Design of Staged Alert System with a Wastewater Signal

Wastewater-Based Epidemiology Seminar Series

Shuotao (Sonny) Diao, Mar. 27, 2024
Joint work with Guyi Chen and David Morton

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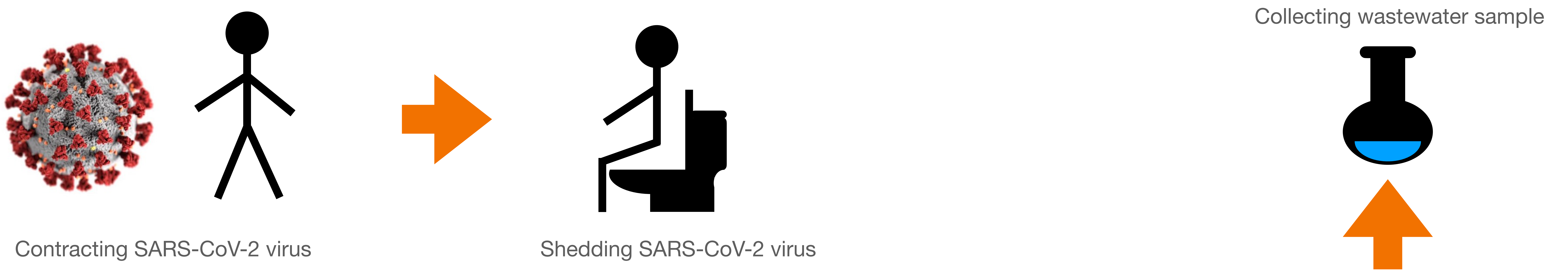
Outline

- SARS-CoV-2 virus in the wastewater
- Staged-alert system and SEIR-V model
- Retrospective analysis of staged-alert system with a wastewater signal

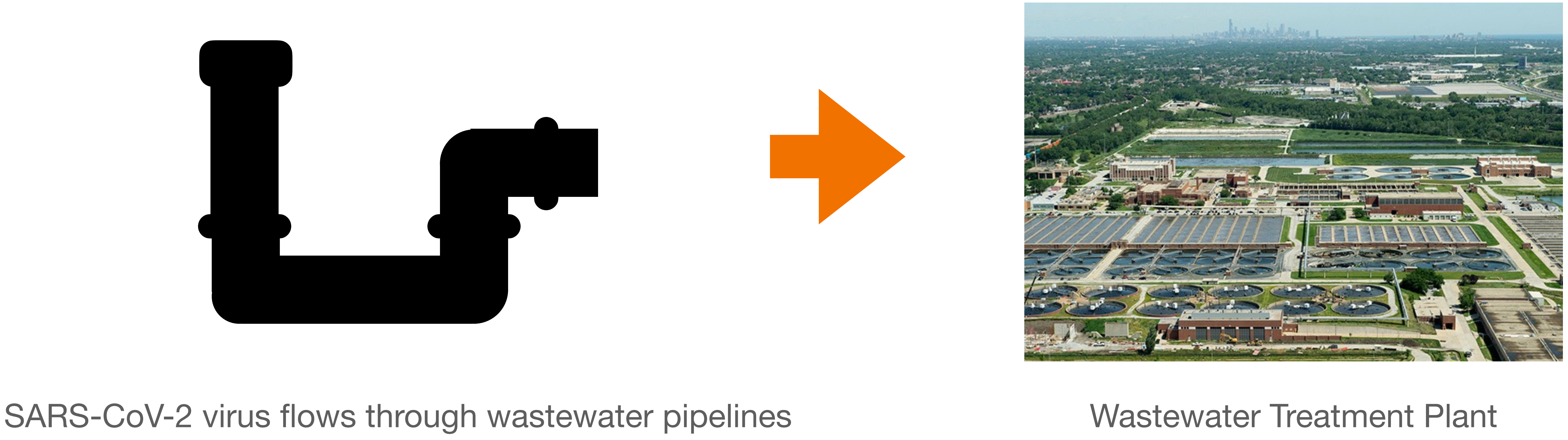
Outline

- **SARS-CoV-2 virus in the wastewater**
- Staged alert system and SEIR-V model
- Retrospective analysis of staged alert system with a wastewater signal

How does SARS-CoV-2 virus appear in the wastewater?

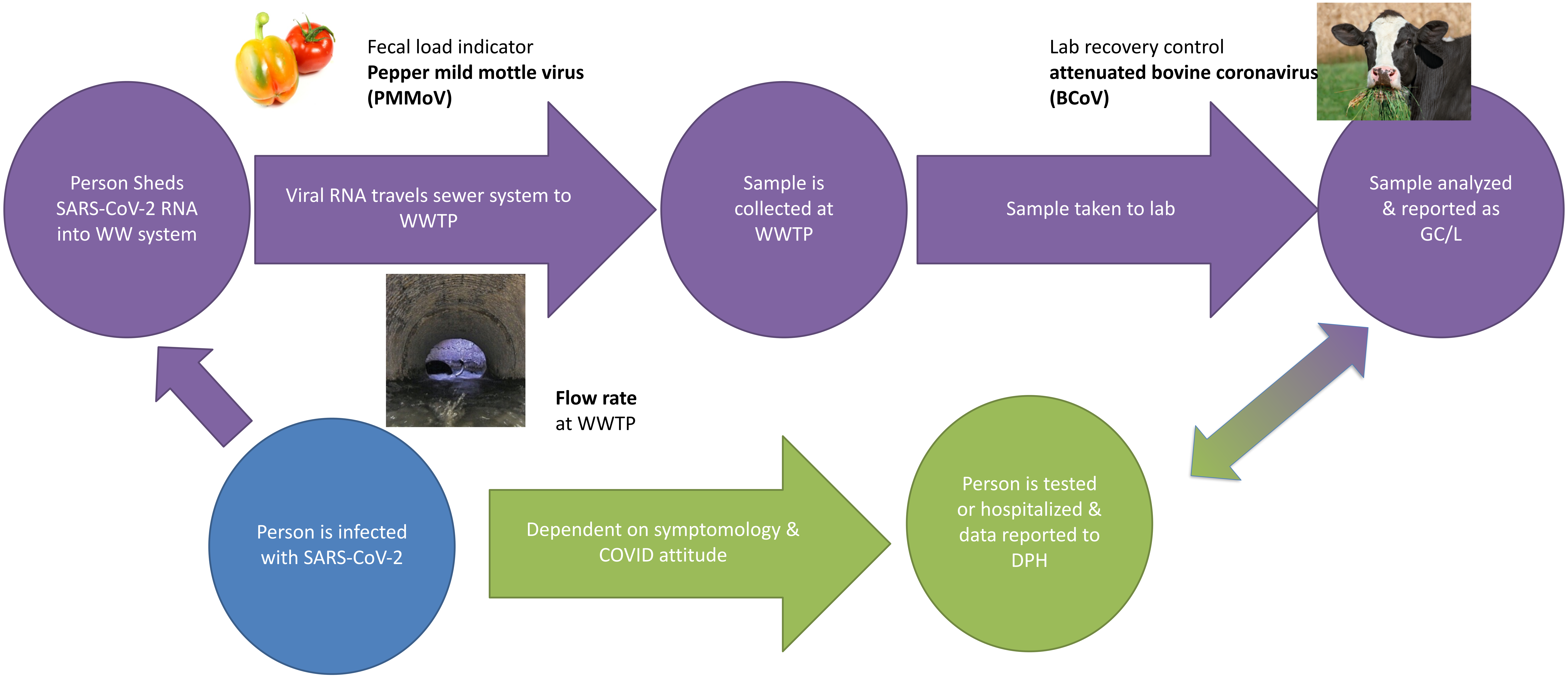


Motivation:
We want to know how many people are sick.
Solutions:
Use wastewater to estimate how severe the pandemic is.
Challenges:
It is not straightforward to connect wastewater to prevalence because of flow rate, temperature, chemical composition, population changes, etc.



Credits:
1. COVID-19 virus image is from https://phil.cdc.gov/details.aspx?pid=23312
2. Calumet WRP image is from https://legacy.mwrd.org/irj/portal/anonymous?NavigationTarget=navurl://1e47bf16ca721c69e2e239f32ce809ca

Relating RNA in wastewater to public health (Leisman, et al., 2024)



Leisman, Katelyn Plaisier, et al. "A modeling pipeline to relate municipal wastewater surveillance and regional public health data." *Water Research* 252 (2024): 121178.

Outline

- SARS-CoV-2 virus in the wastewater
- Staged alert system and SEIR-V model
- Retrospective analysis of staged alert system with a wastewater signal

Model the pandemic (i.e., how a disease spreads,
how public interventions may affect the outcome of the pandemic)

Mitigate a future surge of the pandemic

Outline

- SARS-CoV-2 virus in the wastewater
- **Staged-alert system and SEIR-V model**
  - **Basic SEIR-V Model**
  - **Finite-Difference Equations of SEIR-V Model**
  - **High-Fidelity Model**
  - **Threshold Optimization Problem**
- Retrospective analysis of staged-alert system with a wastewater signal

How does the staged-alert system work?

Question: How do we model the performance of the staged-alert system?

Applications of the Staged-Alert System

Example: Staged-Alert System used by Austin, Texas

COVID-19: Risk-Based Guidelines

	Practice Good Hygiene / Stay Home If Sick / Avoid Sick People	Maintain Social Distancing	Wear Facial Coverings	Higher Risk Individuals (Age over 65, diabetes, high blood pressure, heart, lung and kidney disease, immunocompromised, obesity)			Lower Risk Individuals (No substantial underlying health conditions)			Workplaces Open
				Avoid Gatherings	Avoid Non-Essential Travel	Avoid Dining/ Shopping	Avoid Gatherings	Avoid Non-Essential Travel	Avoid Dining/ Shopping	
Stage 1	•			greater than 25		except with precautions	gathering size TBD			all businesses
Stage 2	•	•	•	greater than 10		except as essential	greater than 25		except with precautions	essential and re-opened businesses
Stage 3	•	•	•	social and greater than 10	•	except as essential	social and greater than 10		except with precautions	essential and re-opened businesses
Stage 4	•	•	•	social and greater than 2	•	except as essential	social and greater than 10	•	except expanded essential businesses	expanded essential businesses
Stage 5	•	•	•	outside of household	•	except as essential	outside of household	•	except as essential	essential businesses only

Use this color-coded alert system to understand the stages of risk. This chart provides recommendations on what people should do to stay safe during the pandemic. Individual risk categories identified pertain to known risks of complication and death from COVID-19. This chart is subject to change as the situation evolves.

AustinTexas.gov/COVID19 Published: May 13, 2020

APH Austin Public Health
PREVENT. PROMOTE. PROTECT.

Applications of the Staged-Alert System

Example: Staged-Alert System used by UK

Coronavirus alert levels in UK

Stage of outbreak	Level	Measures in place
Risk of healthcare services being overwhelmed	5	Extremely strict social distancing
Transmission is high or rising exponentially	4	Social distancing continues
Virus is in general circulation	3	Gradual relaxation of restrictions
Number of cases and transmission is low	2	Minimal social distancing, enhanced tracing
Covid-19 no longer present in UK	1	Routine international monitoring

Source : UK government

BBC

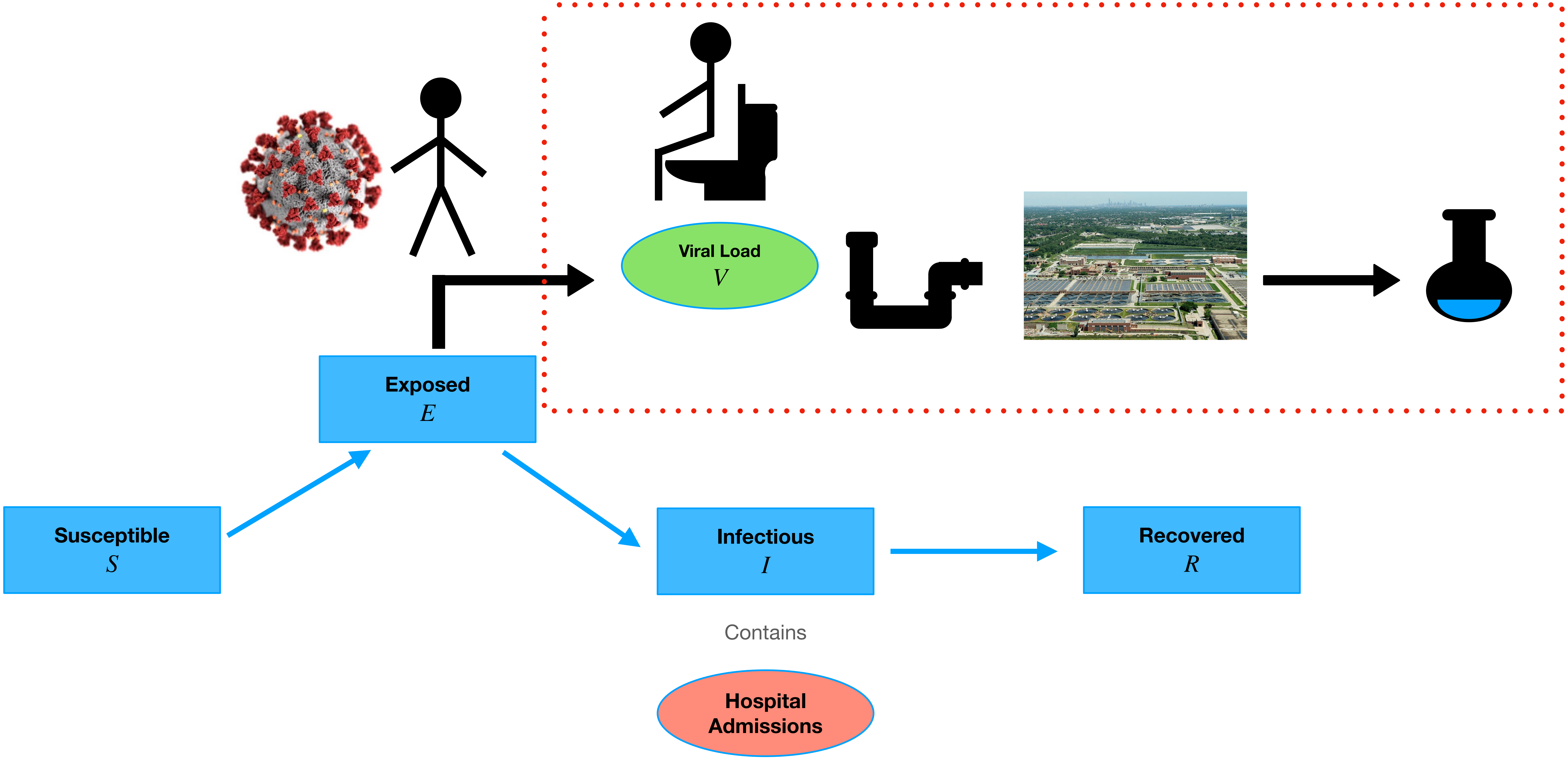
Applications of the Staged-Alert System

Example: Staged-Alert System used by CDC

CDC's Staged Alert System

COVID-19 Community Levels – Use the Highest Level that Applies to Your Community				
New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High
Fewer than 200	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	<10.0%	10.0-14.9%	≥15.0%
200 or more	New COVID-19 admissions per 100,000 population (7-day total)	NA	<10.0	≥10.0
	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	NA	<10.0%	≥10.0%

