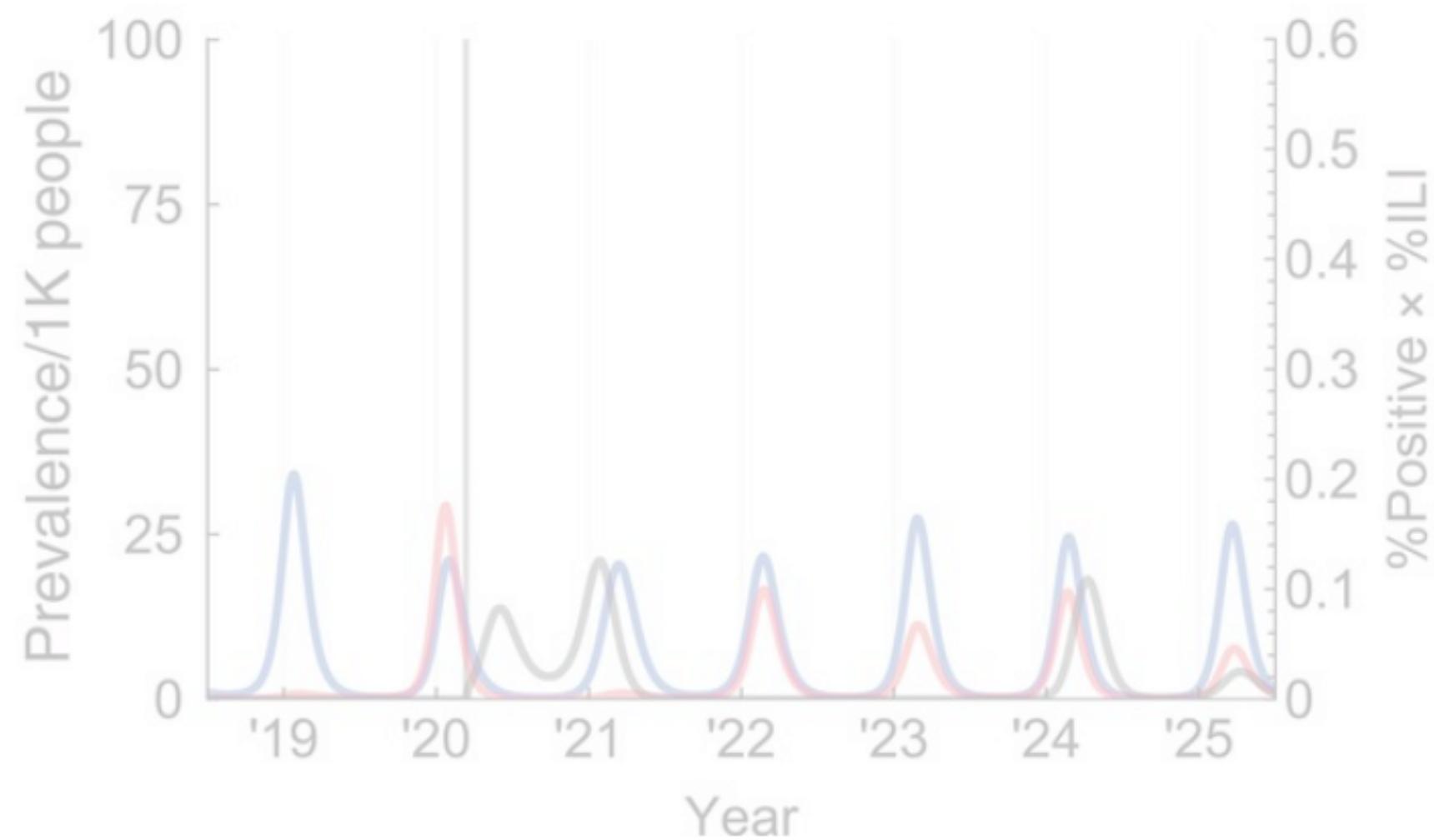


**Reductions in commuting mobility correlate with geographic differences in SARS-CoV-2 prevalence in New York City**

Stephen M. Kissler, Nishant Kishore, Malavika Prabhu, Dena Goffman, Yaakov Beilin, Ruth Landau, Cynthia Gyamfi-Bannerman, Brian T. Bateman, Jon Snyder, Armin S. Razavi, Daniel Katz, Jonathan Gal, Angela Bianco, Joanne Stone, Daniel Larremore, Caroline O. Buckee & Yonatan H. Grad



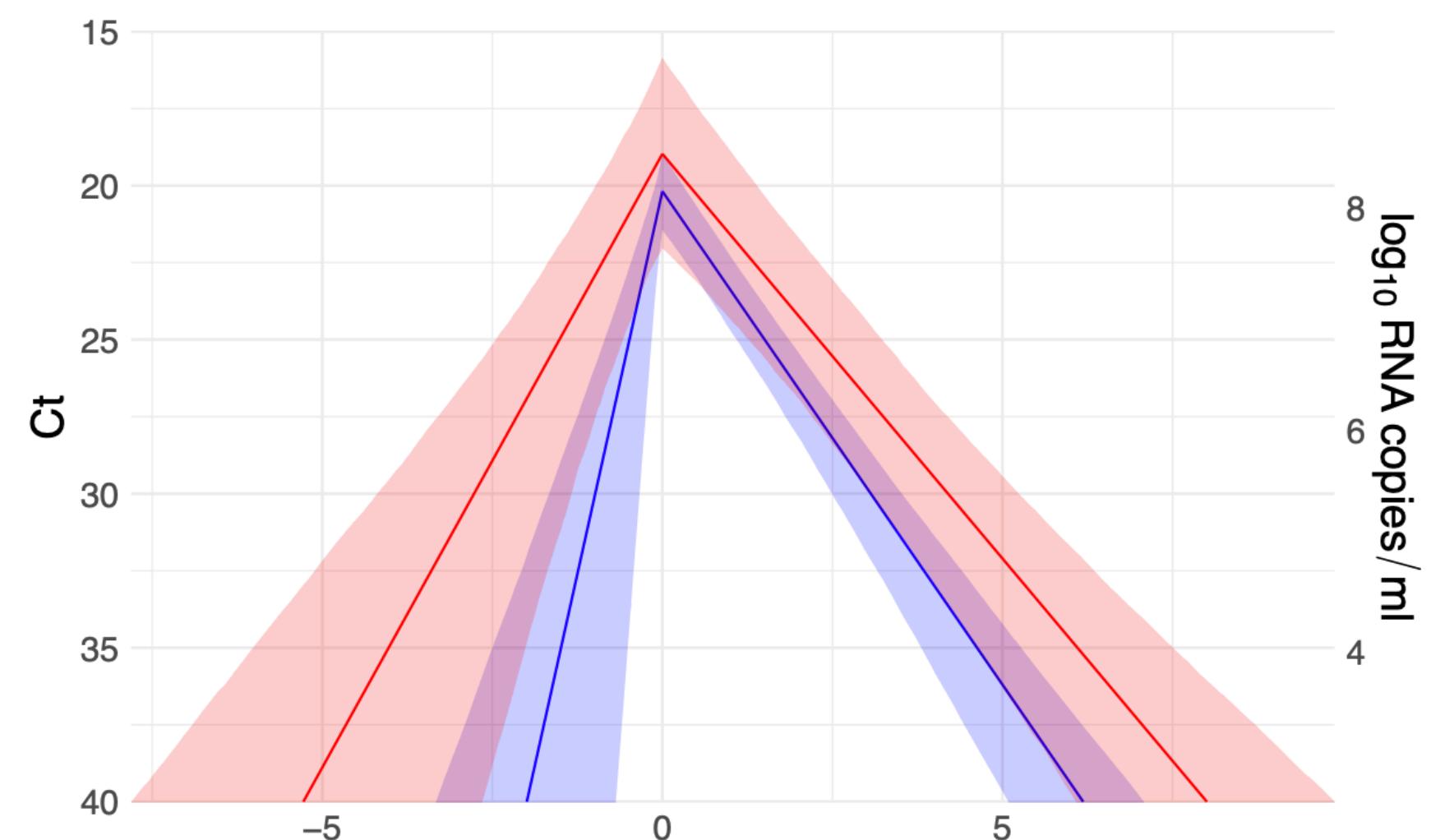
### I. Long-term global spread of SARS-CoV-2



### II. Measuring SARS-CoV-2 prevalence in New York City



### III. Viral dynamics of SARS-CoV-2 variants



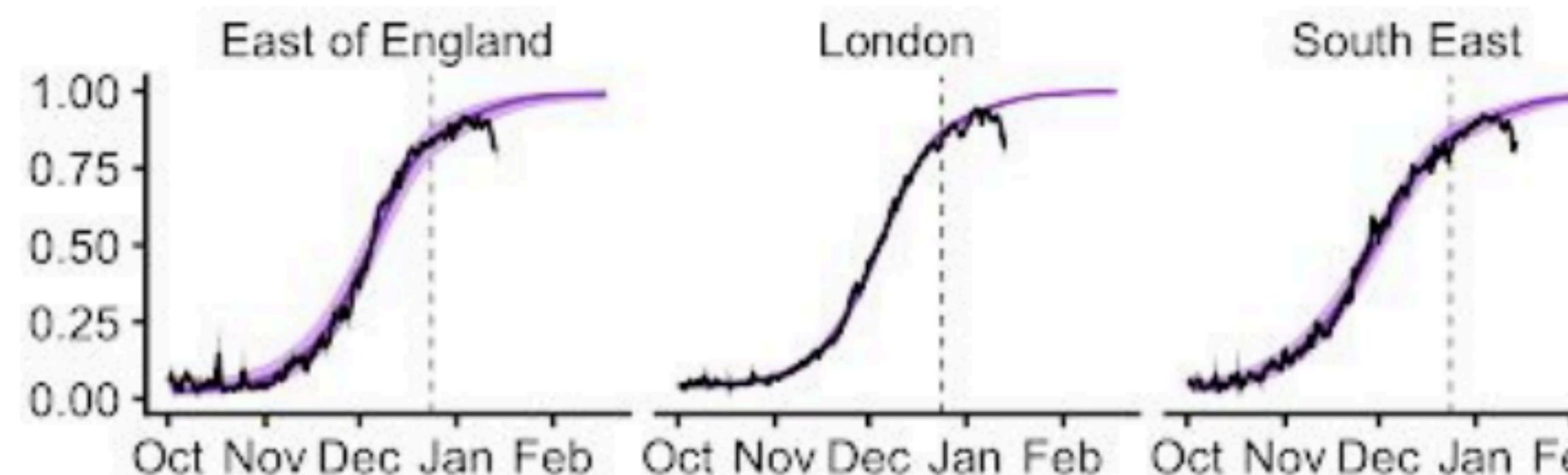
# Why is B.1.1.7 more transmissible?

## Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England

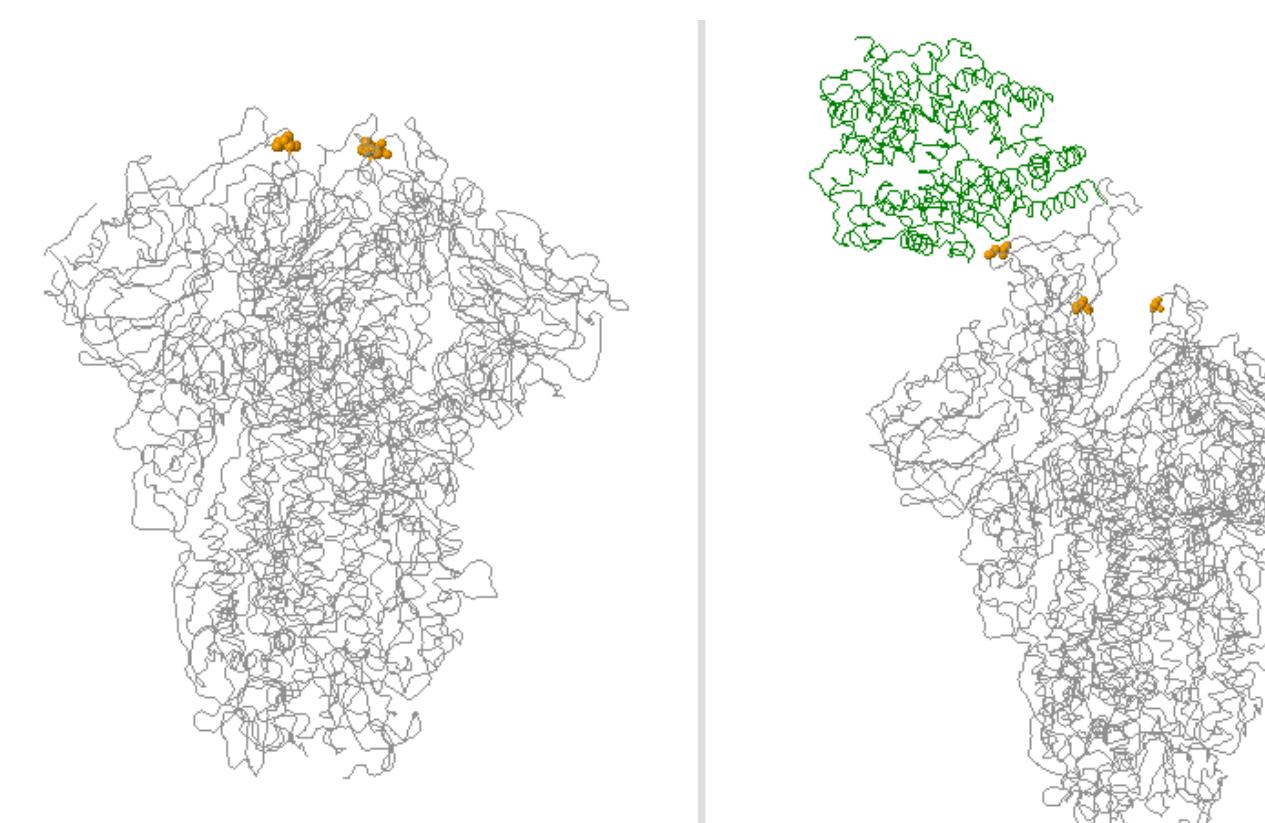
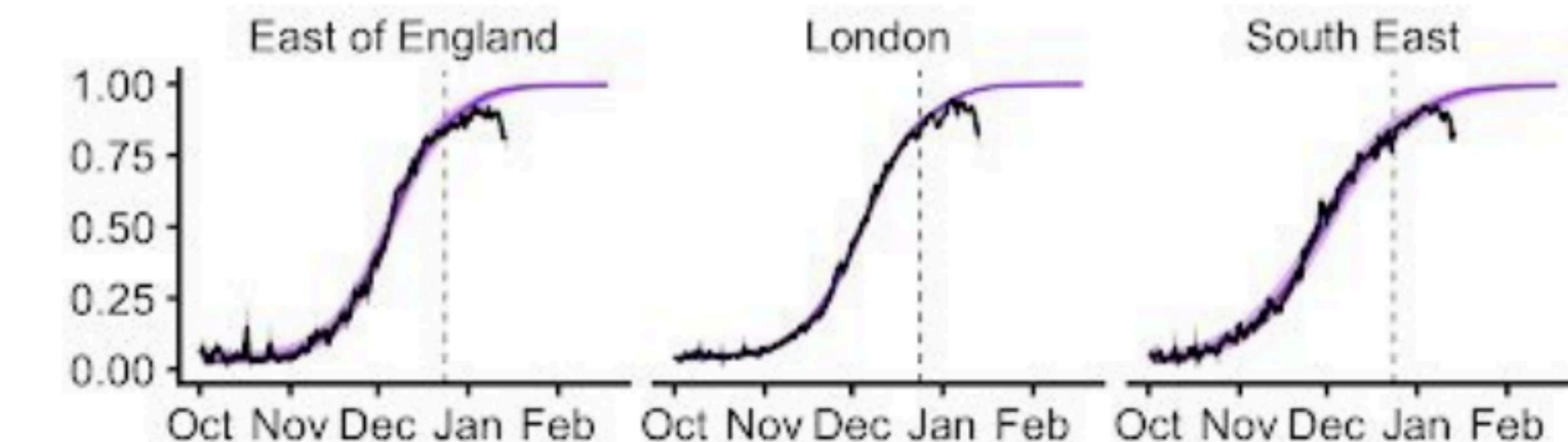
Nicholas G. Davies<sup>1†</sup>, Sam Abbott<sup>1\*</sup>, Rosanna C. Barnard<sup>1\*</sup>, Christopher I. Jarvis<sup>1\*</sup>, Adam J. Kucharski<sup>1\*</sup>, James Munday<sup>1\*</sup>, Carl A. B. Pearson<sup>1\*</sup>, Timothy W. Russell<sup>1\*</sup>, Damien C. Tully<sup>1\*</sup>, Alex D. Washburne<sup>2\*</sup>, Tom Wenseleers<sup>3\*</sup>, Amy Gimma<sup>1</sup>, William Waites<sup>1</sup>, Kerry LM Wong<sup>1</sup>, Kevin van Zandvoort<sup>1</sup>, Justin D. Silverman<sup>4</sup>, CMMID COVID-19 Working Group, Karla Diaz-Ordaz<sup>5</sup>, Ruth Keogh<sup>5</sup>, Rosalind M. Eggo<sup>1</sup>, Sebastian Funk<sup>1</sup>, Mark Jit<sup>1</sup>, Katherine E. Atkins<sup>1,6</sup>, W. John Edmunds<sup>1</sup>

A

### Increased transmissibility



### Increased duration of infectiousness



???

# The data

- 65 participants had confirmed novel infections, with **58 non-B.1.1.7** and **7 B.1.1.7** 

**Densely sampled viral trajectories suggest longer duration of acute infection with B.1.1.7 variant relative to non-B.1.1.7 SARS-CoV-2**

Stephen M. Kissler<sup>\*1</sup>, Joseph R. Fauver<sup>\*2</sup>, Christina Mack<sup>\*3,4</sup>, Caroline G. Tai<sup>3</sup>, Mallory I. Breban<sup>2</sup>, Anne E. Watkins<sup>2</sup>, Radhika M. Samant<sup>3</sup>, Deverick J. Anderson<sup>5</sup>, David D. Ho<sup>6</sup>, Nathan D. Grubaugh<sup>†2</sup>, Yonatan H. Grad<sup>†1</sup>

<sup>1</sup> Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, MA

<sup>2</sup> Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT

<sup>3</sup> IQVIA, Real World Solutions, Durham, NC

<sup>4</sup> Department of Epidemiology, University of North Carolina-Chapel Hill, Chapel Hill, NC

<sup>5</sup> Duke Center for Antimicrobial Stewardship and Infection Prevention, Durham, NC

<sup>6</sup> Aaron Diamond AIDS Research Center, Columbia University Vagelos College of Physicians and Surgeons, New York, NY

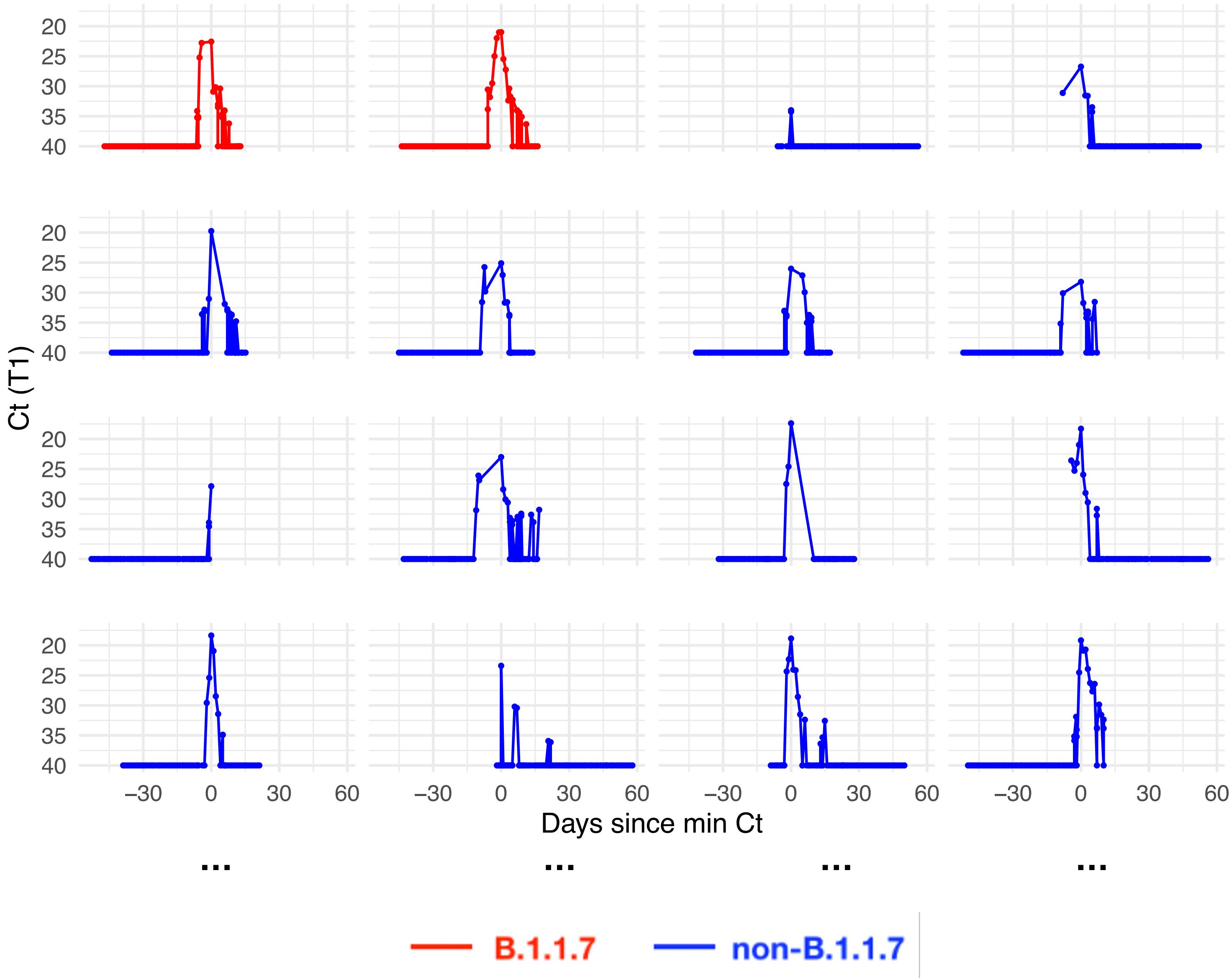
\* denotes equal contribution

† denotes co-senior authorship

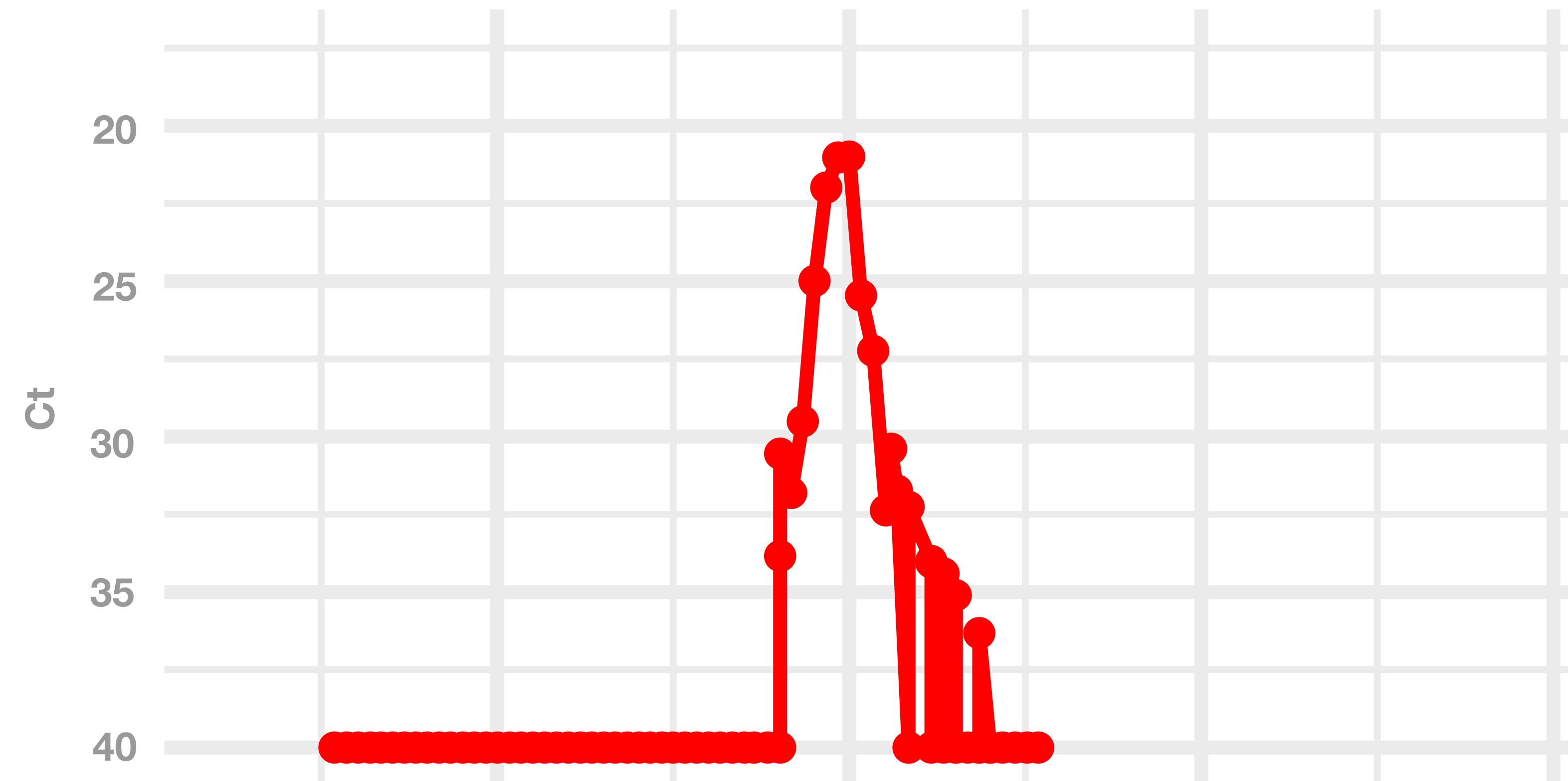
<https://www.medrxiv.org/content/10.1101/2021.02.16.21251535v1>

[https://github.com/skissler/CtTrajectories\\_B117](https://github.com/skissler/CtTrajectories_B117)