SEIR-V Compartmental Model



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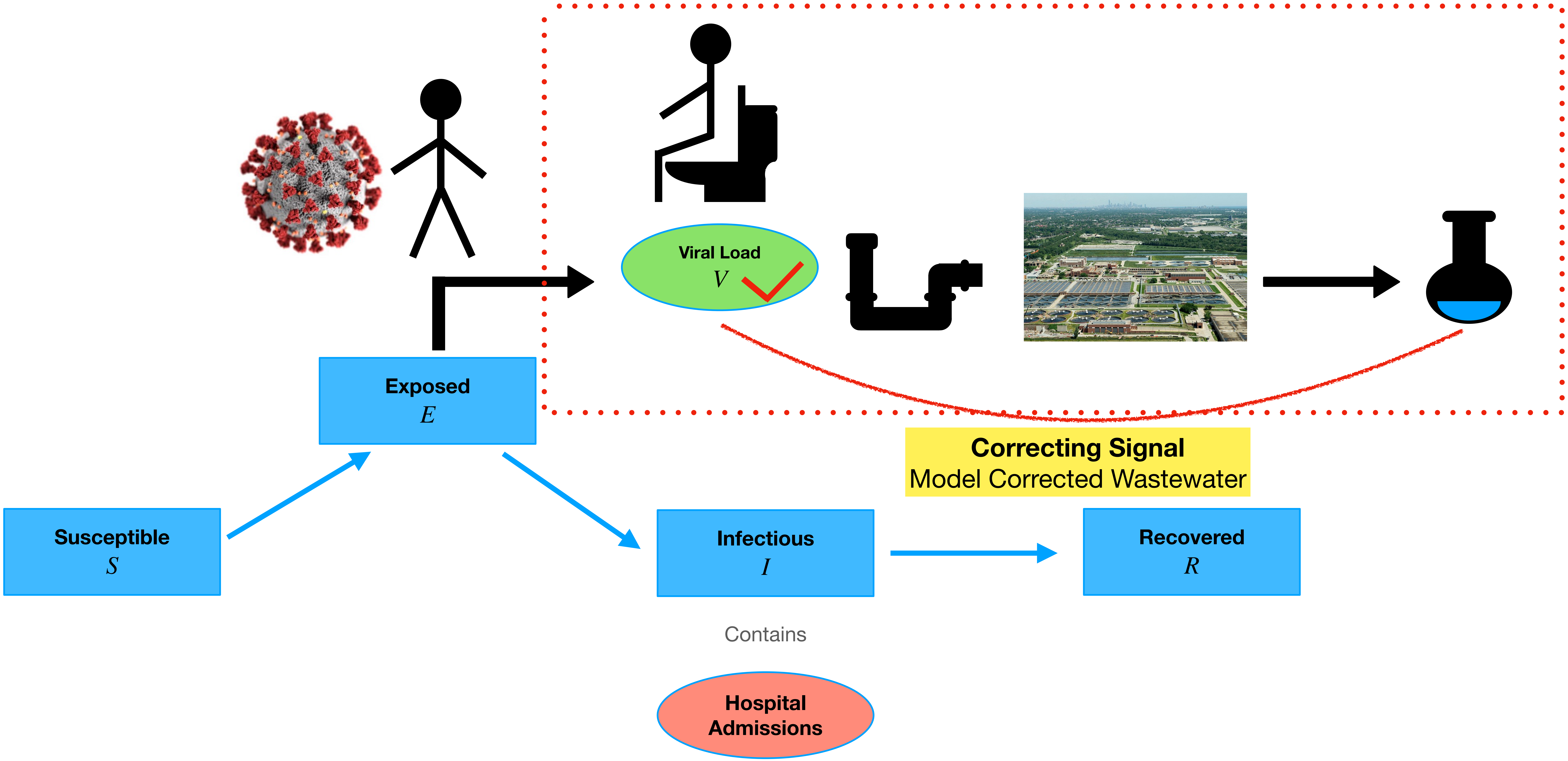

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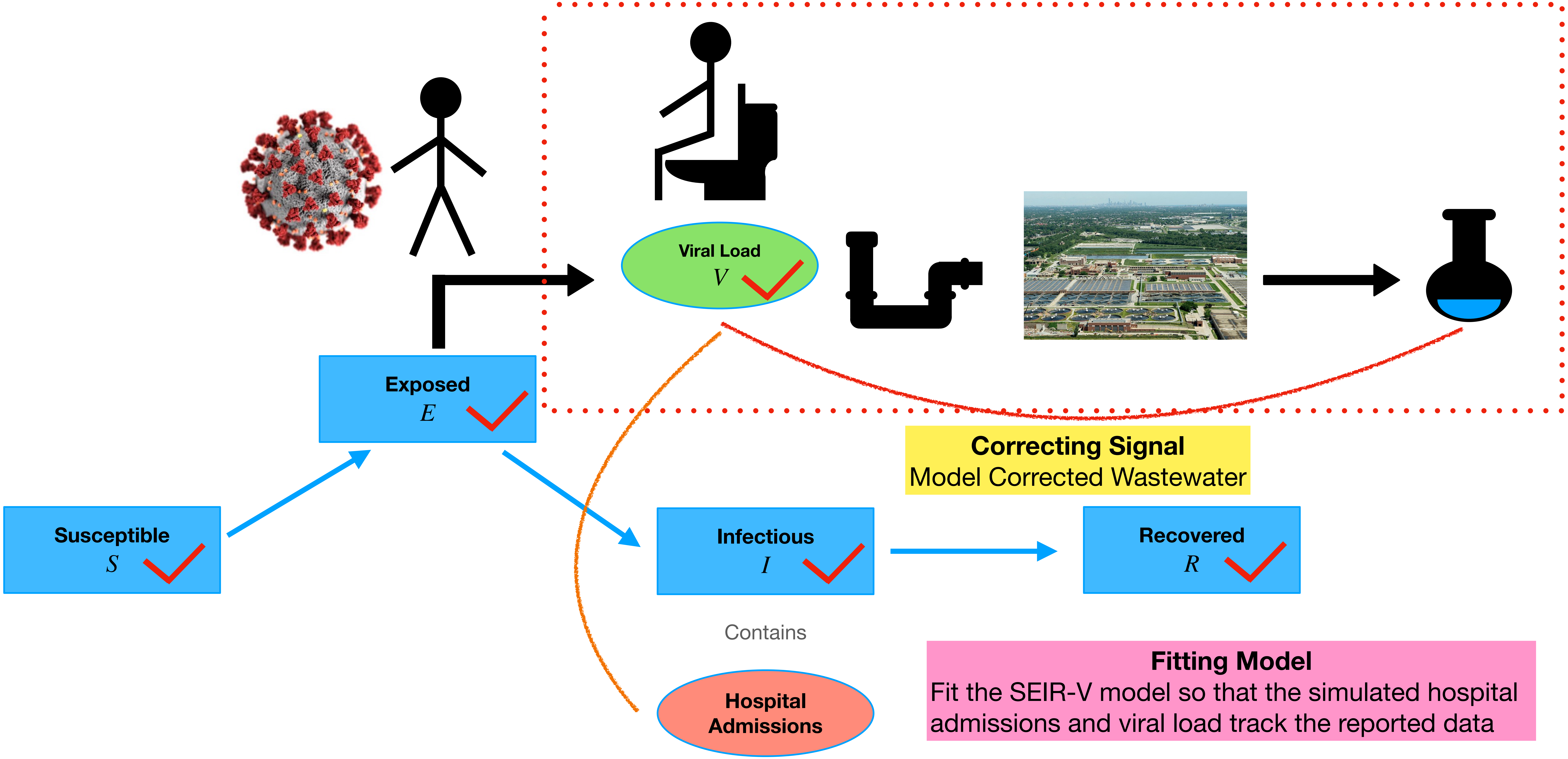

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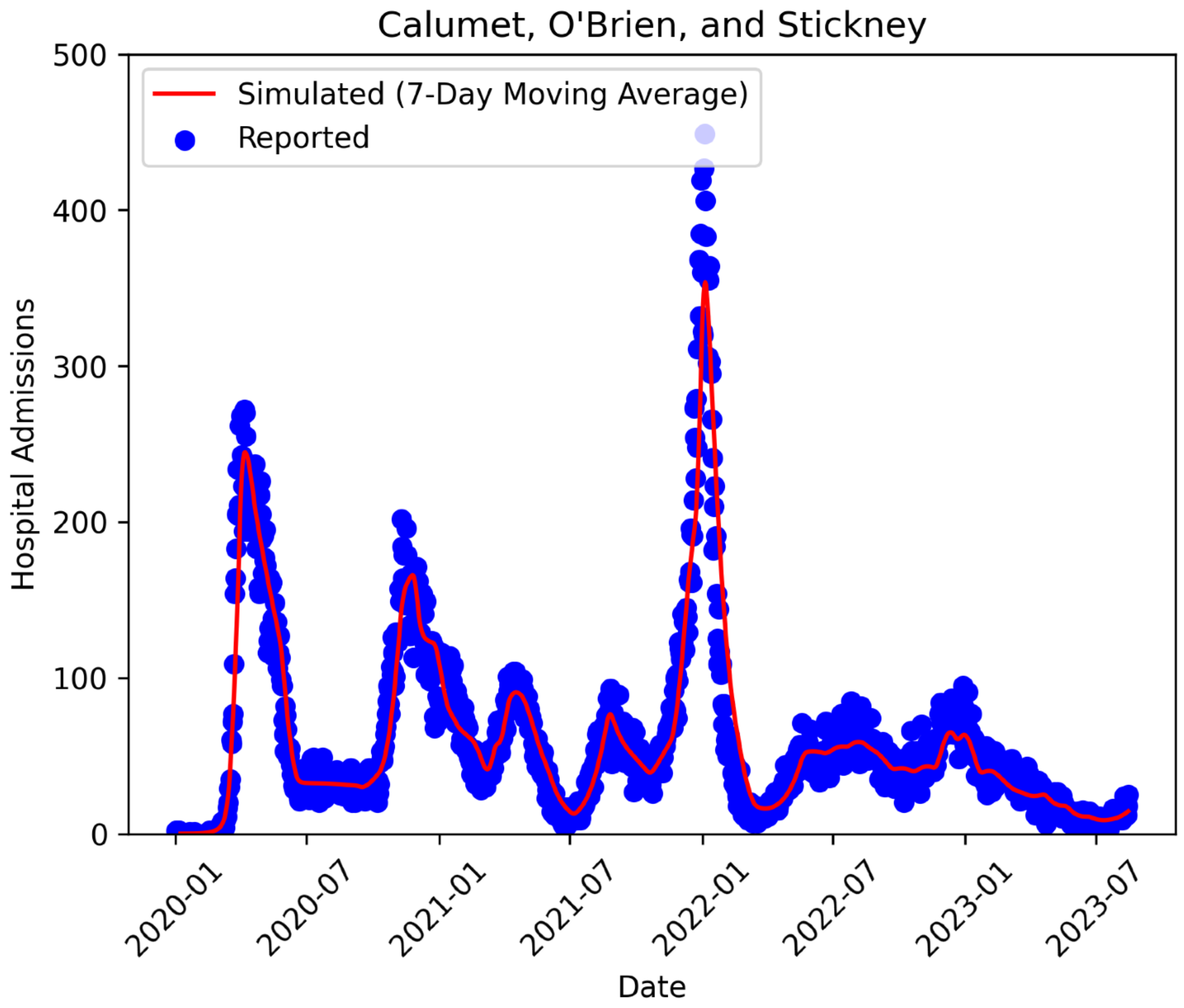
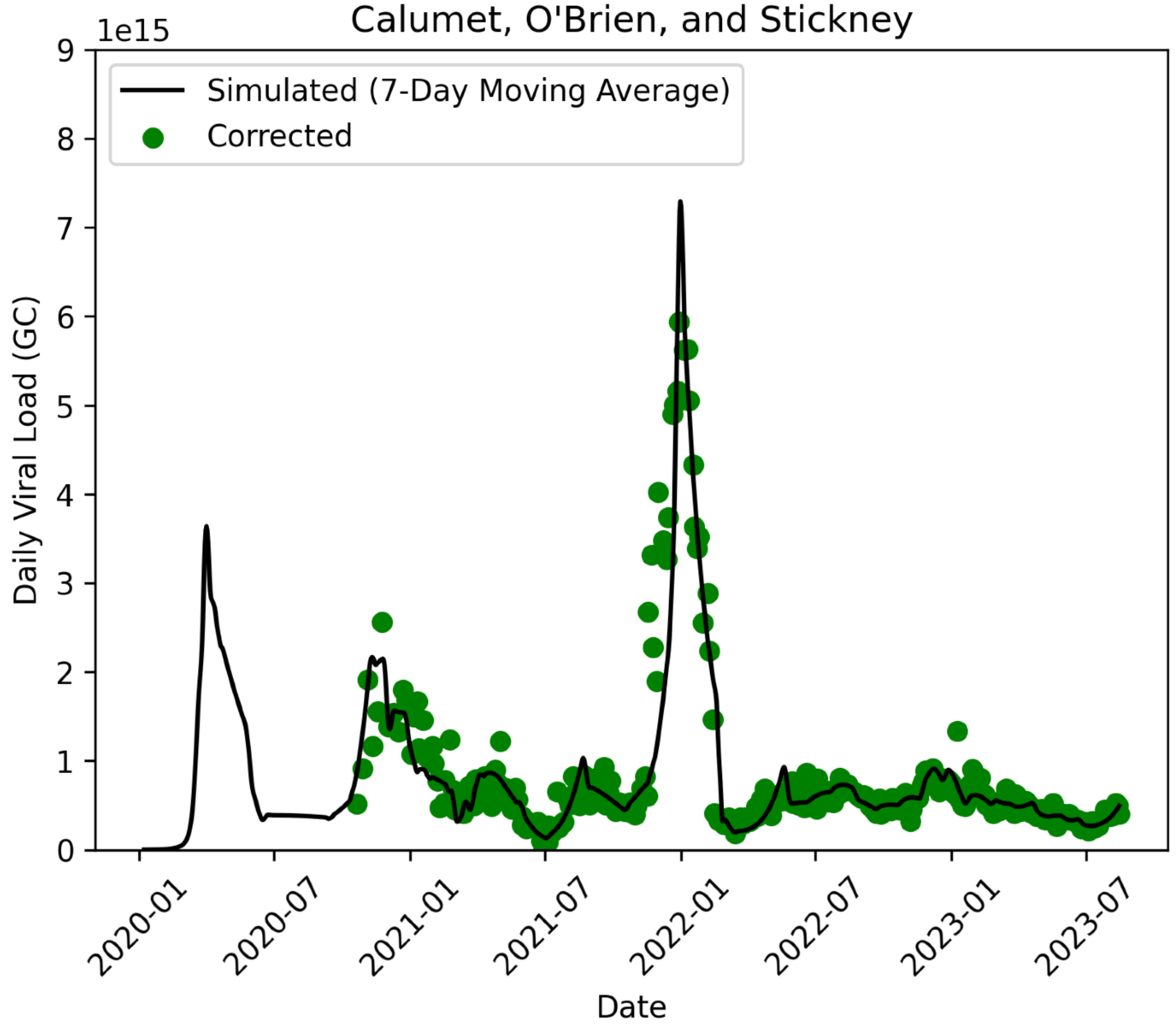




Load

V

Susce

S

Infectious

I

R

Contains

Hospital Admissions

Fitting Model

Fit the SEIR-V model so that the simulated hospital admissions and viral load track the reported data

SEIR-V Compartmental Model

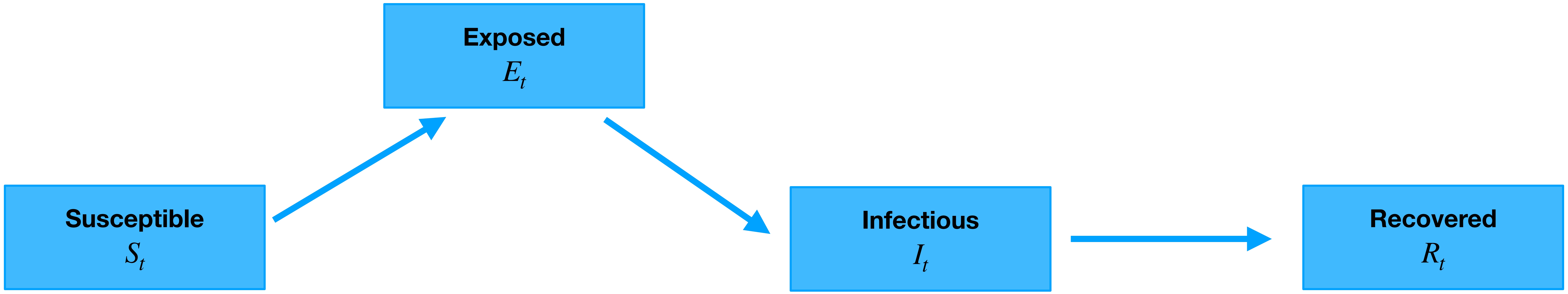
Deterministic SEIR Model

Daily exposed individuals: $$S(t+1) - S(t) = -\Delta S(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right]$$

Daily change in the compartment E: $$E(t+1) - E(t) = S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right] - \lambda E(t)$$

Daily change in the compartment I: $$I(t+1) - I(t) = \lambda E(t) - \gamma I(t)$$

Daily change in the compartment R: $$R(t+1) - R(t) = \gamma I(t)$$



SEIR-V Compartmental Model

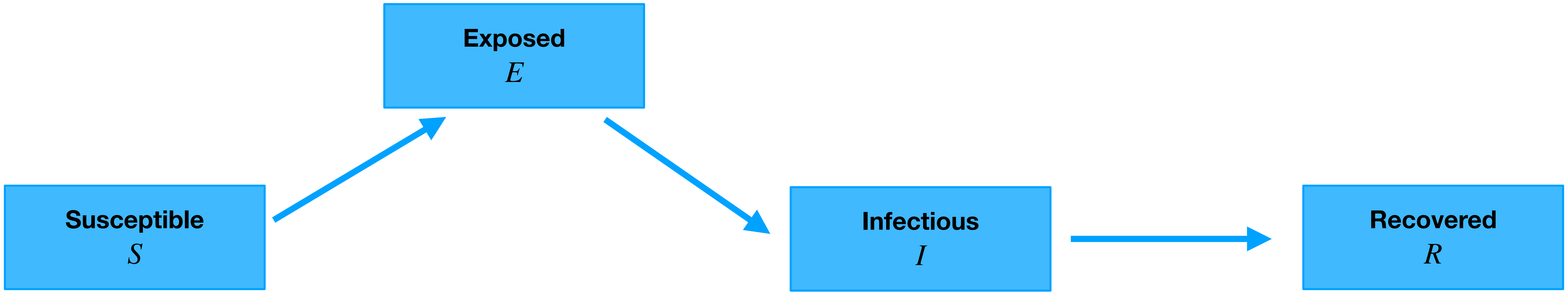
Stochastic SEIR Model

Daily exposed individuals: $\tilde{S}(t+\Delta t) - \tilde{S}(t) = -\tilde{\xi}_1,\ \tilde{\xi}_1 \sim \text{Binomial}\left(\tilde{S}(t), \frac{(1-\kappa(t))\beta}{N}\tilde{I}(t)\Delta t\right)$

Daily change in the compartment E: $\tilde{E}(t+\Delta t) - \tilde{E}(t) = \tilde{\xi}_1 - \tilde{\xi}_2,\ \tilde{\xi}_2 \sim \text{Binomial}(\tilde{E}(t), \lambda\Delta t)$

Daily change in the compartment I: $\tilde{I}(t+\Delta t) - \tilde{I}(t) = \tilde{\xi}_2 - \tilde{\xi}_3,\ \tilde{\xi}_3 \sim \text{Binomial}\left(\tilde{I}(t), \gamma\Delta t\right)$

Daily change in the compartment R: $\tilde{R}(t+\Delta t) - \tilde{R}(t) = \tilde{\xi}_3$



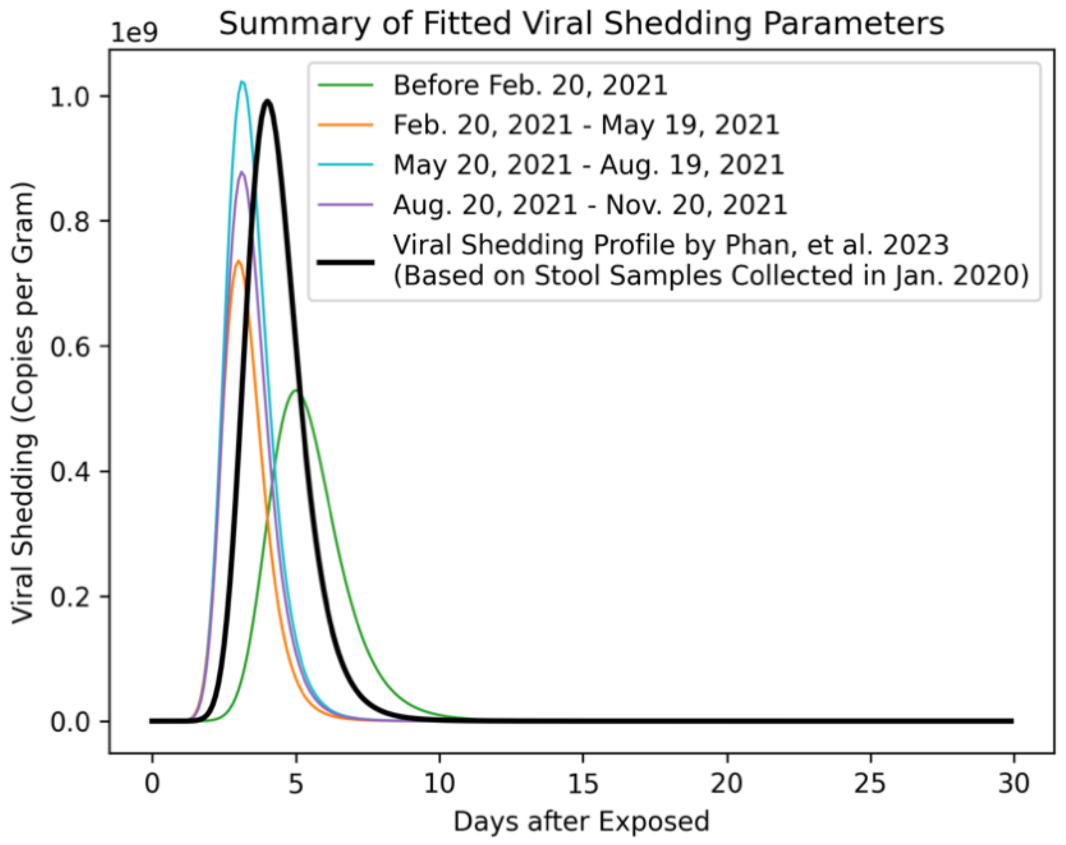
SEIR-V Compartmental Model

Viral Load Model

Daily exposed individuals: $$S(t+\Delta t) - S(t) = -\Delta S(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\Delta t\right]$$

Daily viral load: $$V(t) = \sum_{i=0}^{N} \phi_{i\Delta t:(i+1)\Delta t}(\omega)\Delta S(t - i\Delta t)$$

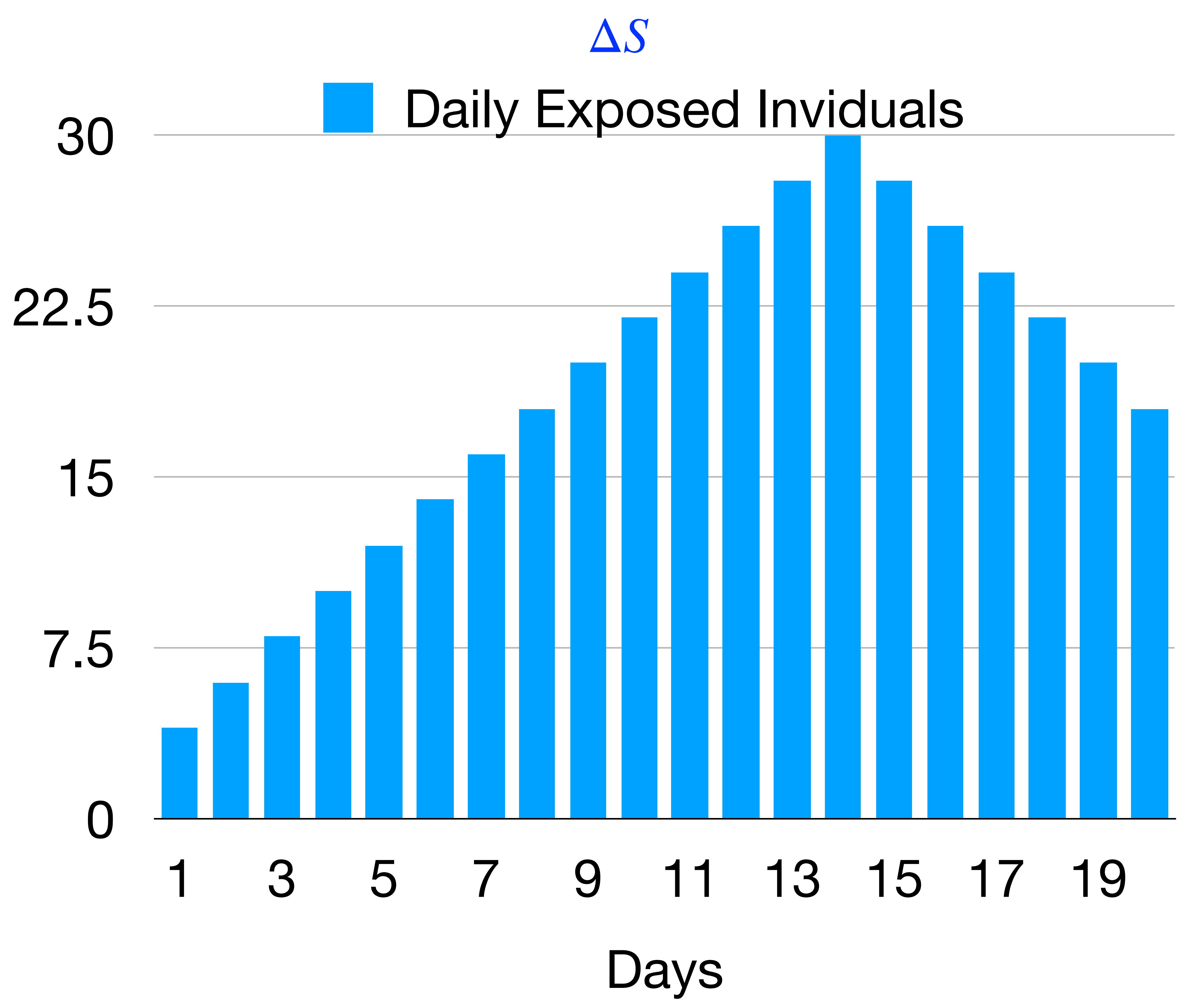
Viral Shedding Function: $$f(t;\omega) = 10^{\frac{\omega_1 t}{\omega_2^2 + t^2}} \qquad \phi_{i\Delta t:(i+1)\Delta t}(\omega) = \int_{i\Delta t}^{(i+1)\Delta t} f(t;\omega)dt$$