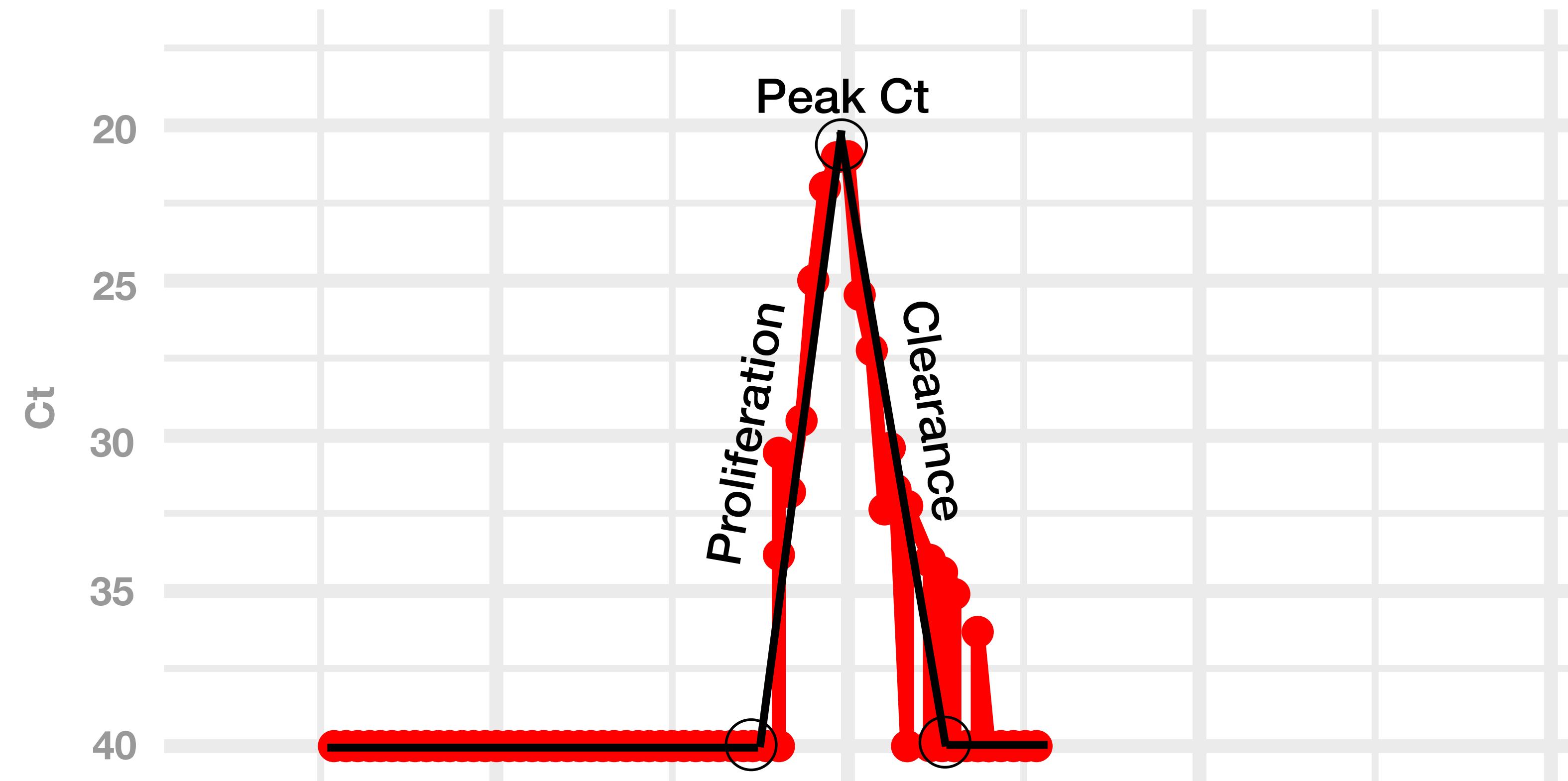
**Ct ~ log(viral concentration)**



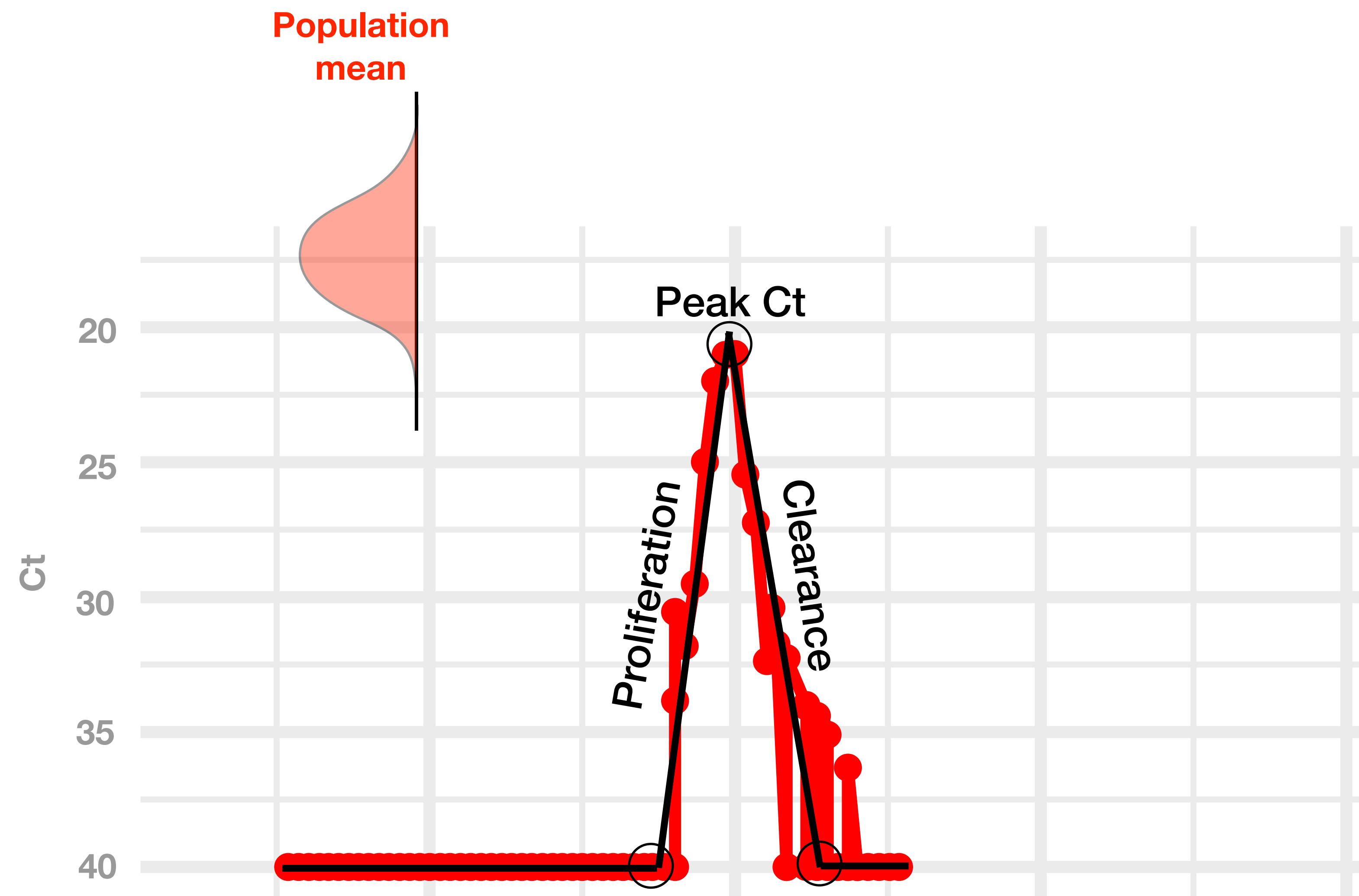
# The model



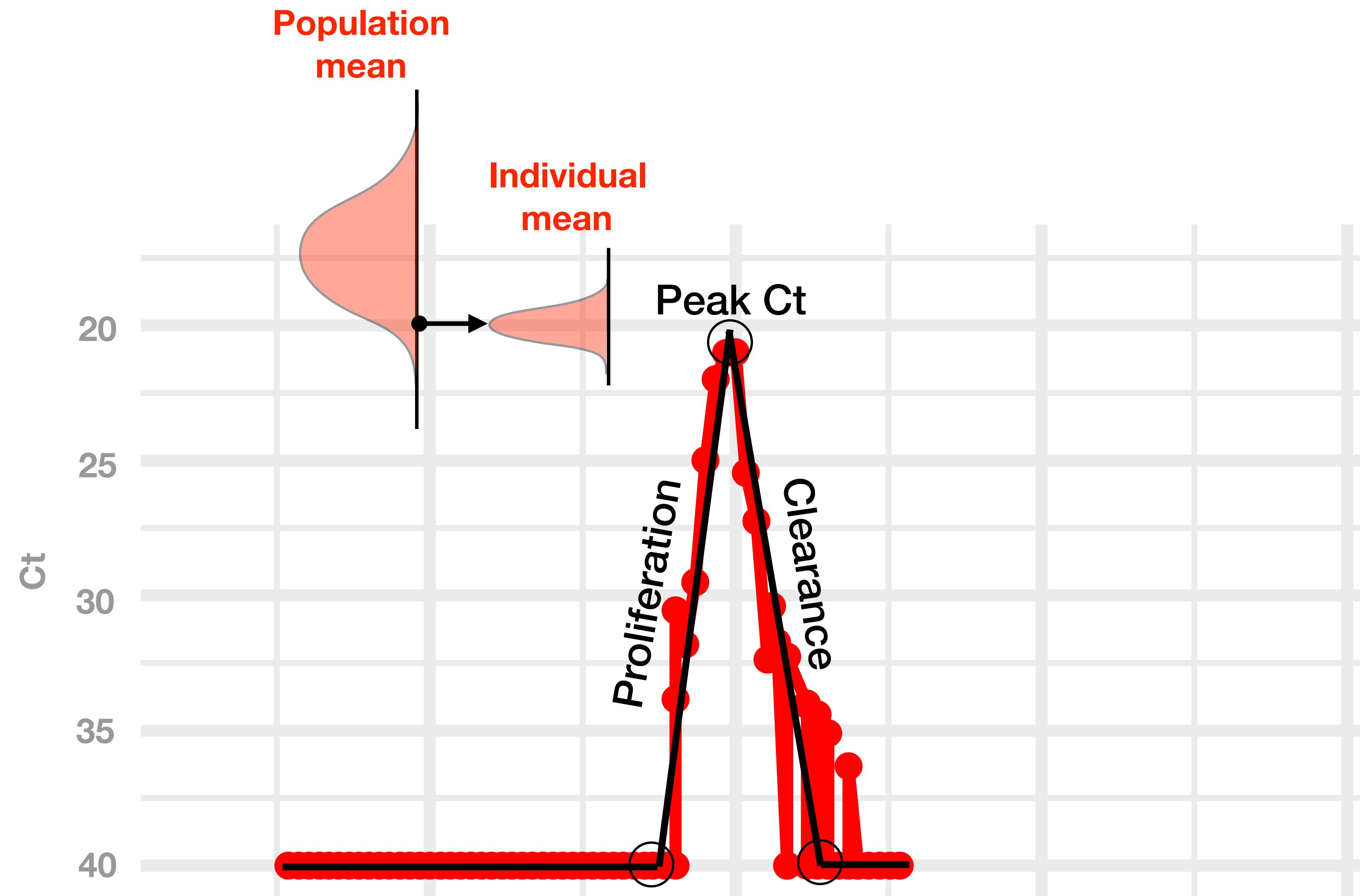
# The model



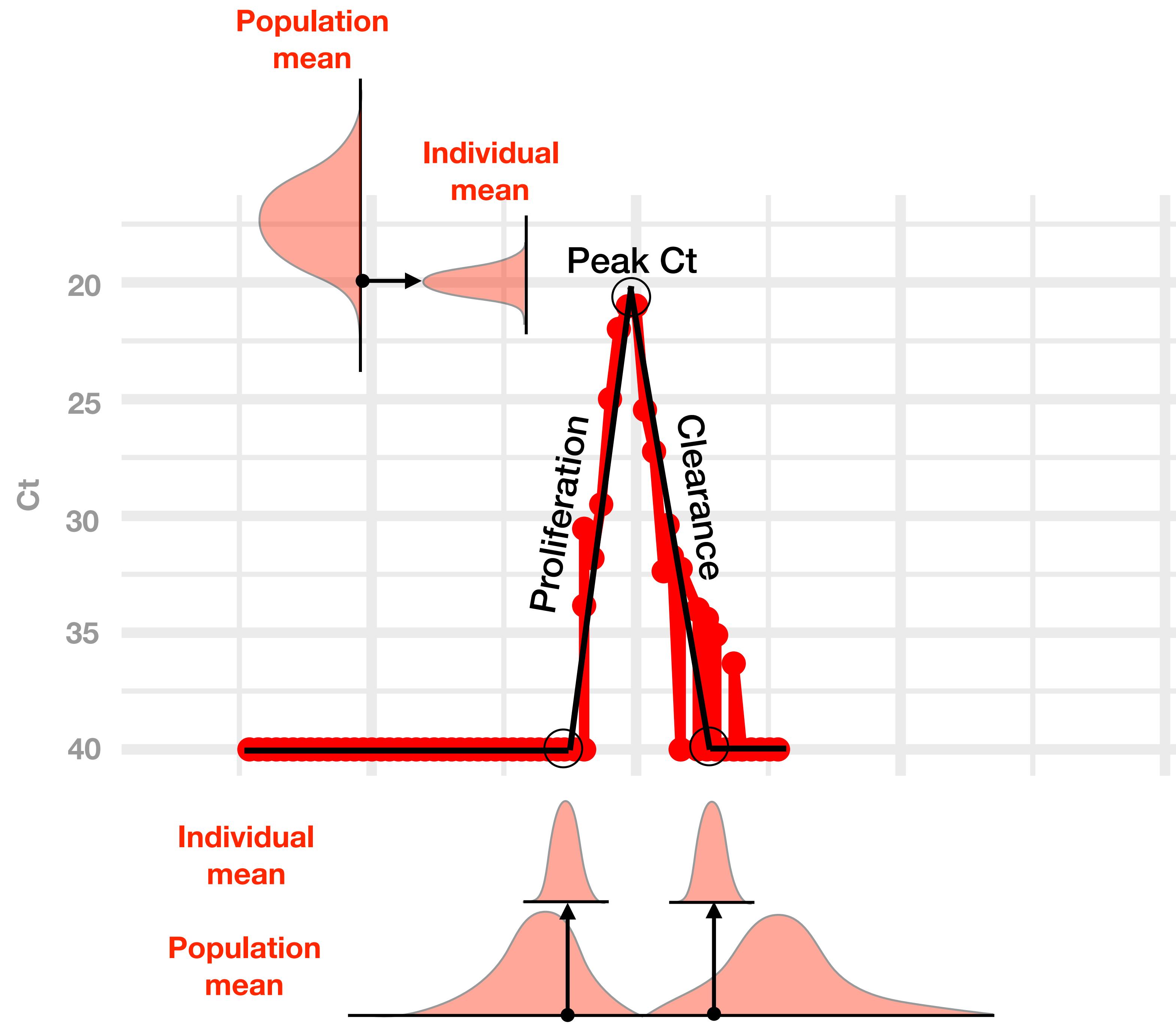