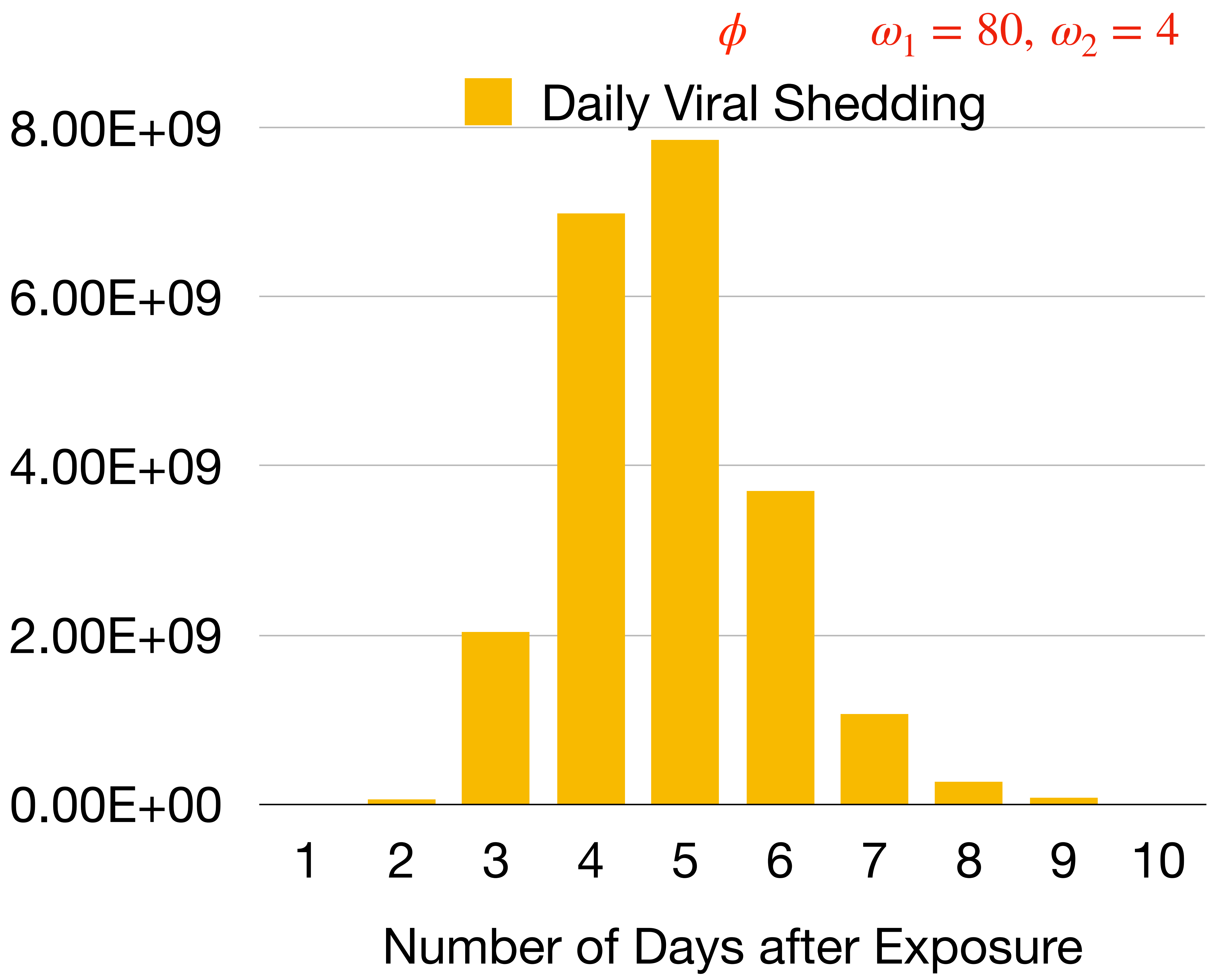


Susceptible S_t → **Exposed** E_t → **Infectious** I_t → **Recovered** R_t

SEIR-V Compartmental Model

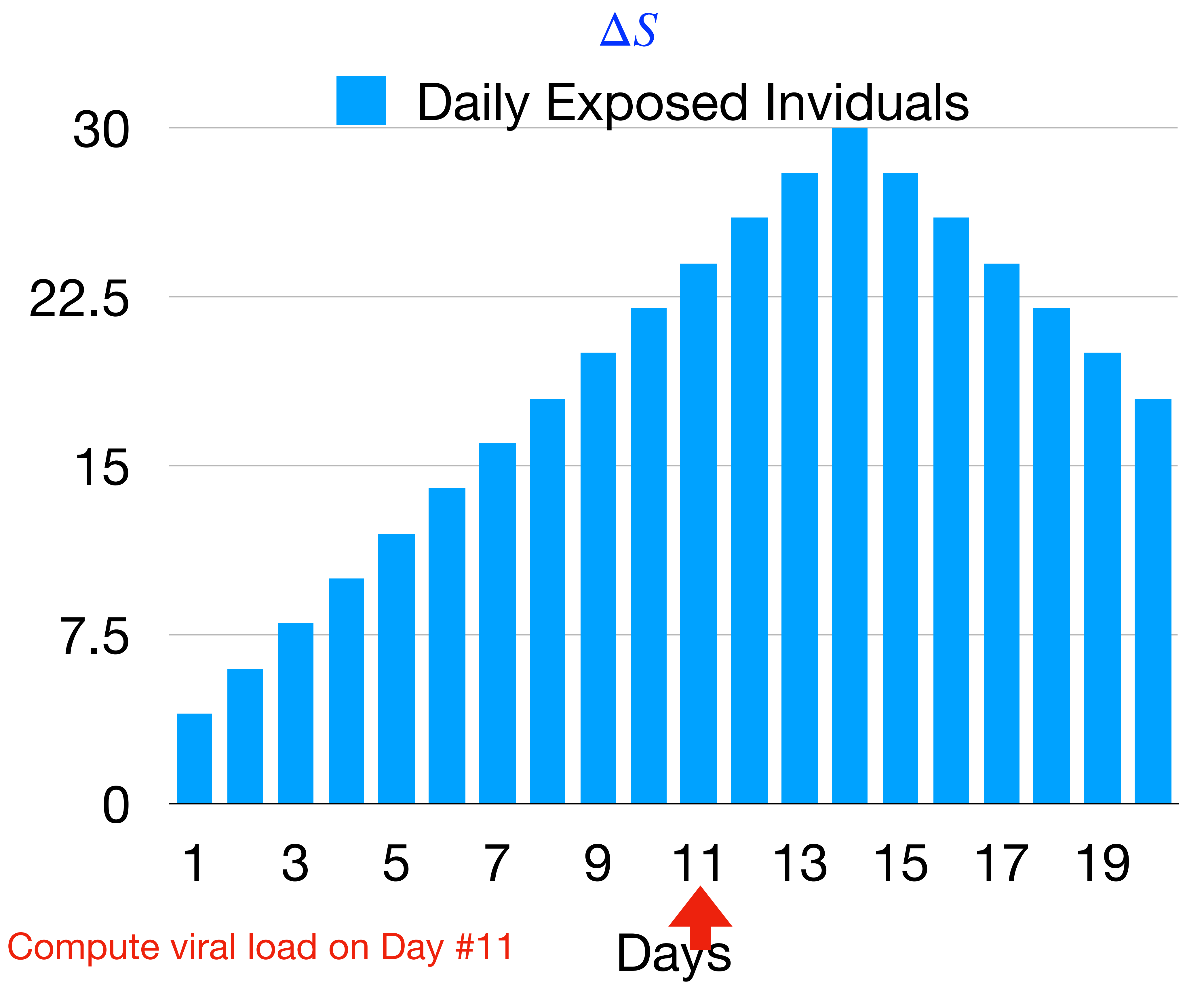
An Illustrative Example: $\Delta t = 1$, daily weight of feces = 1g

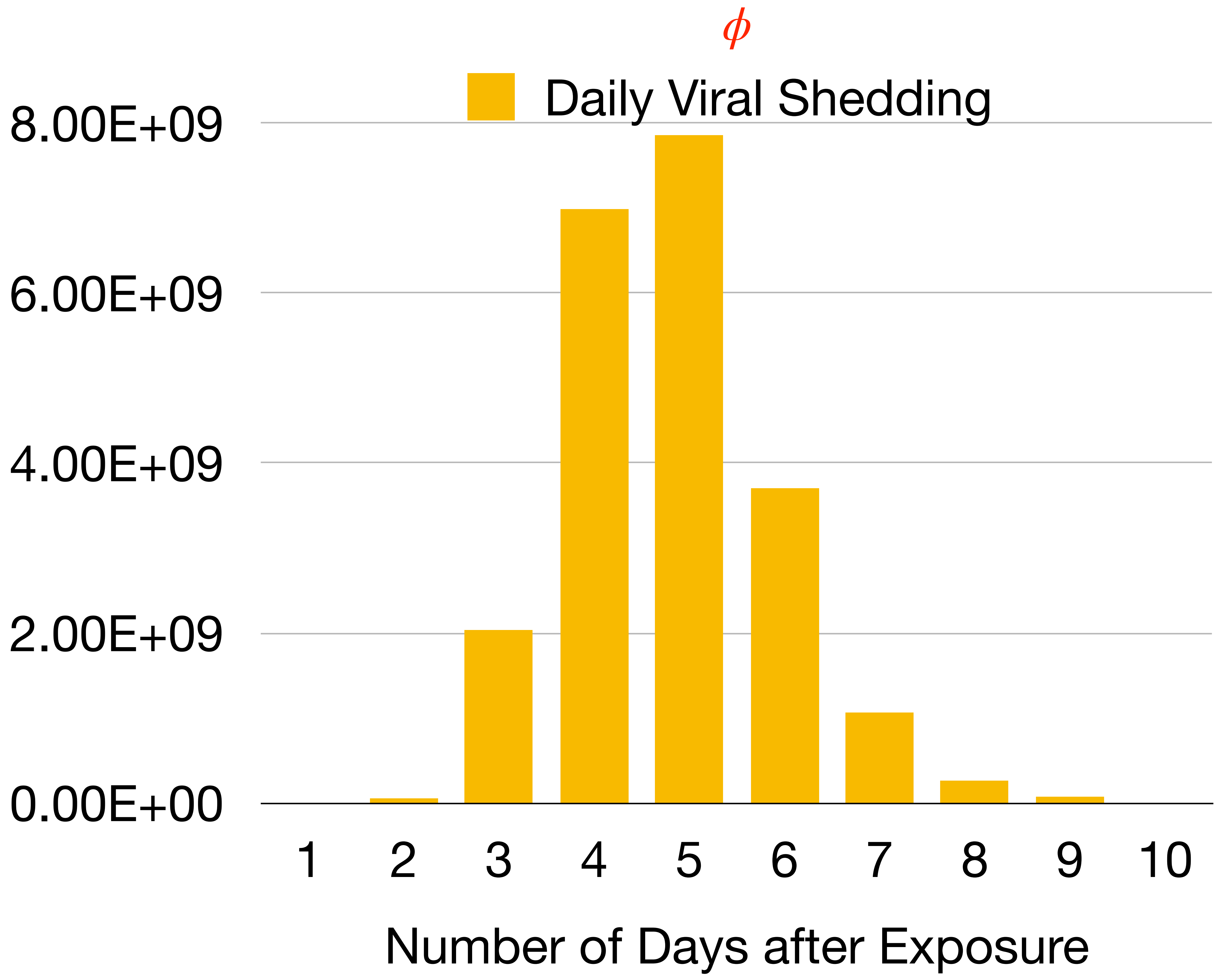




SEIR-V Compartmental Model

An Illustrative Example: $\Delta t = 1$, daily weight of feces = 1g





$$V_t = \sum_{i=0}^{N} \phi_{i:i+1}(\omega)\Delta S_{t-i}$$

SEIR-V Compartmental Model

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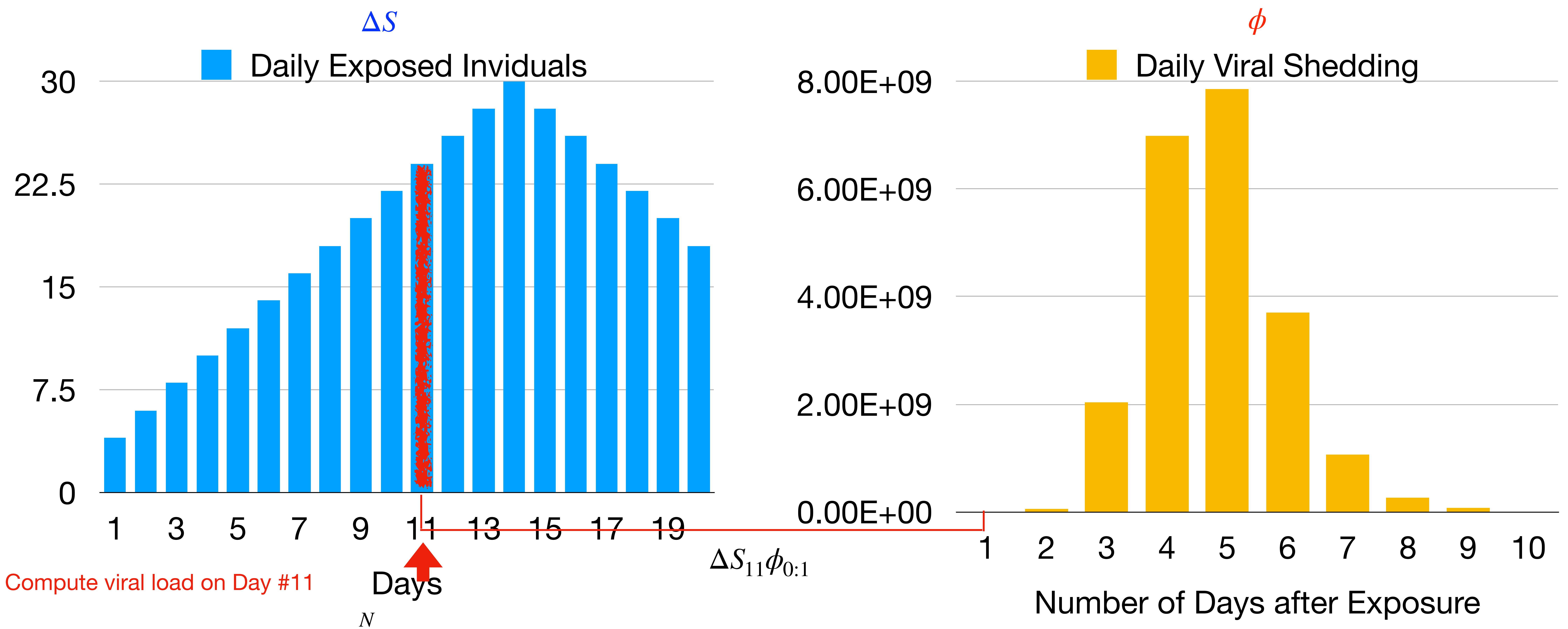

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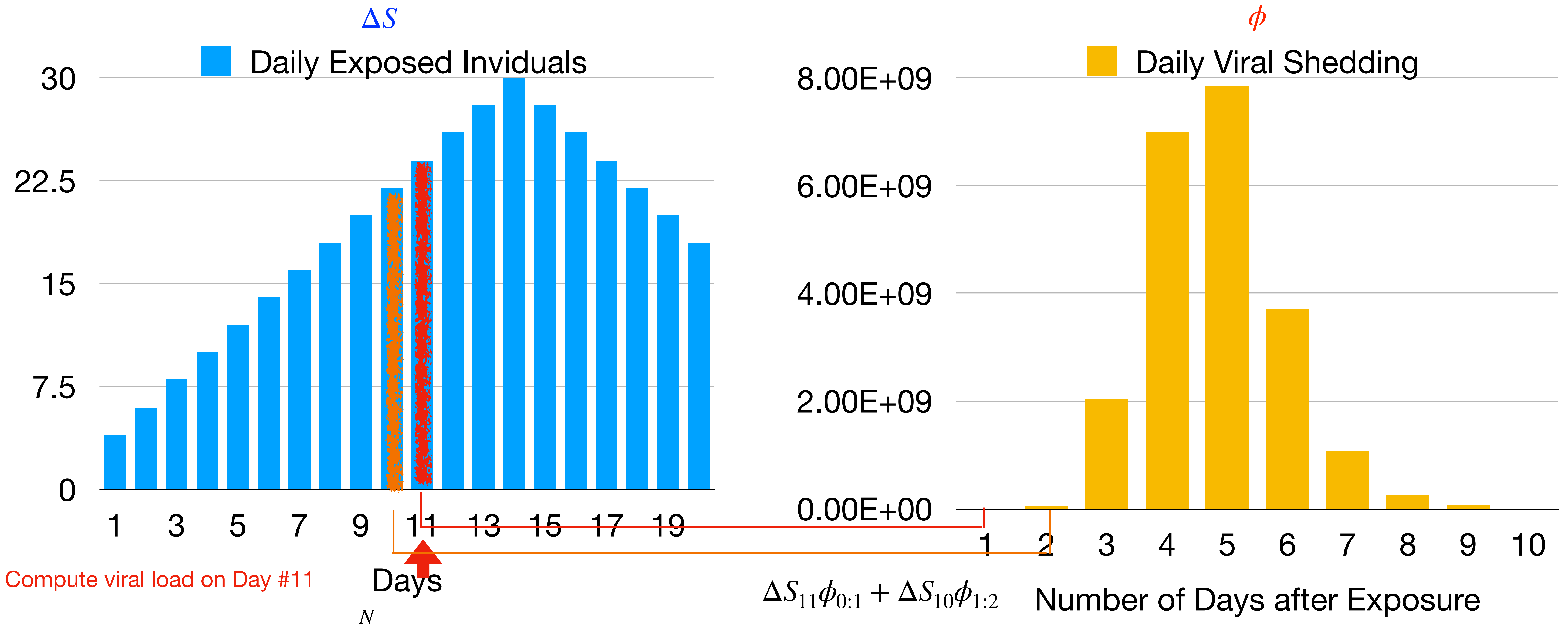
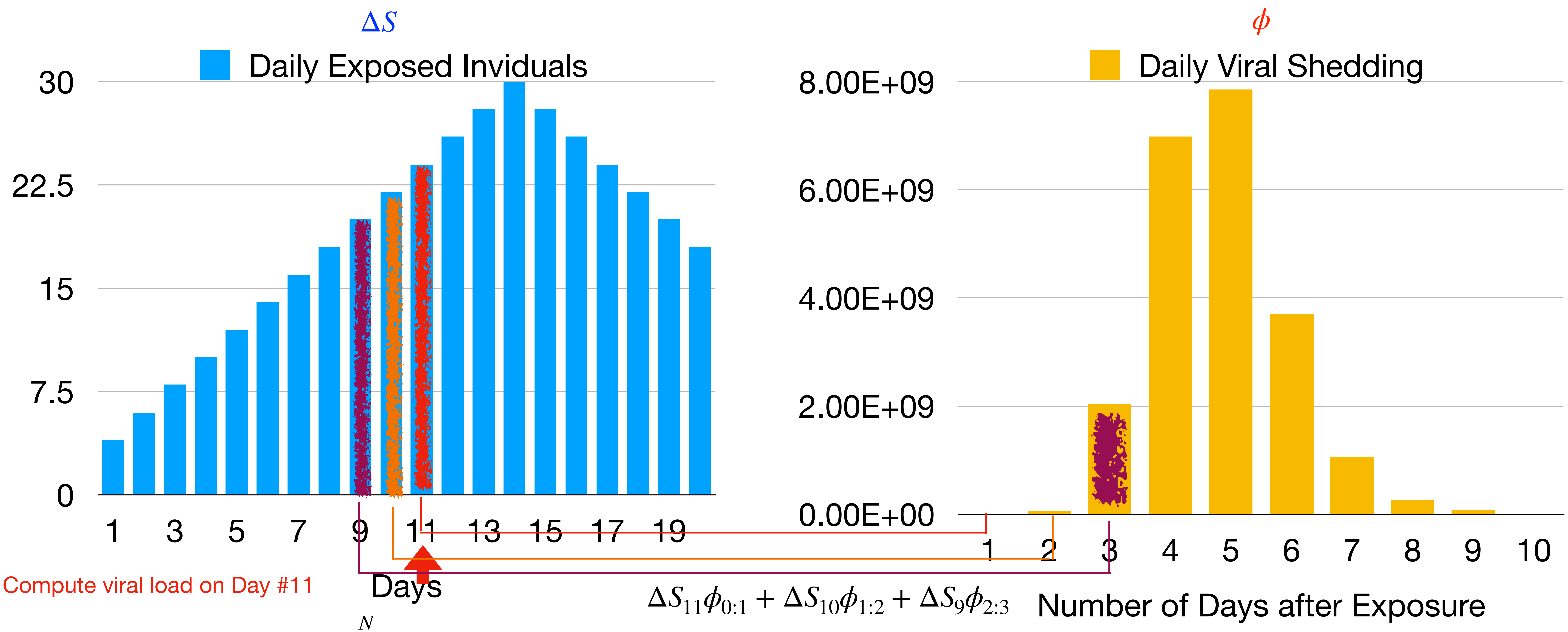