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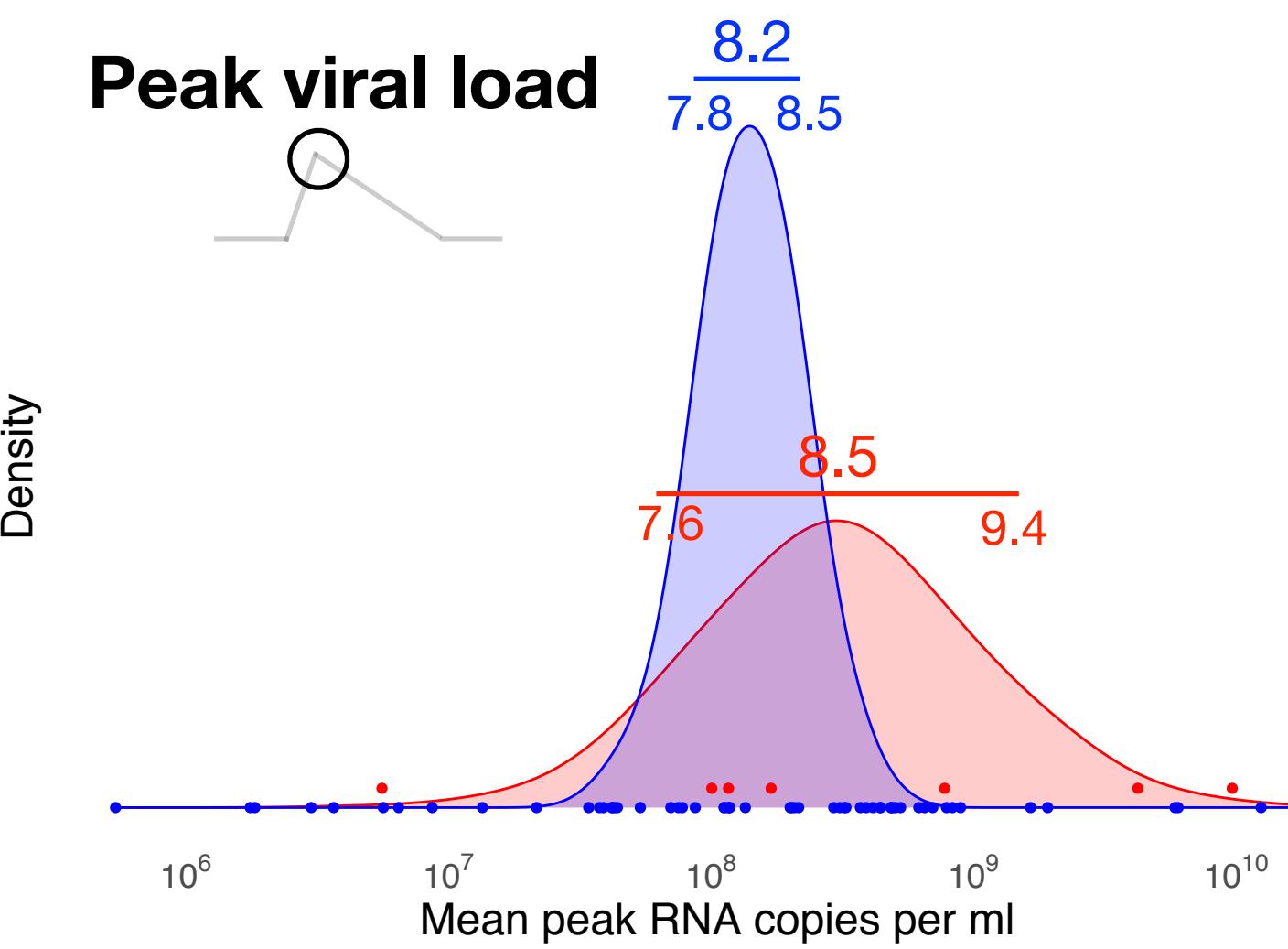
# The model



# The model

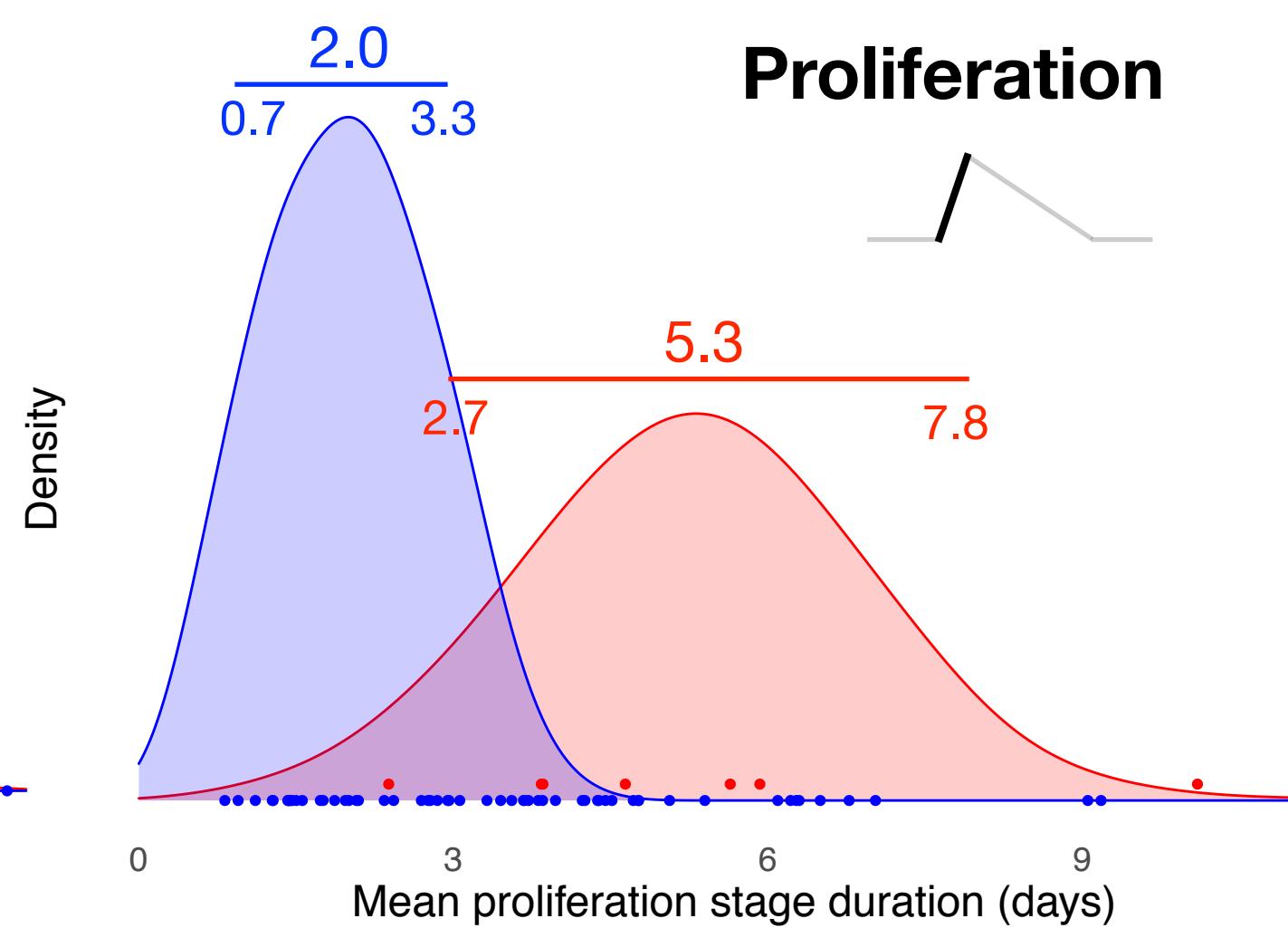
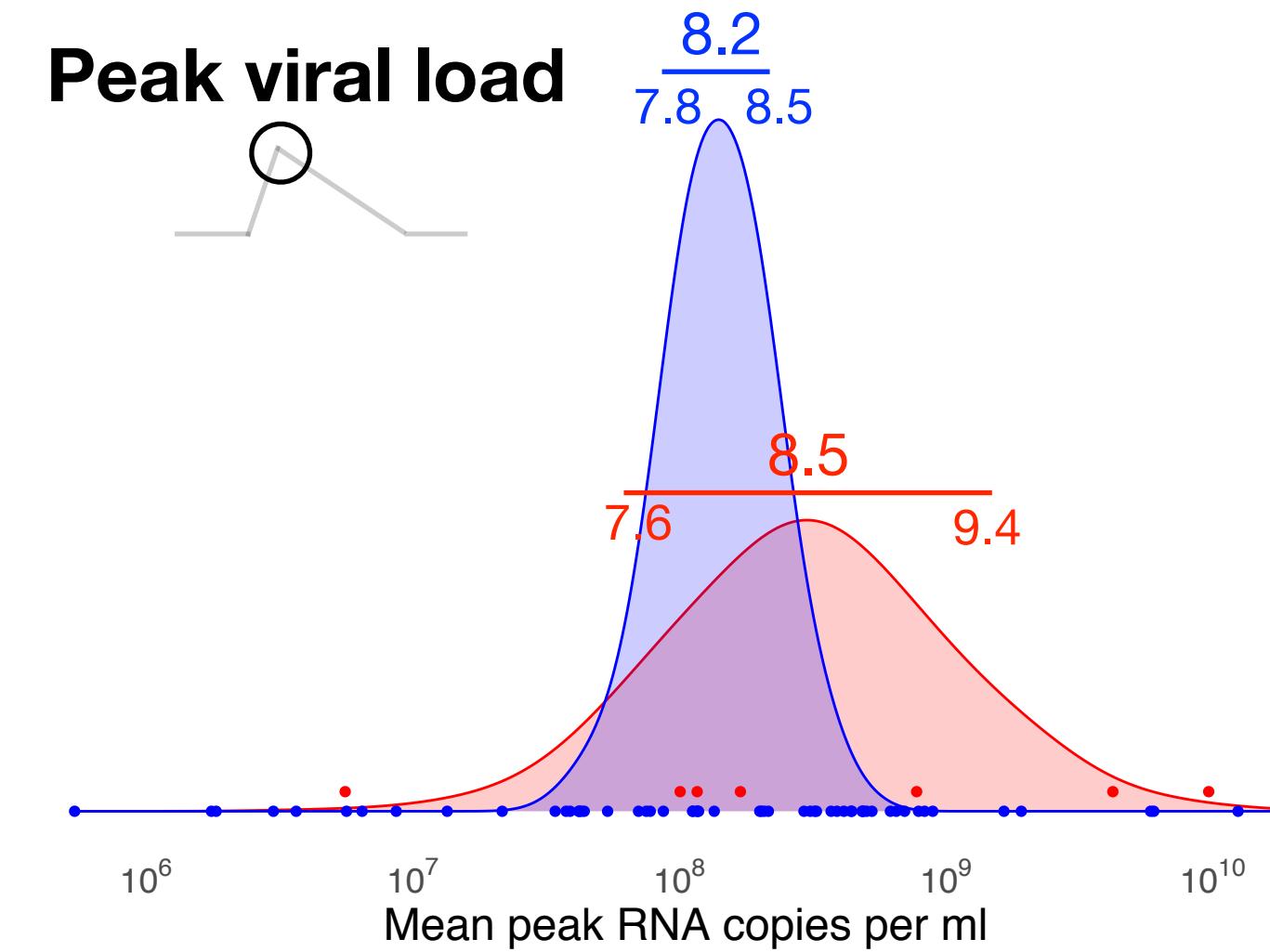