$$V_t = \sum_{i=0}^{N} \phi_{i:i+1}(\omega)\Delta S_{t-i}$$

SEIR-V Compartmental Model

An Illustrative Example: $\Delta t = 1$, daily weight of feces = 1g

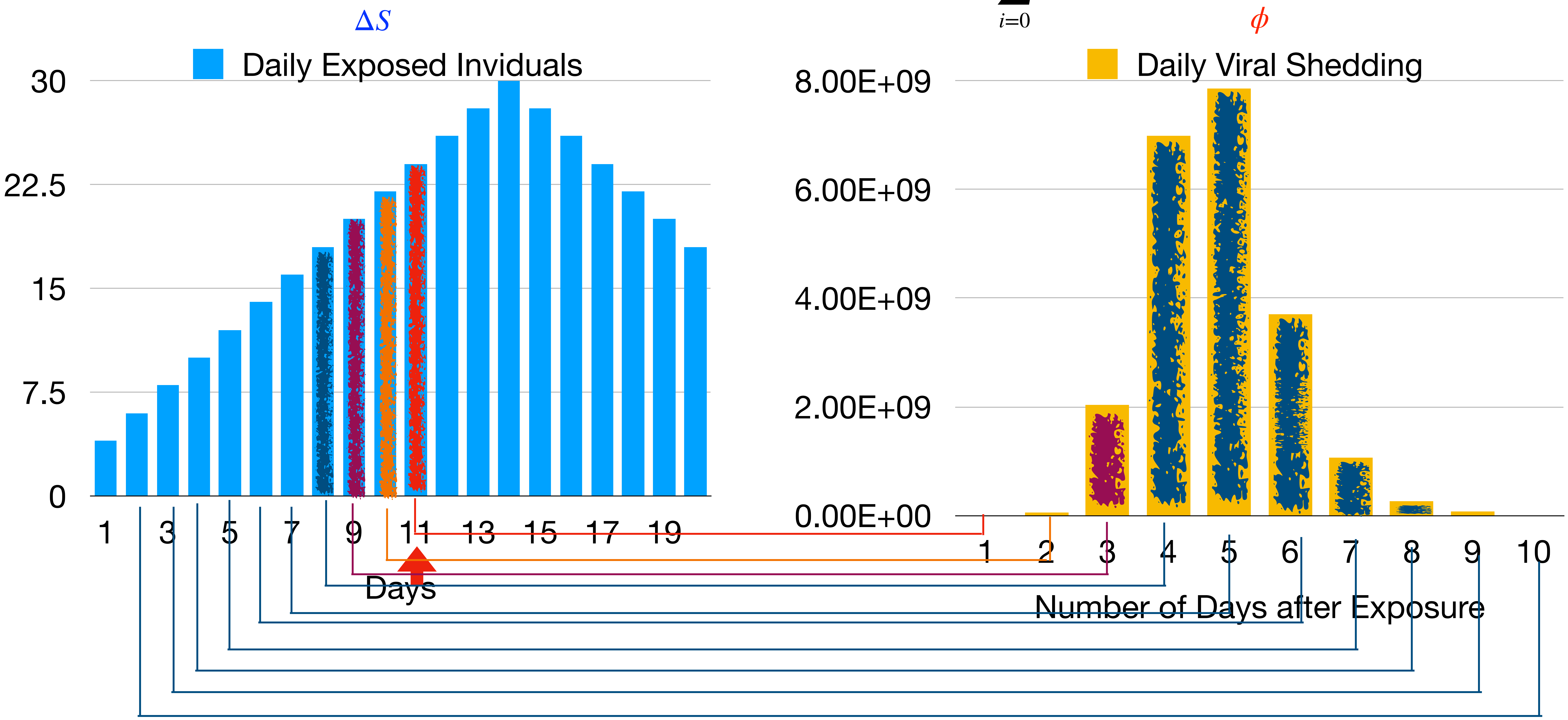


$$V_t = \sum_{i=0}^{N} \phi_{i:i+1}(\omega)\Delta S_{t-i}$$

SEIR-V Compartmental Model

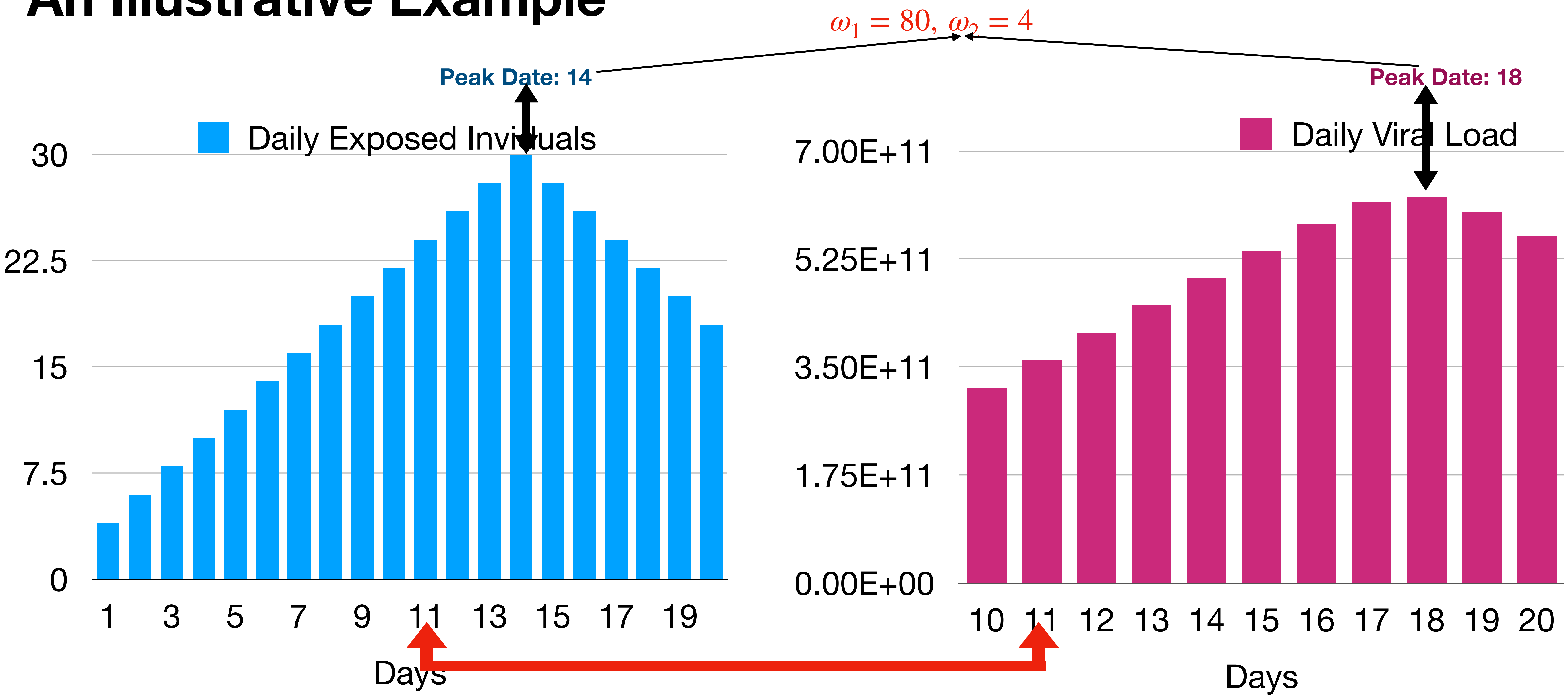
An Illustrative Example

Compute viral load on Day #11 $$V_{11} = \sum_{i=0}^{9} \phi_{i:i+1}(\omega) \Delta S_{11-i}$$



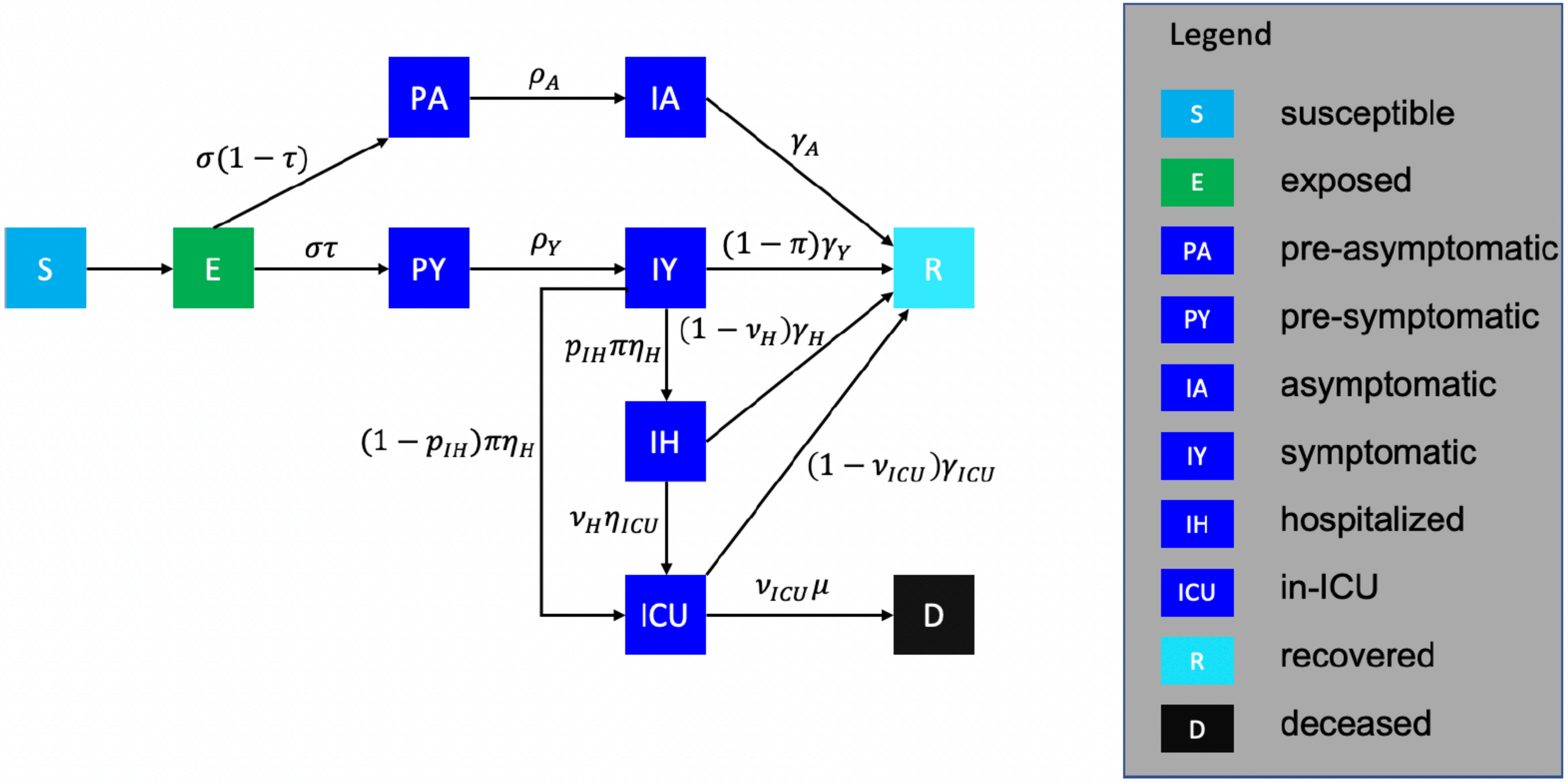
SEIR-V Compartmental Model

An Illustrative Example



SEIR-V Compartmental Model

High-Fidelity Model



SEIR-V Compartmental Model

General Model: Ordinary Differential Equations

Daily exposed individuals: $S(t+1) - S(t) = -\Delta S(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right]$

$$dS(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right] dt$$

Daily change in the compartment E: $E(t+1) - E(t) = S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right] - \lambda E(t)$

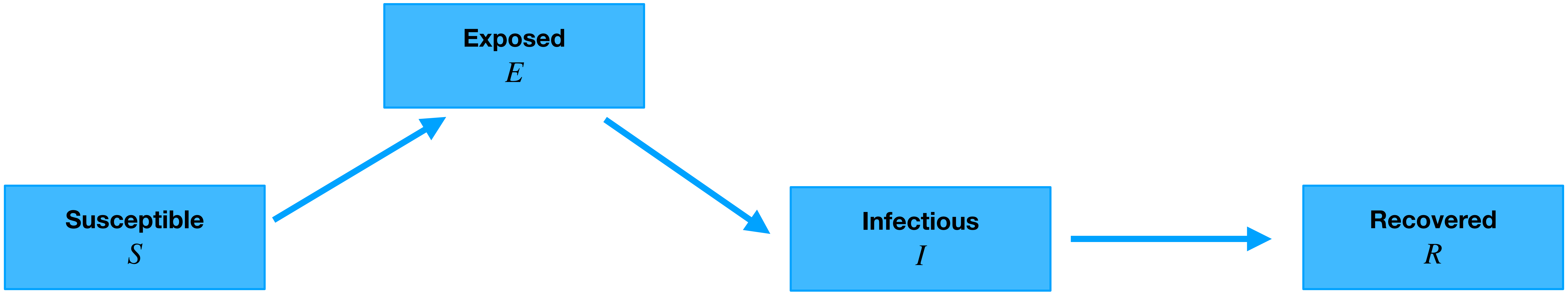
$$dE(t) = \left[S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right] - \lambda E(t)\right] dt$$

Daily change in the compartment I: $I(t+1) - I(t) = \lambda E(t) - \gamma I(t)$

$$dI(t) = \left[\lambda E(t) - \gamma I(t)\right] dt$$

Daily change in the compartment R: $R(t+1) - R(t) = \gamma I(t)$

$$dR(t) = \gamma I(t) dt$$



SEIR-V Compartmental Model

General Model: Ordinary Differential Equations

Daily exposed individuals:

$$S(t+1) - S(t) = -\Delta S(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right]$$

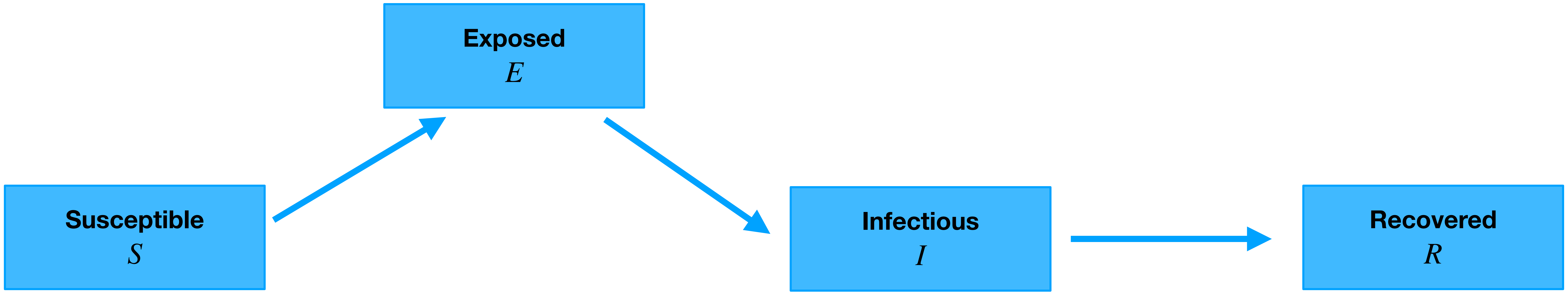
$$dS(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right] dt$$

Daily viral load:

$$V(t) = \int_0^T S(t-s)\left[\frac{(1-\kappa(t-s))\beta}{N} I(t-s)\right] f(s;\omega)\, ds$$

Viral Shedding Function:

$$f(t;\omega) = 10^{\frac{\omega_1 t}{\omega_2^2 + t^2}}$$



Threshold Optimization Problem

How to find the optimal thresholds in the Staged Alert System

Daily exposed individuals: $S(t+1) - S(t) = -\Delta S(t) = -S(t)\left[\frac{(1-\kappa(t))\beta}{N} I(t)\right]$

Transmission reduction is controlled by the threshold and critical stat (e.g., hospital admissions, wastewater signals):

Threshold Optimization Problem
Minimize social-economic-cost(history-of-stages) Subject to history-of-stages from SEIR-V(thresholds) ICU is not overwhelmed from SEIR-V(thresholds)

Outline

- SARS-CoV-2 virus in the wastewater
- Staged-alert system and SEIR-V model
- **Retrospective analysis of staged-alert system with a wastewater signal**

Experiment

Wastewater Policy versus Hospitalization Policy (Guyi Chen)

Critical Stat

Wastewater Policy

7-Day Moving Average of Viral Load per Person

Hospitalization Policy

7-Day Moving Average of Hospital Admissions

Stages	Transmission reduction	Economic cost
Red	80%	1000
Orange	72.5%	100
Yellow	65%	10
Blue	57.5%	1

Scope:

Population served by Calumet, O'Brien, and Stickney wastewater treatment plants is considered.