# Posterior mean distributions



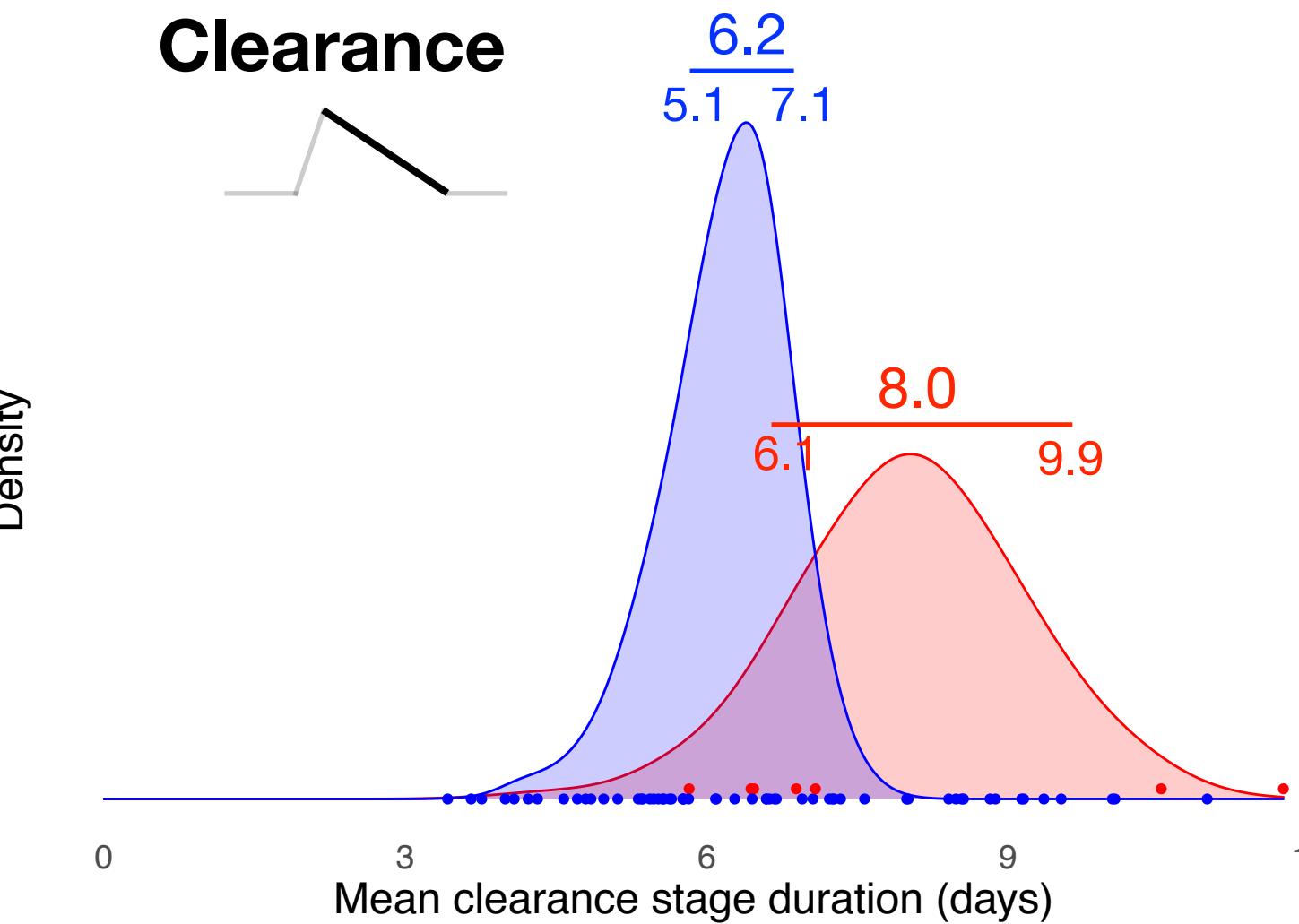
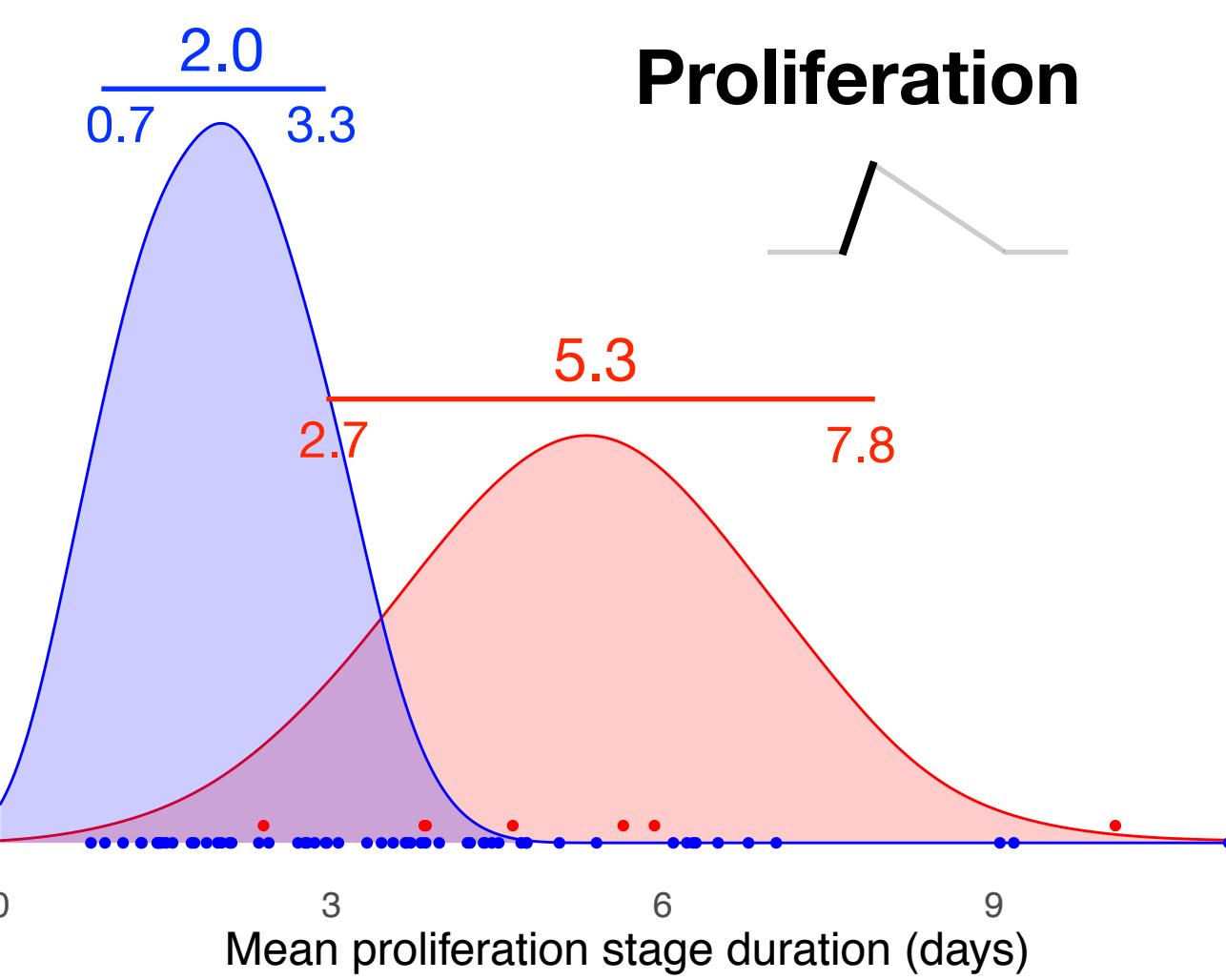
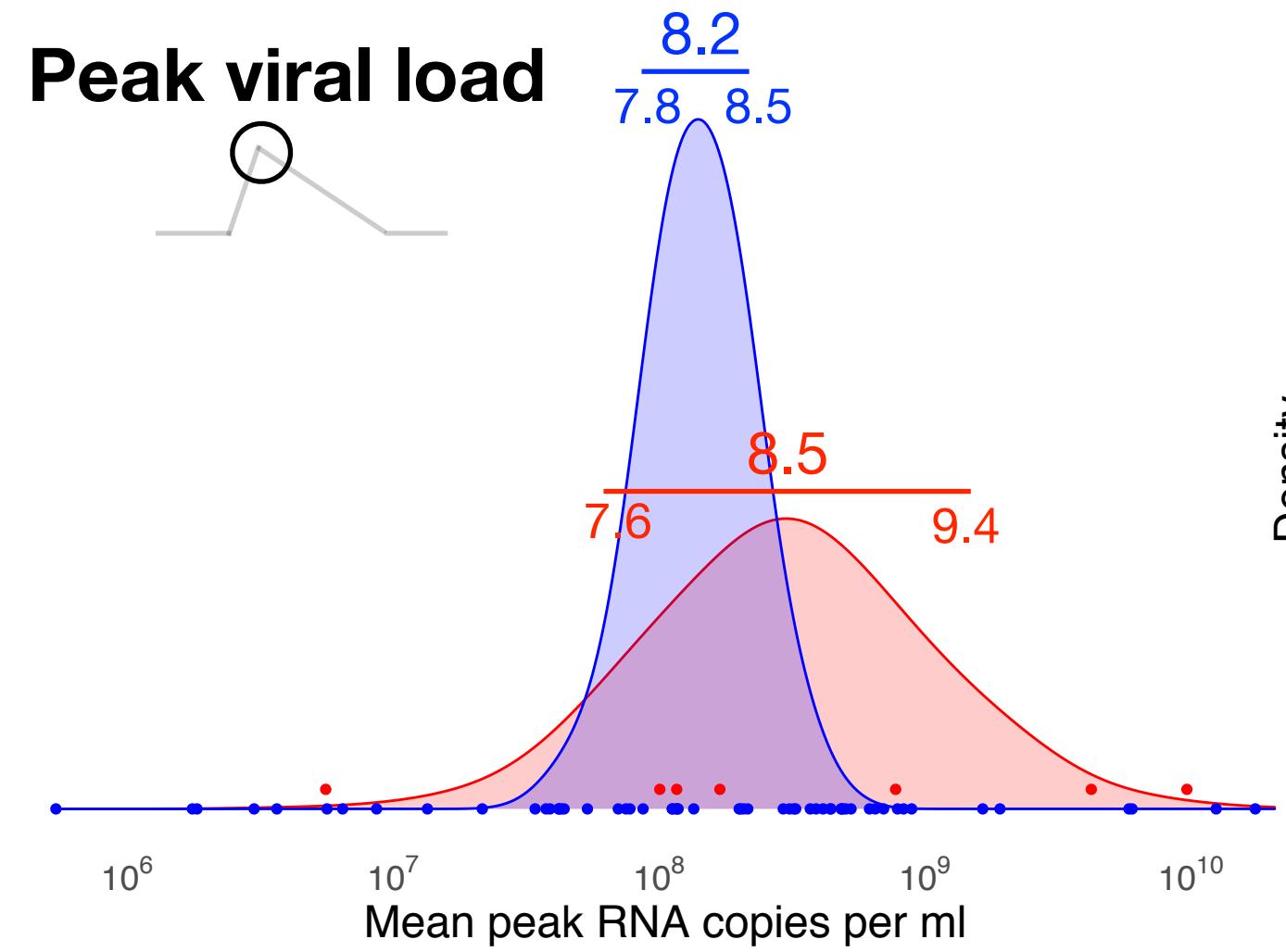
— B.1.1.7    — non-B.1.1.7

# Posterior mean distributions



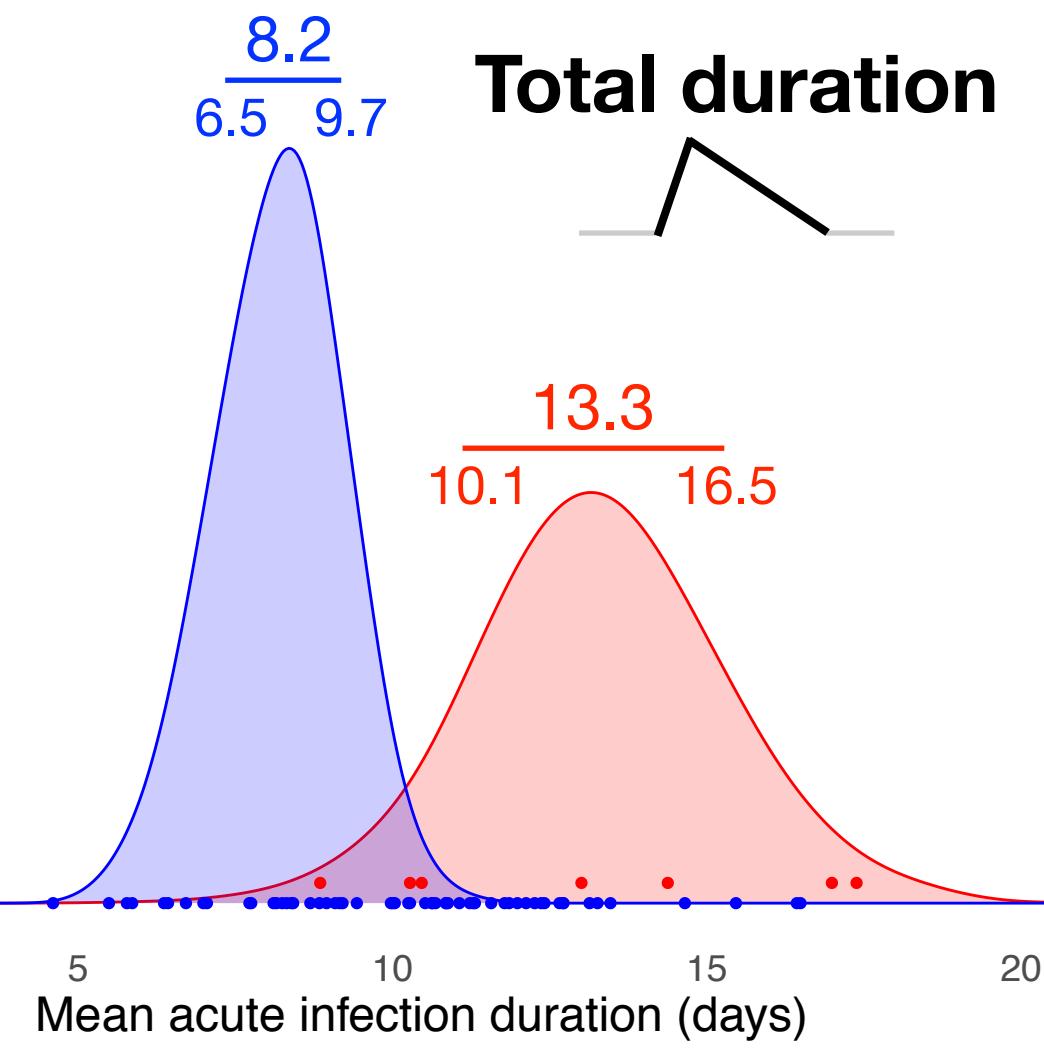
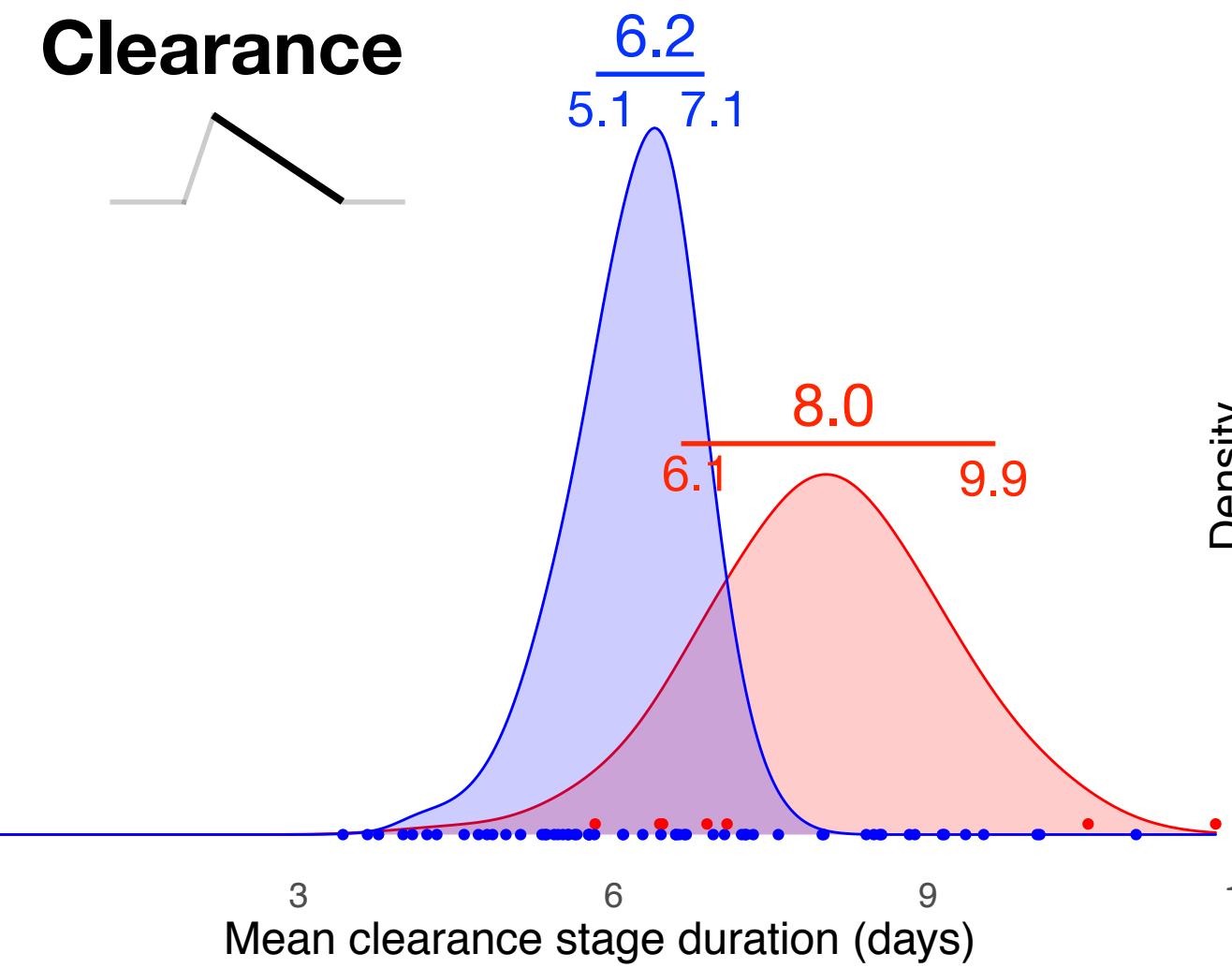
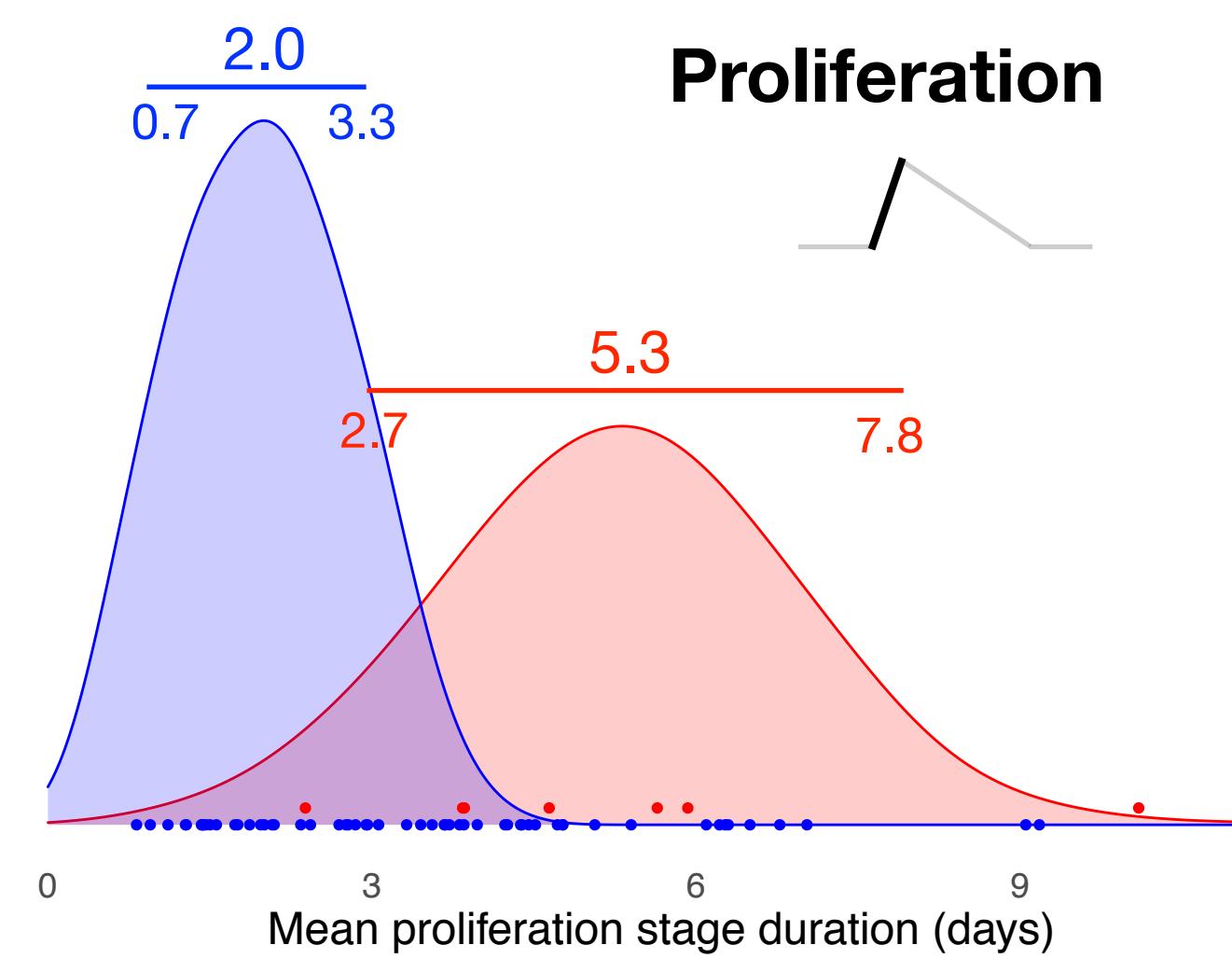
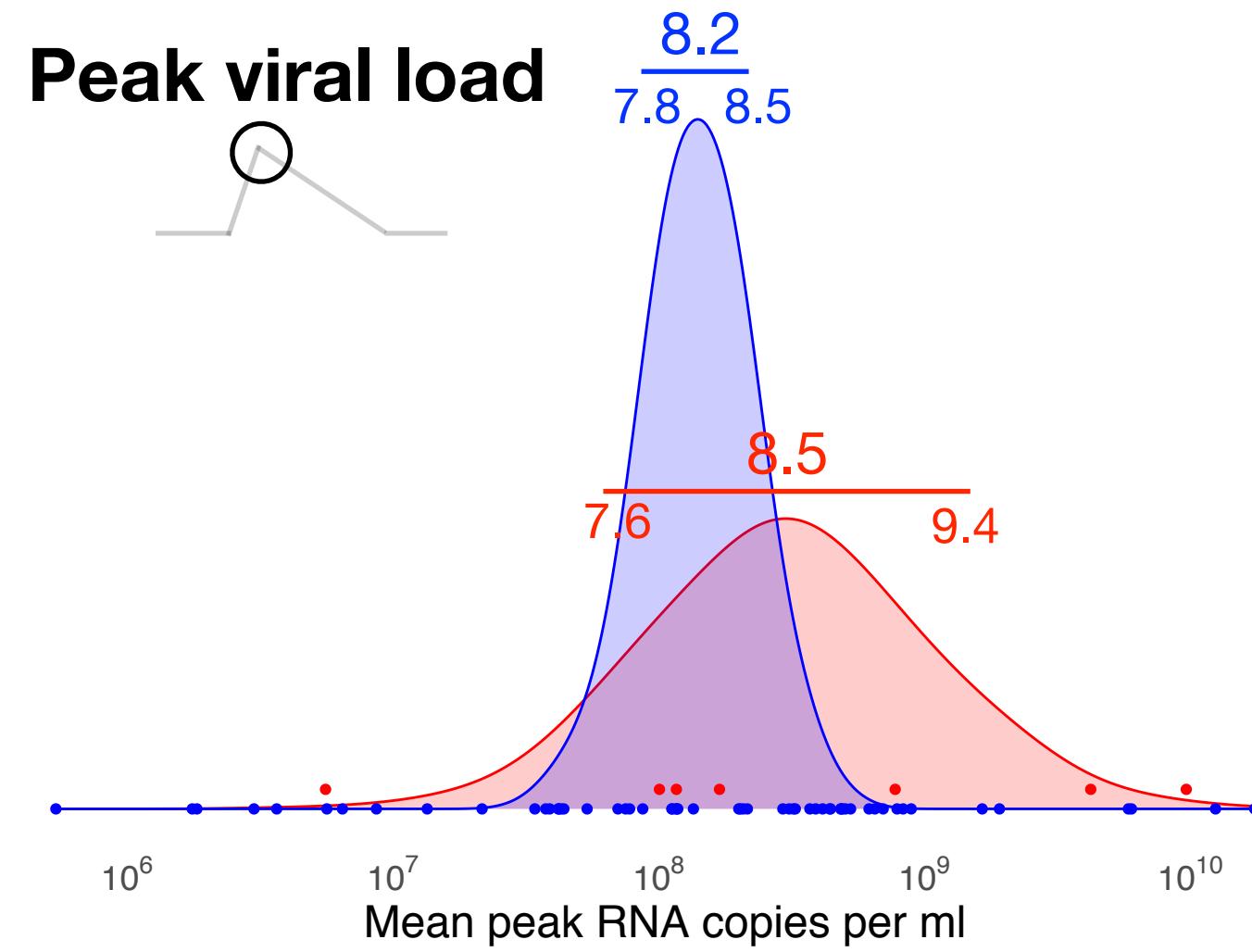
— B.1.1.7    — non-B.1.1.7