Goal:

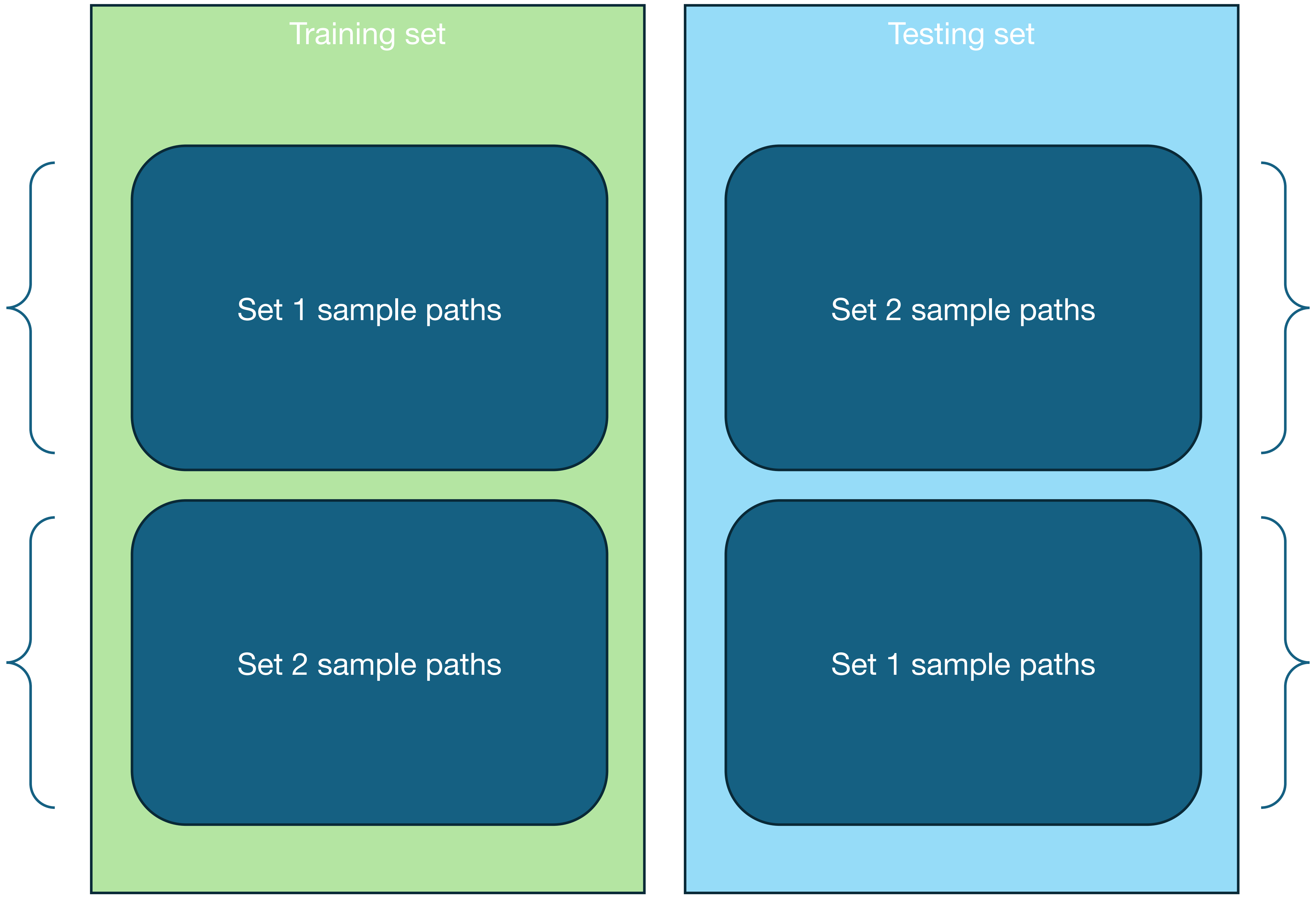
Find the thresholds that have least socioeconomic costs while maintaining occupied ICU beds below the associated capacity.

Remark: Special thanks for Guyi's great contribution for numerical experiment and later retrospective analysis. Also, thanks to the IDPH/DPI data team for providing the clinical data.

Wastewater Policy Versus Hospitalization Policy

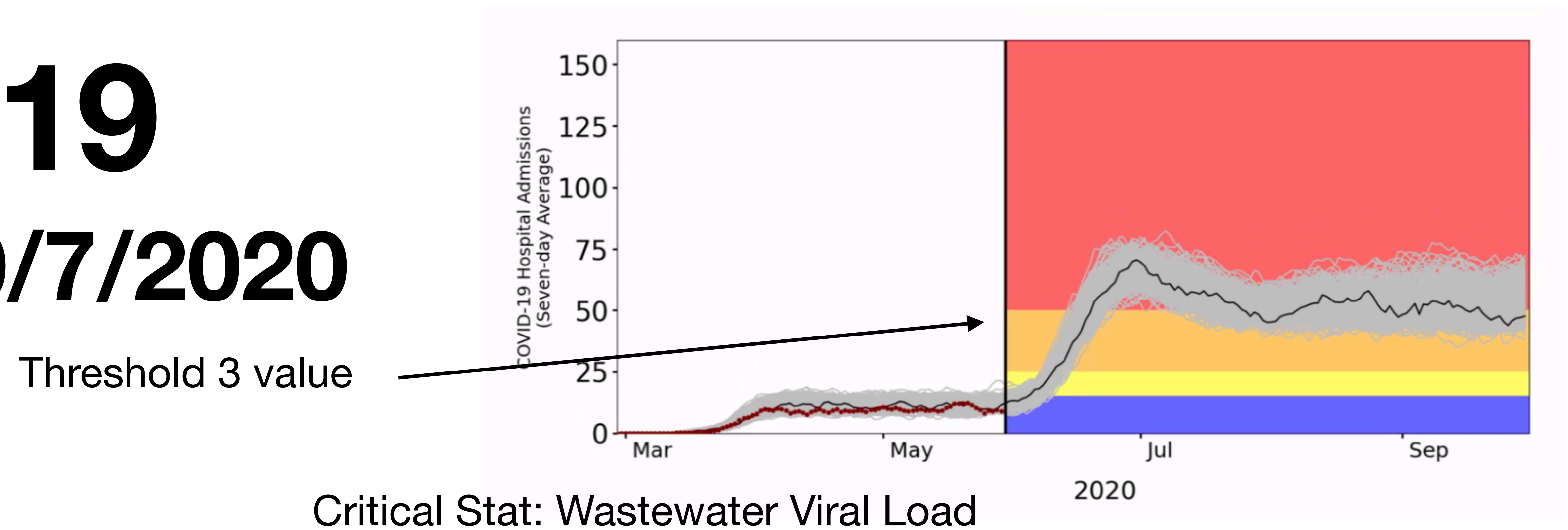
More Details

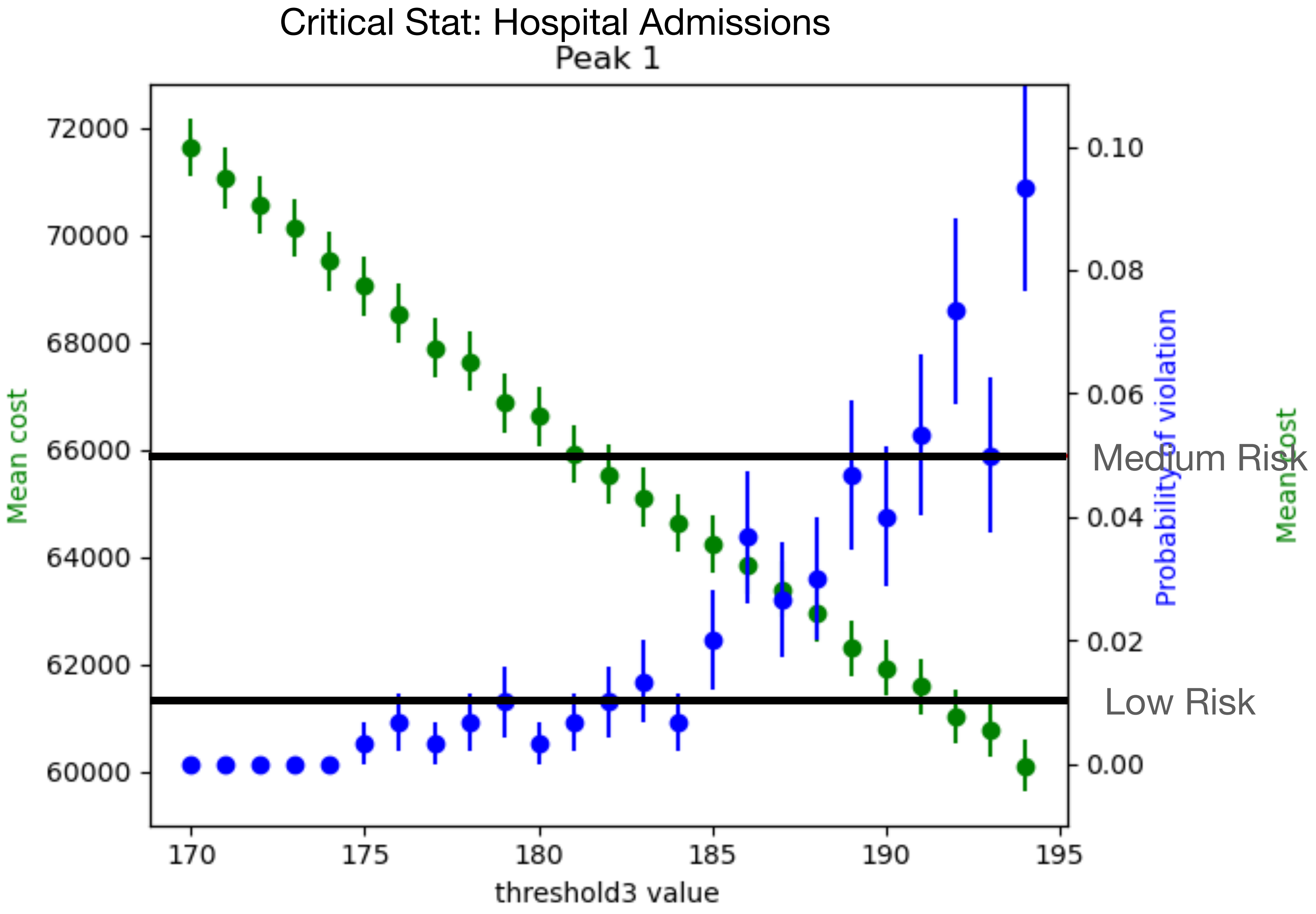
- We consider the following two time periods for the policy optimization and evaluation.
- First surge of COVID-19:
    - from 3/21/2020 to 10/7/2020 (200 days)
    - ICU capacity: **950**
- Second surge of COVID-19:
    - from 10/8/2020 to 3/13/2021 (156 days)
    - ICU capacity: **570**
- We generate two sets of 300 Monte Carlo simulation sample paths, which we use for cross validating the performance of the policies.