# Posterior mean distributions



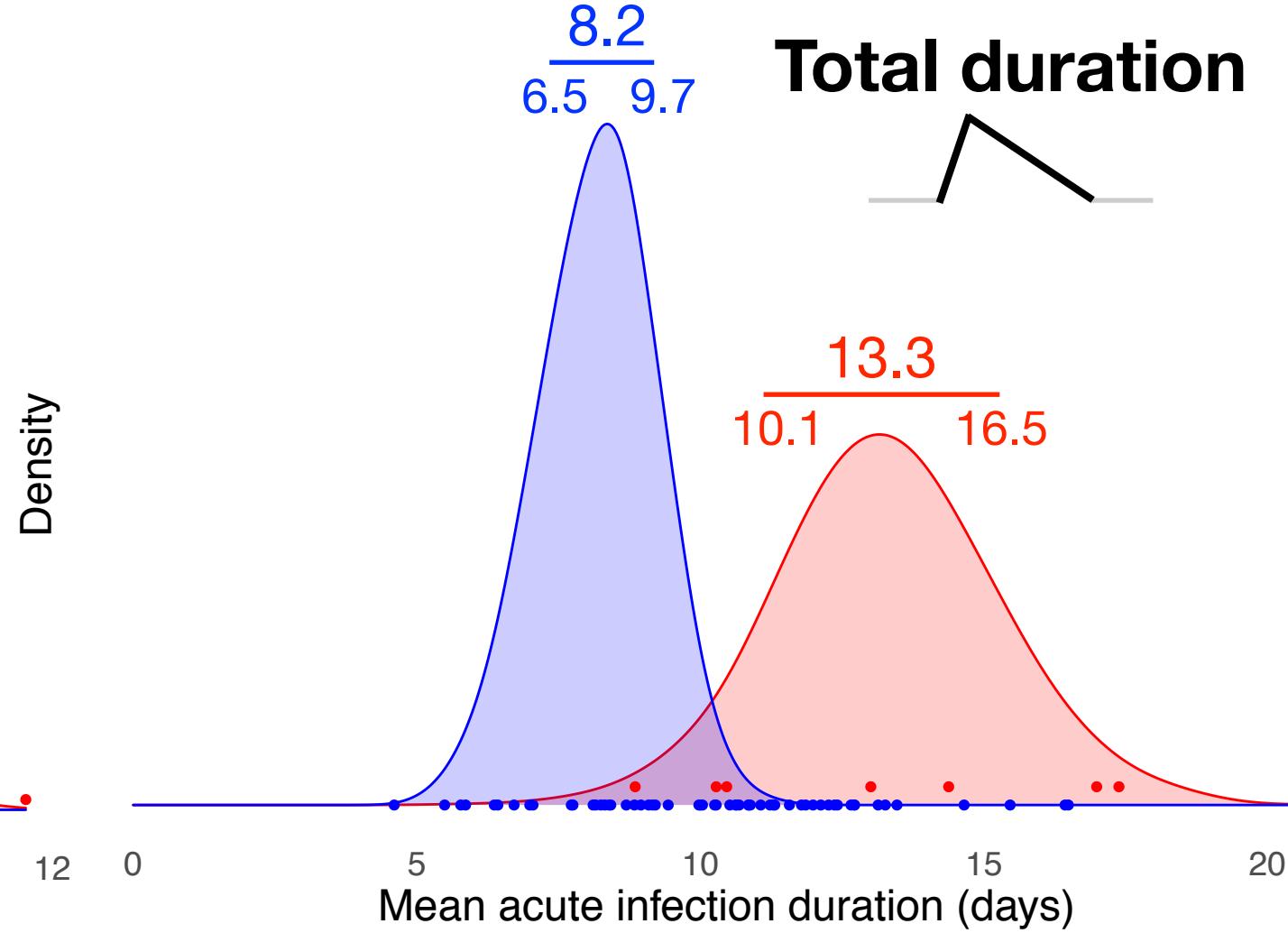
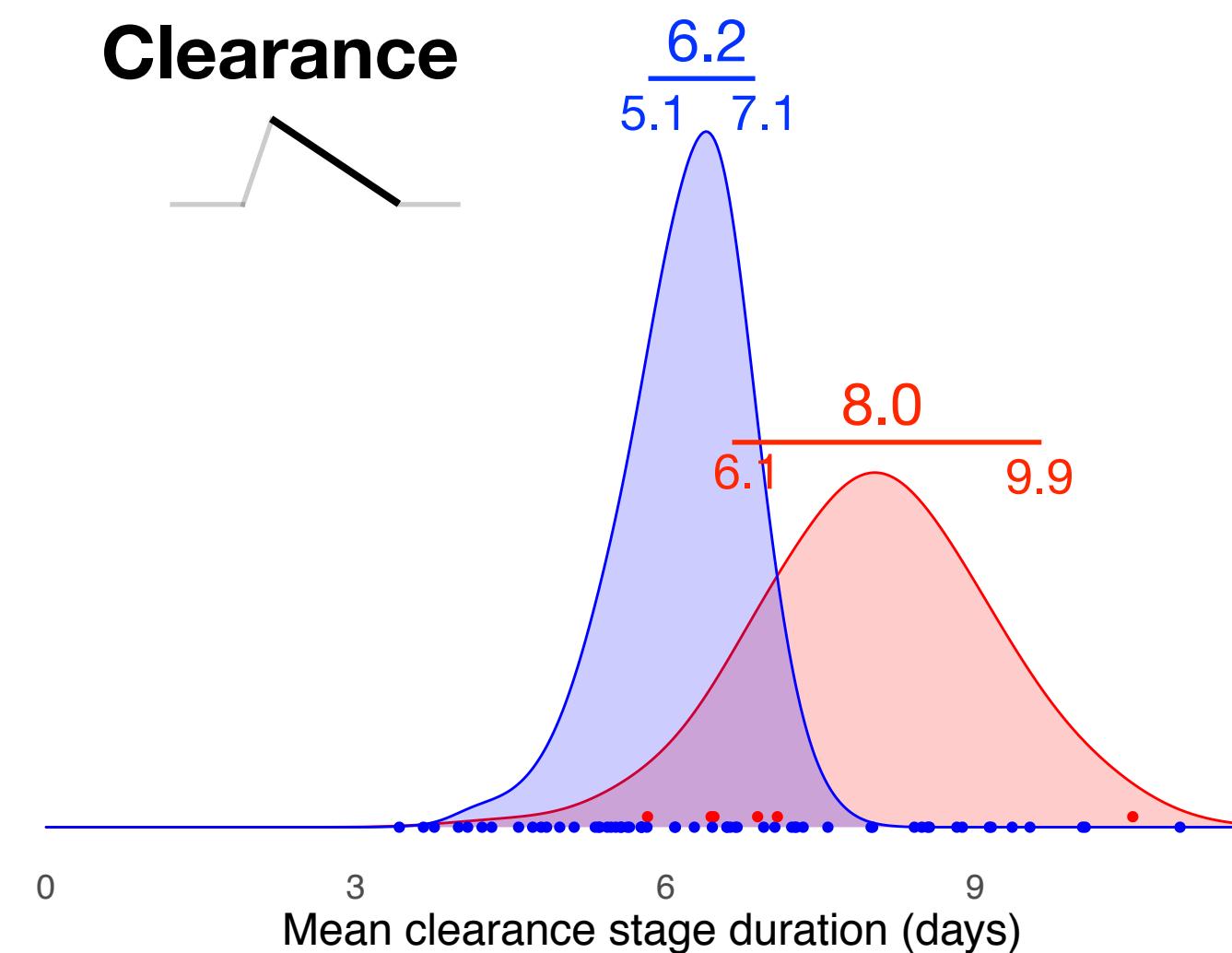
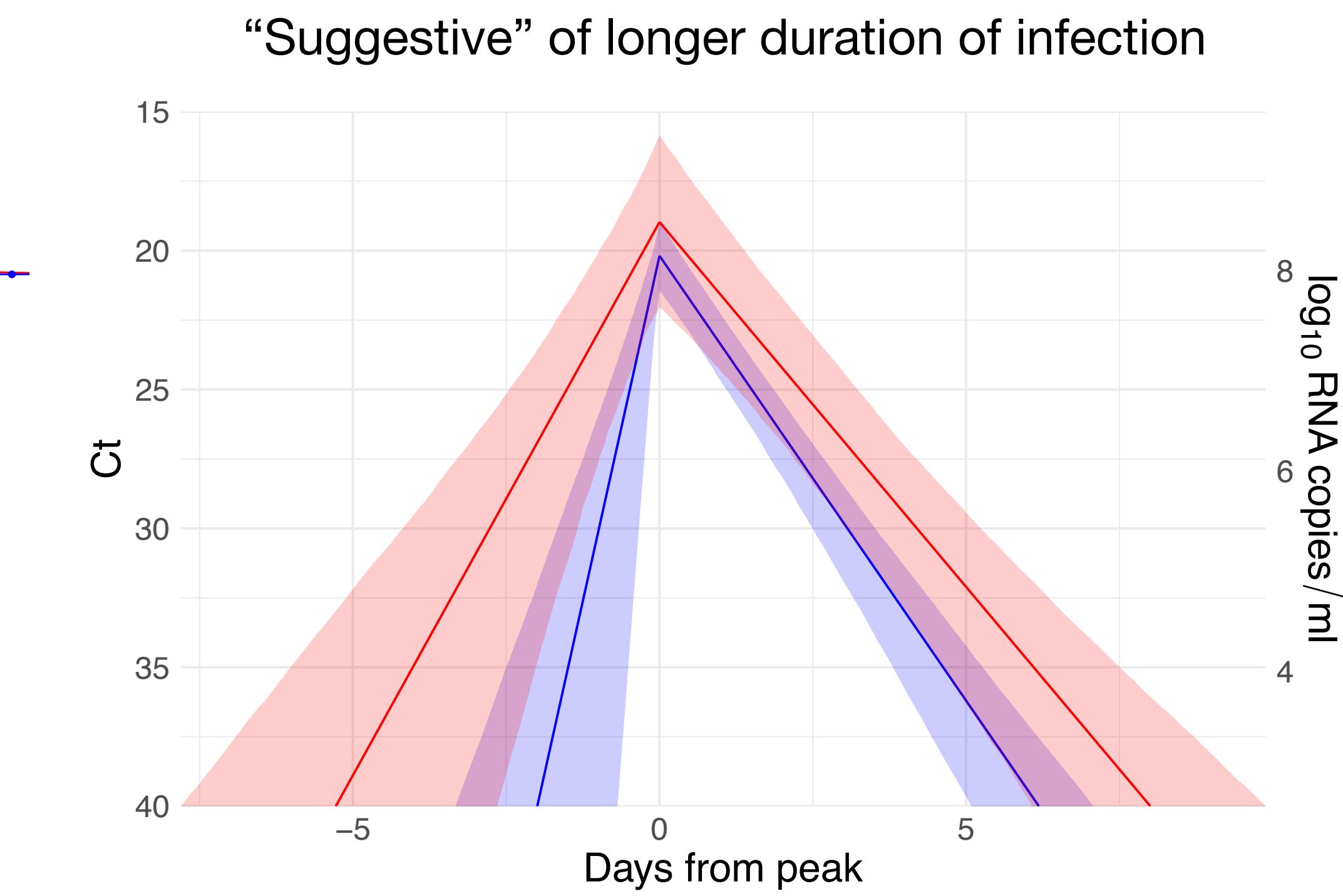
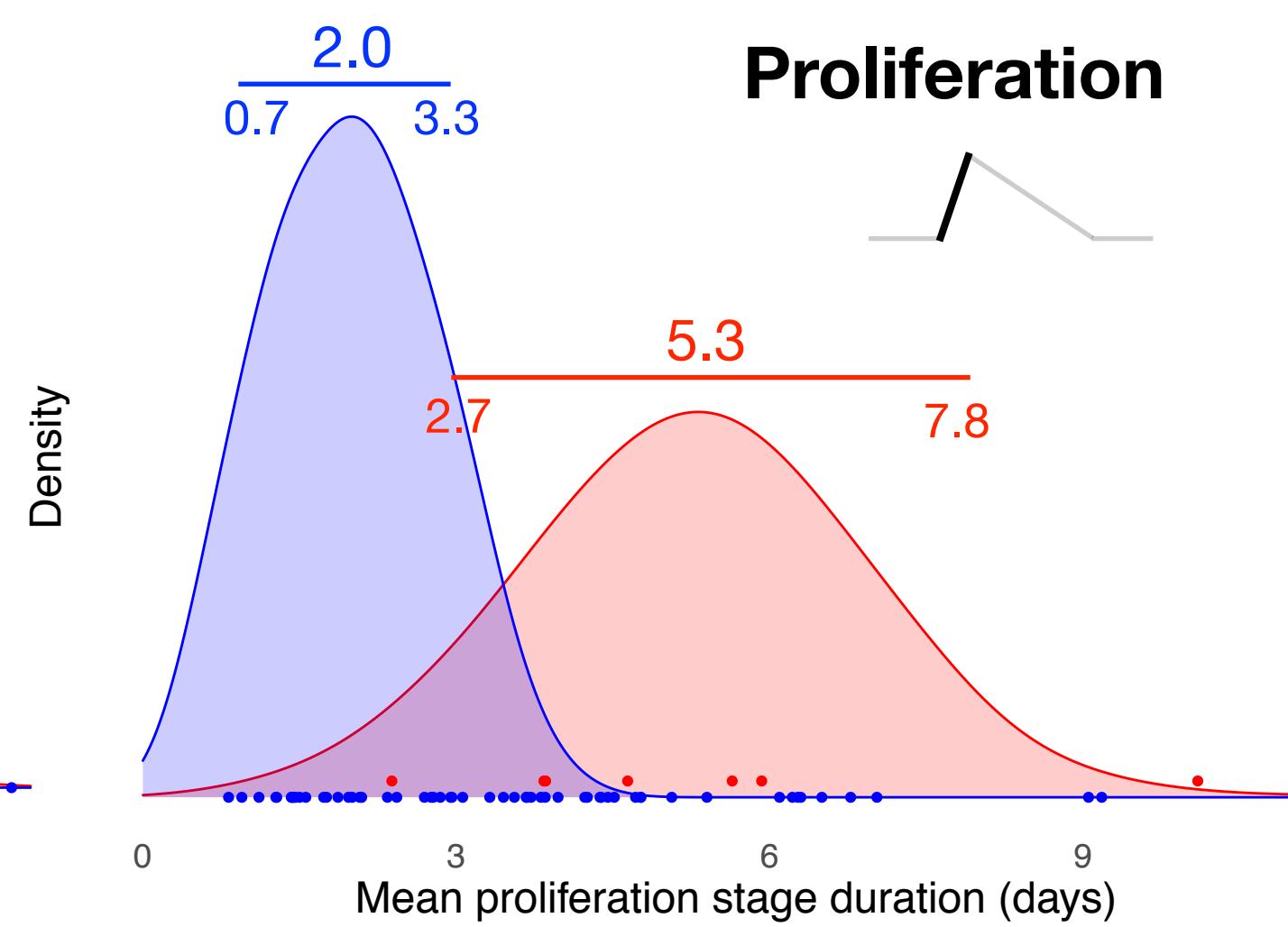
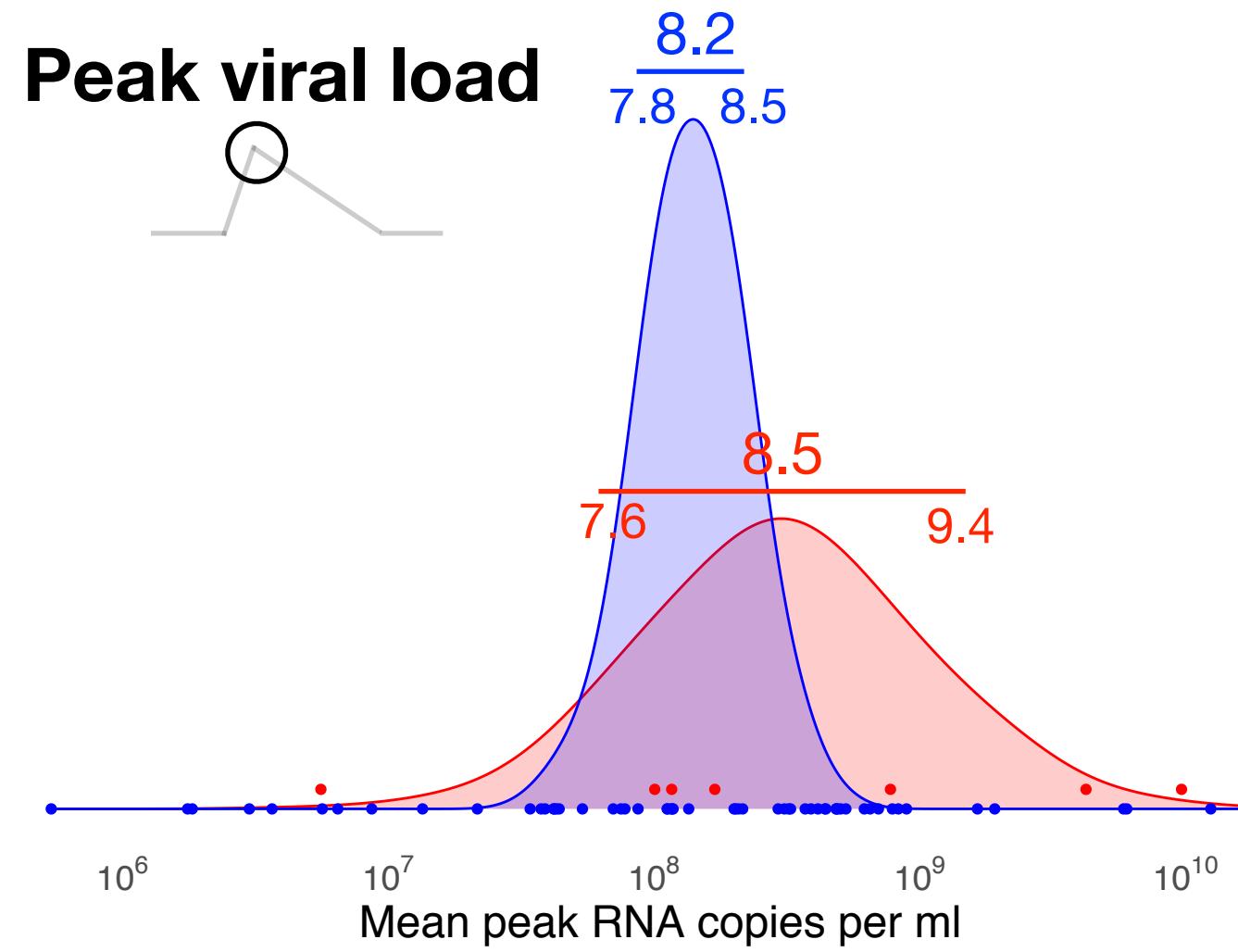
— B.1.1.7    — non-B.1.1.7

# Posterior mean distributions



— B.1.1.7    — non-B.1.1.7

# Posterior mean distributions



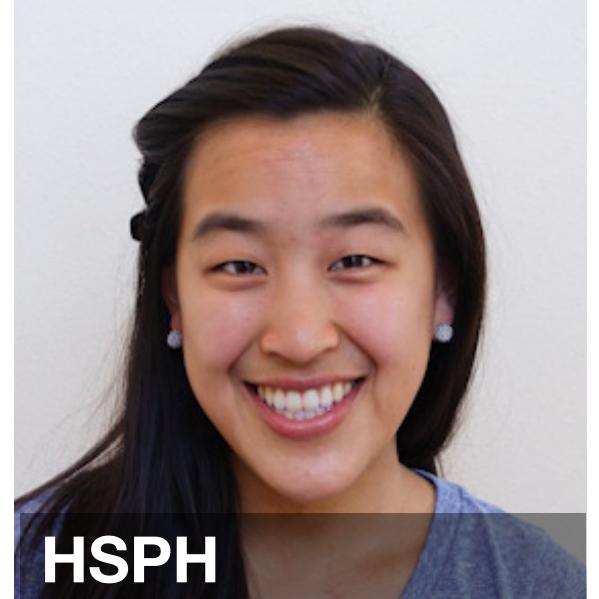
— B.1.1.7    — non-B.1.1.7

## Final thoughts

- Mathematics has improved our understanding of COVID-19 at every level.
- Unprecedented collaboration between mathematicians, epidemiologists, virologists, physicians...
- Which lessons should we carry forward, and how?

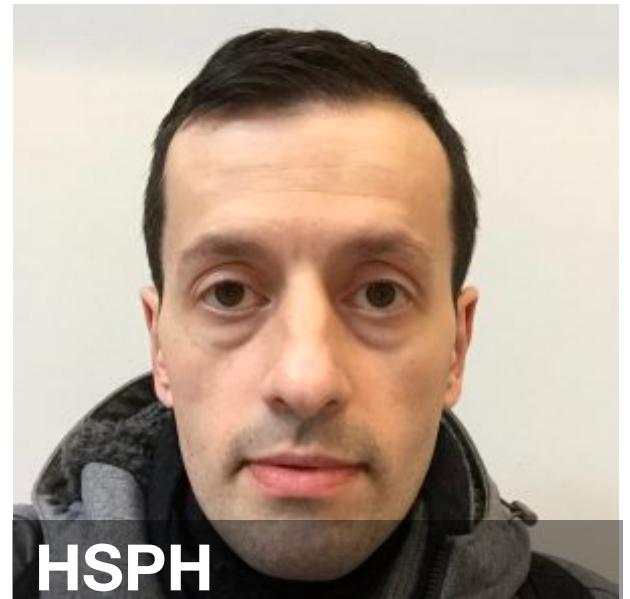
# Acknowledgements

## Long-term projections



HSPH

Christine Tedijanto



HSPH

Ed Goldstein



HSPH

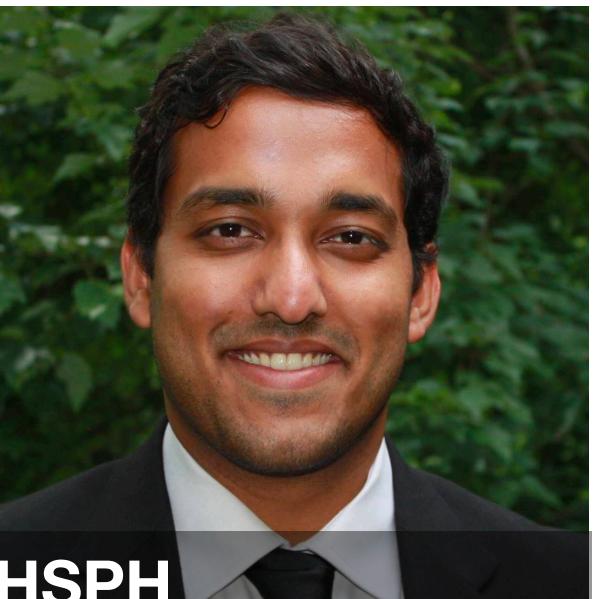
Marc Lipsitch



HSPH

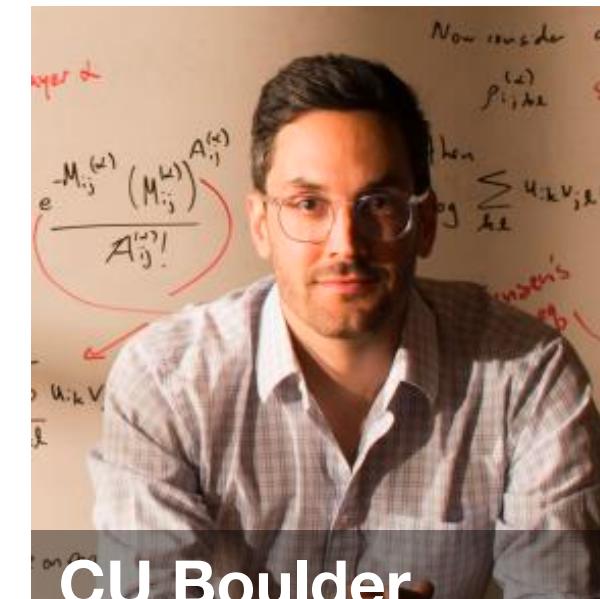
Yonatan Grad

## NYC prevalence



HSPH

Nishant Kishore



CU Boulder

Dan Larremore



HSPH

Caroline Buckee



HSPH

Yonatan Grad

**Weill Cornell Medicine**

Malavika Prabhu\*

Jon Snyder

Armin S. Razavi

**Columbia University**

Dena Goffman\*

Ruth Landau

Cynthia Gyamfi-Bannerman

**Icahn School of Medicine**

Yaakov Beilin\*

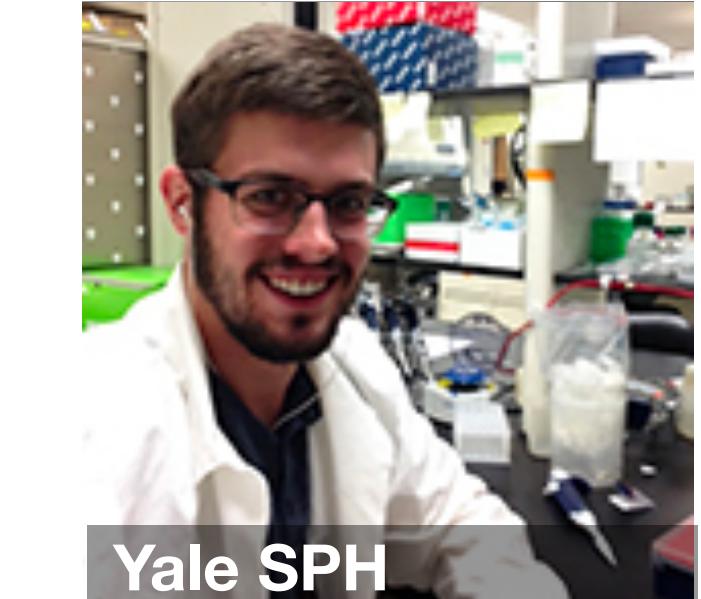
Daniel Katz

Jonathan Gal

Angela Bianco

Joanne Stone

## Viral trajectories



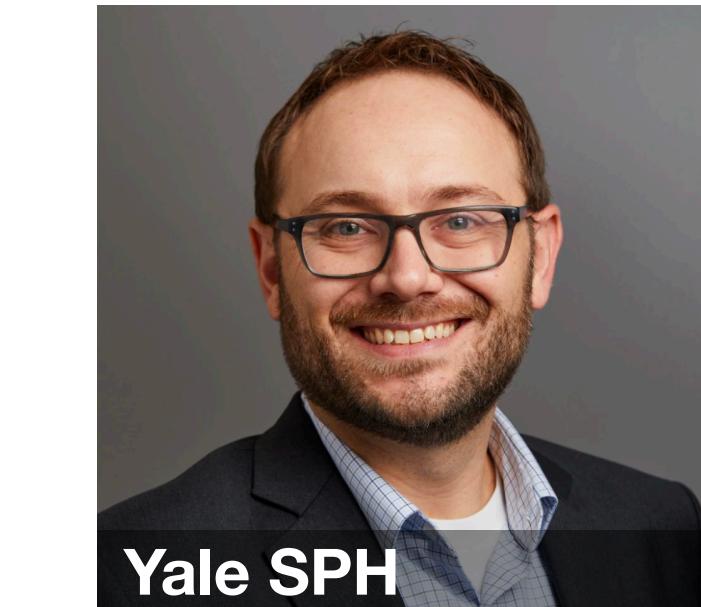
Yale SPH

Joseph Fauver



IQVIA

Christina Mack



Yale SPH

Nathan Grubaugh



HSPH

Yonatan Grad

**IQVIA**

Caroline G. Tai

Radhika M. Samant

**Yale School of Public Health**

Mallery I. Breban

Anne E. Watkins

**Duke University**

Deverick J. Anderson

**Columbia University**

David D. Ho