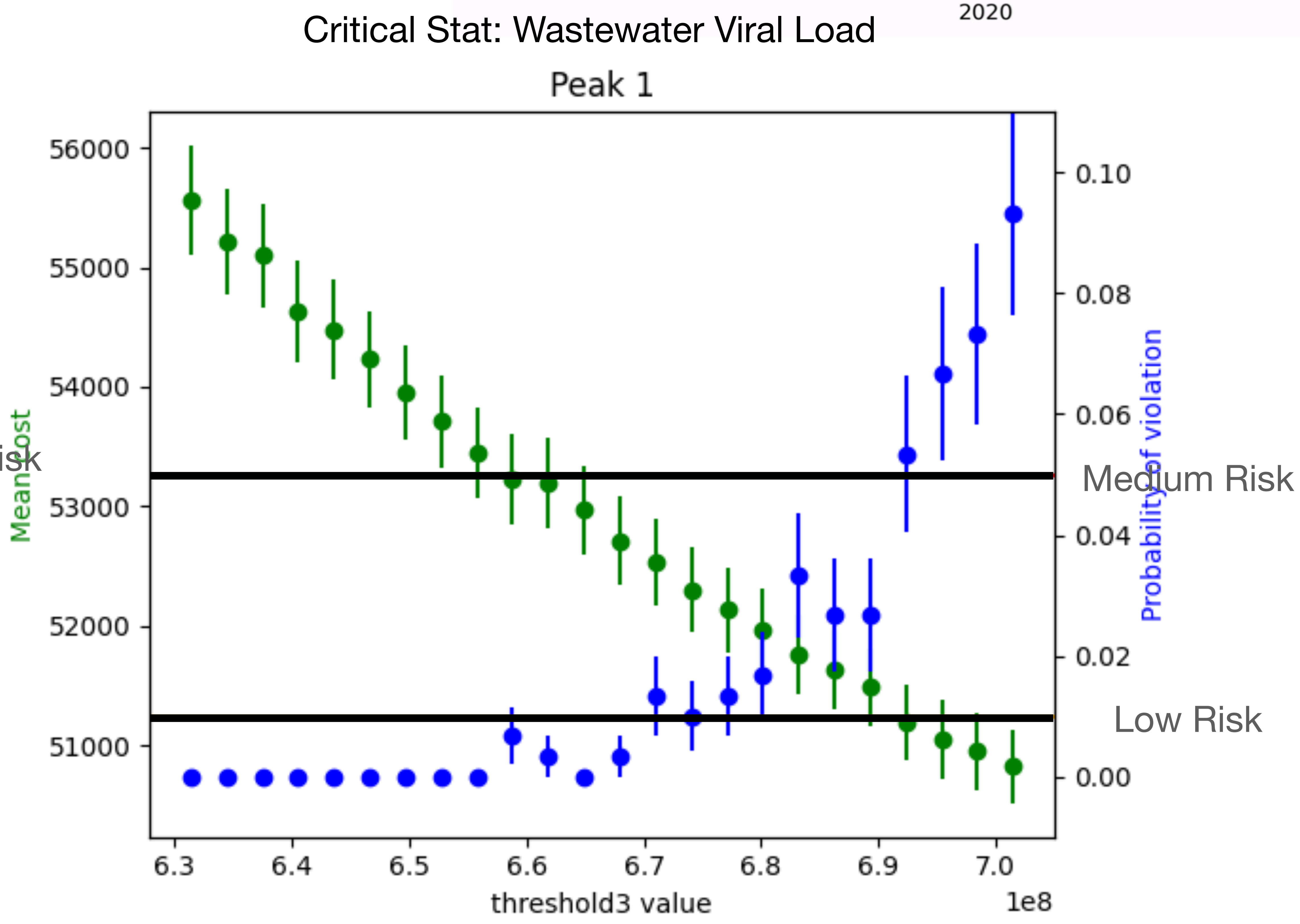


First Surge of COVID-19

Time Span: from 3/21/2020 to 10/7/2020





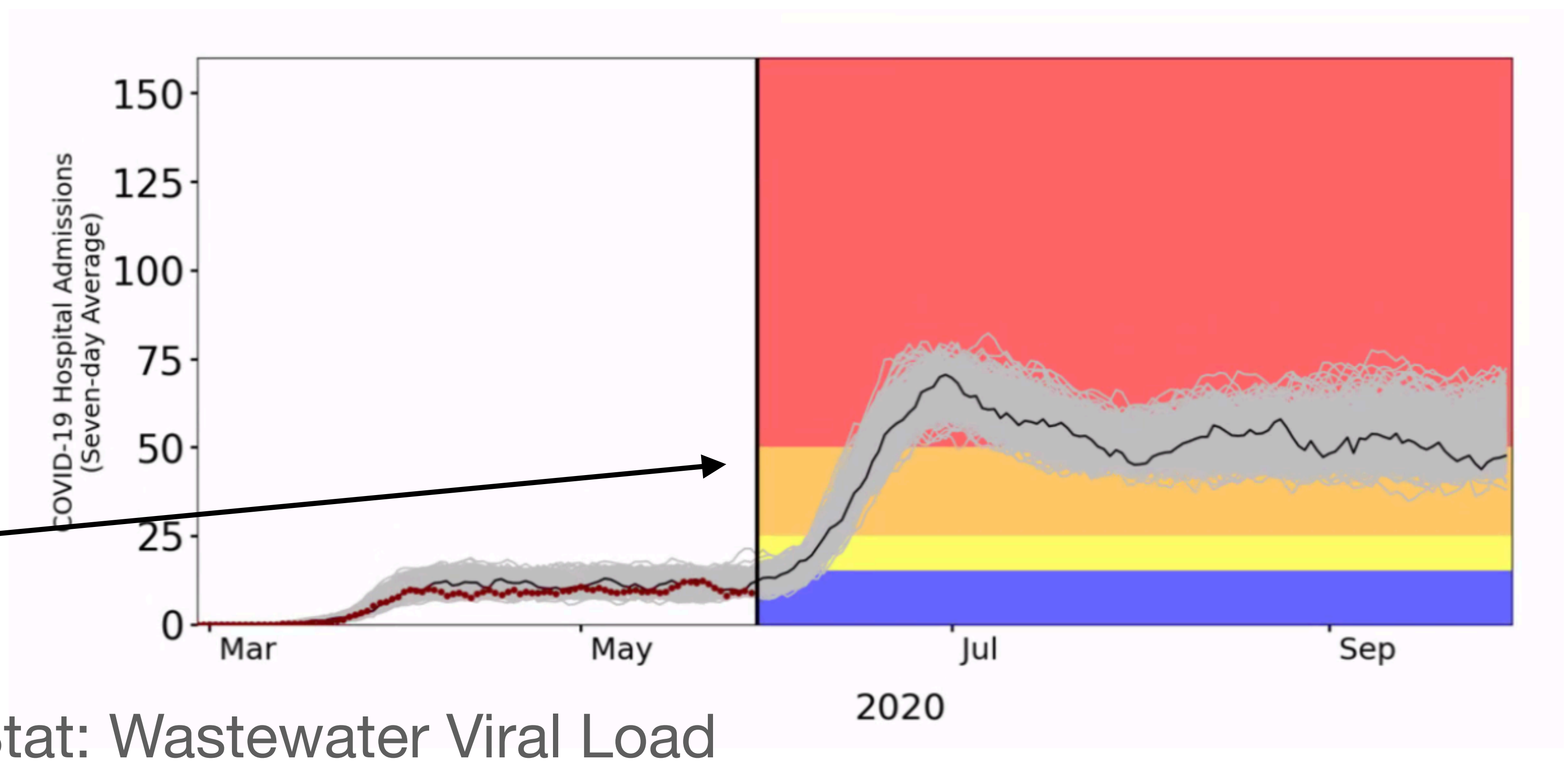


Explanation: If the critical stat is above threshold 3, we are in the red stage (the strictest stage).
Smaller threshold 3 value means more restricted policy.
More risky: More relaxed constraint on the ICU violation, Prob(ICU capacity is violated) $\leq$ 5%.
Less risky: Prob(ICU capacity is violated) $\leq$ 1%.

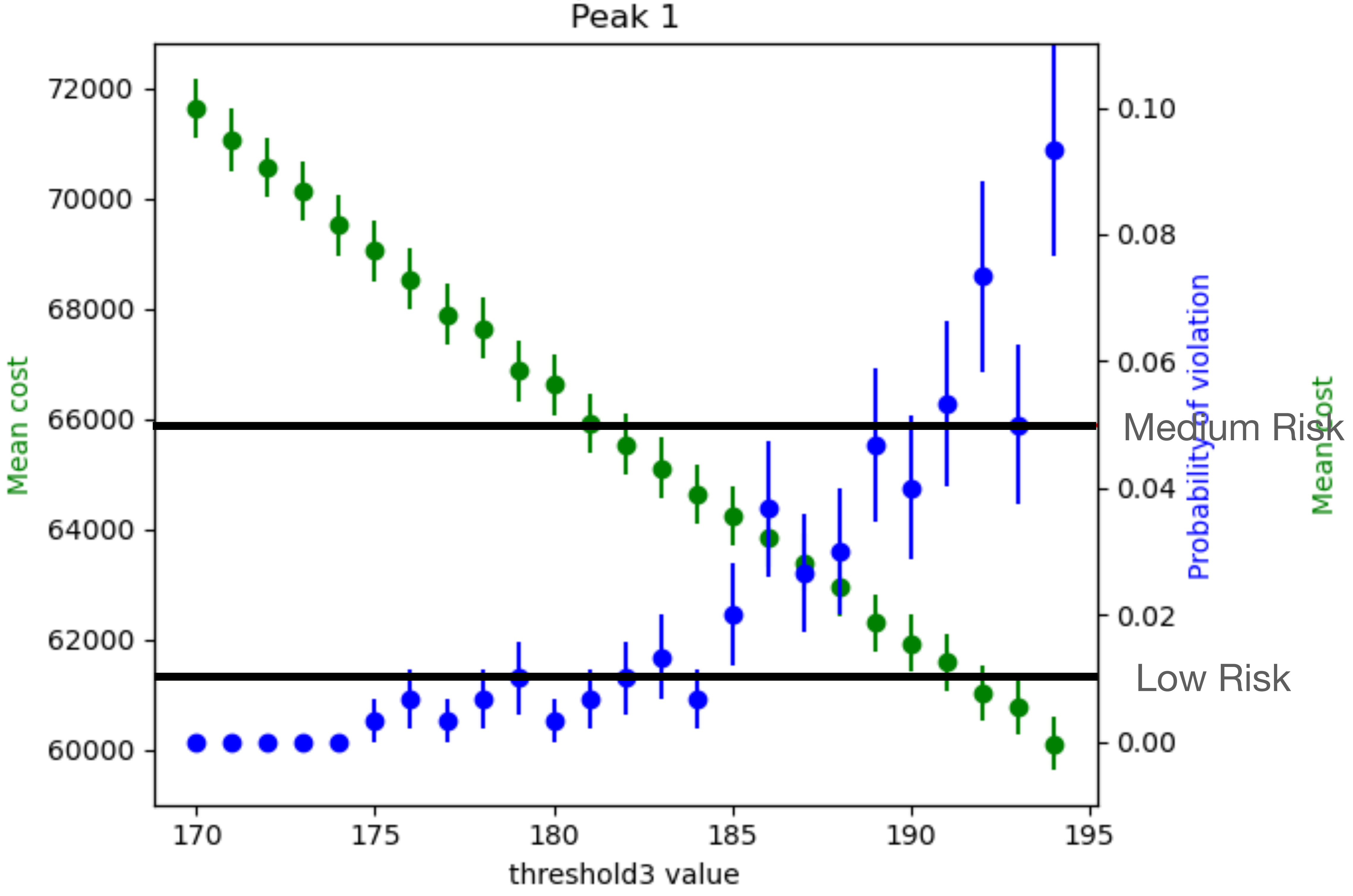
First Surge of COVID-19

Time Span: from 3/21/2020 to 10/7/2020

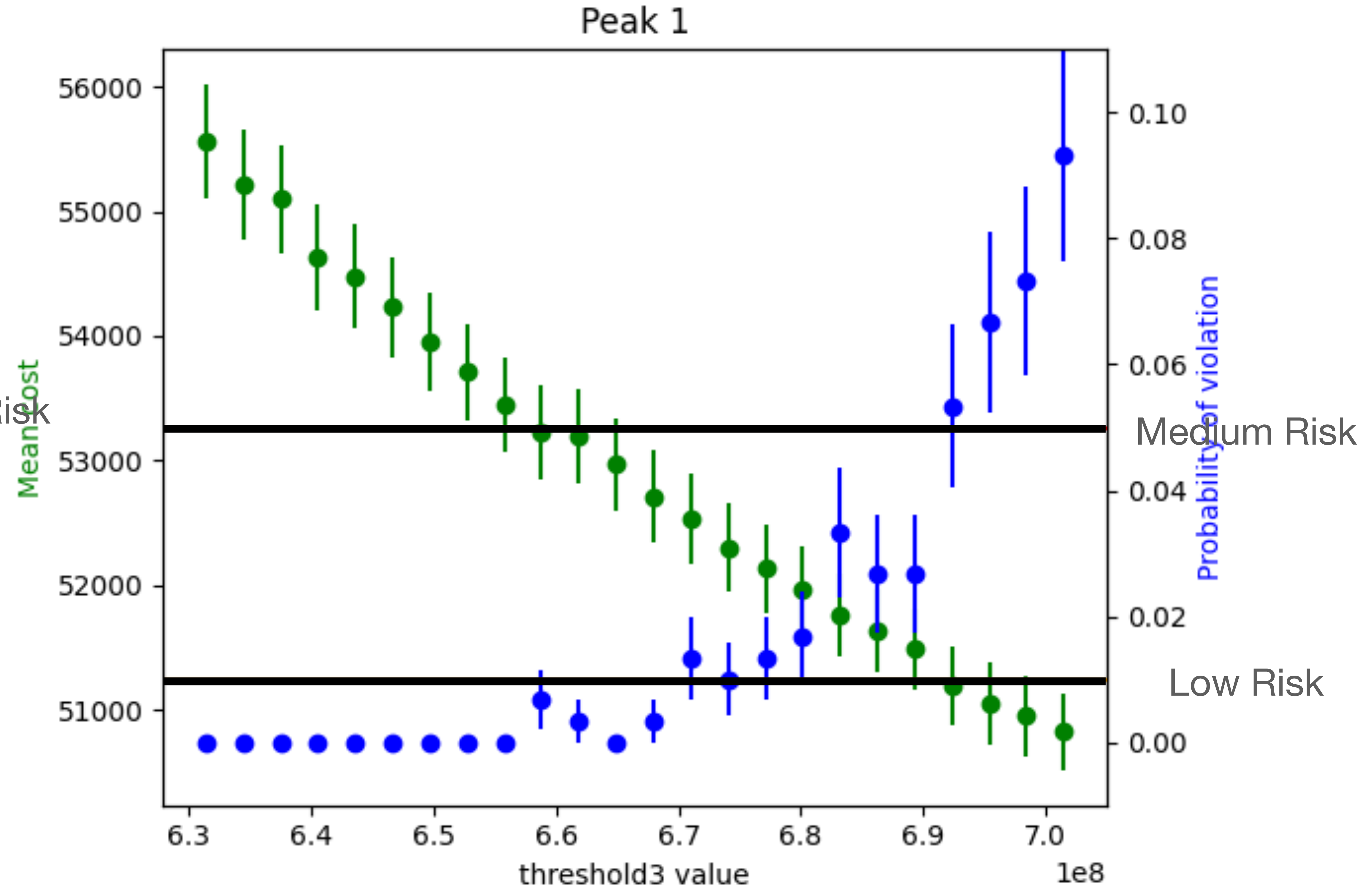
Threshold 3 value



Critical Stat: Hospital Admissions



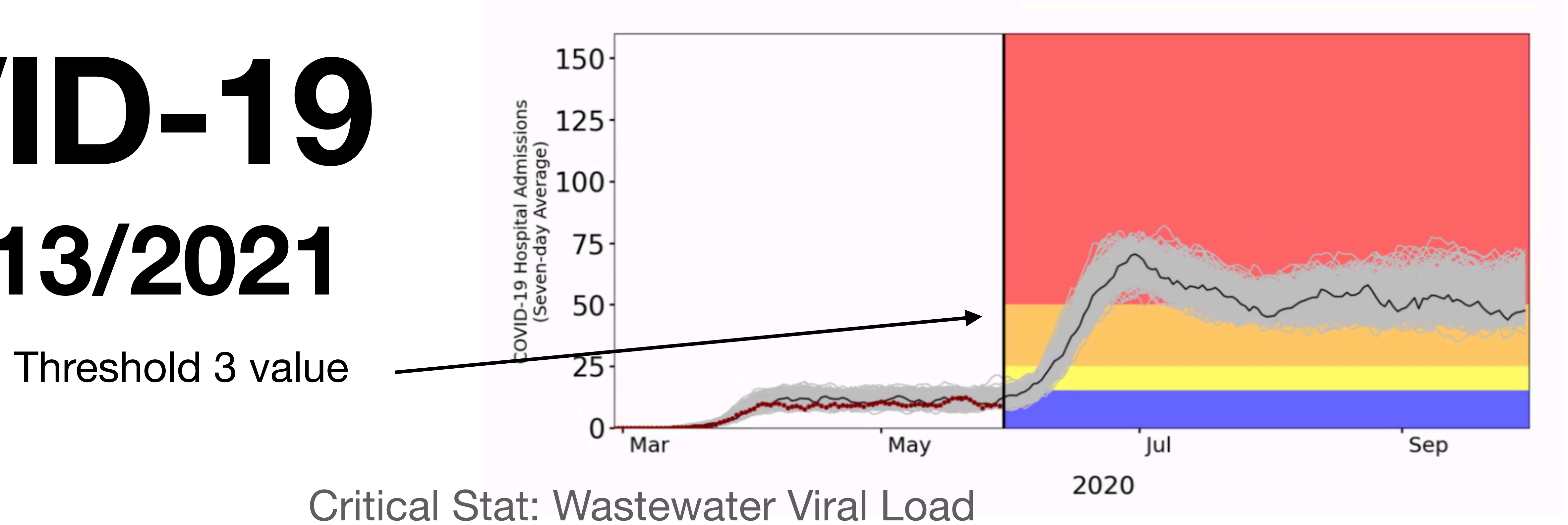
Critical Stat: Wastewater Viral Load



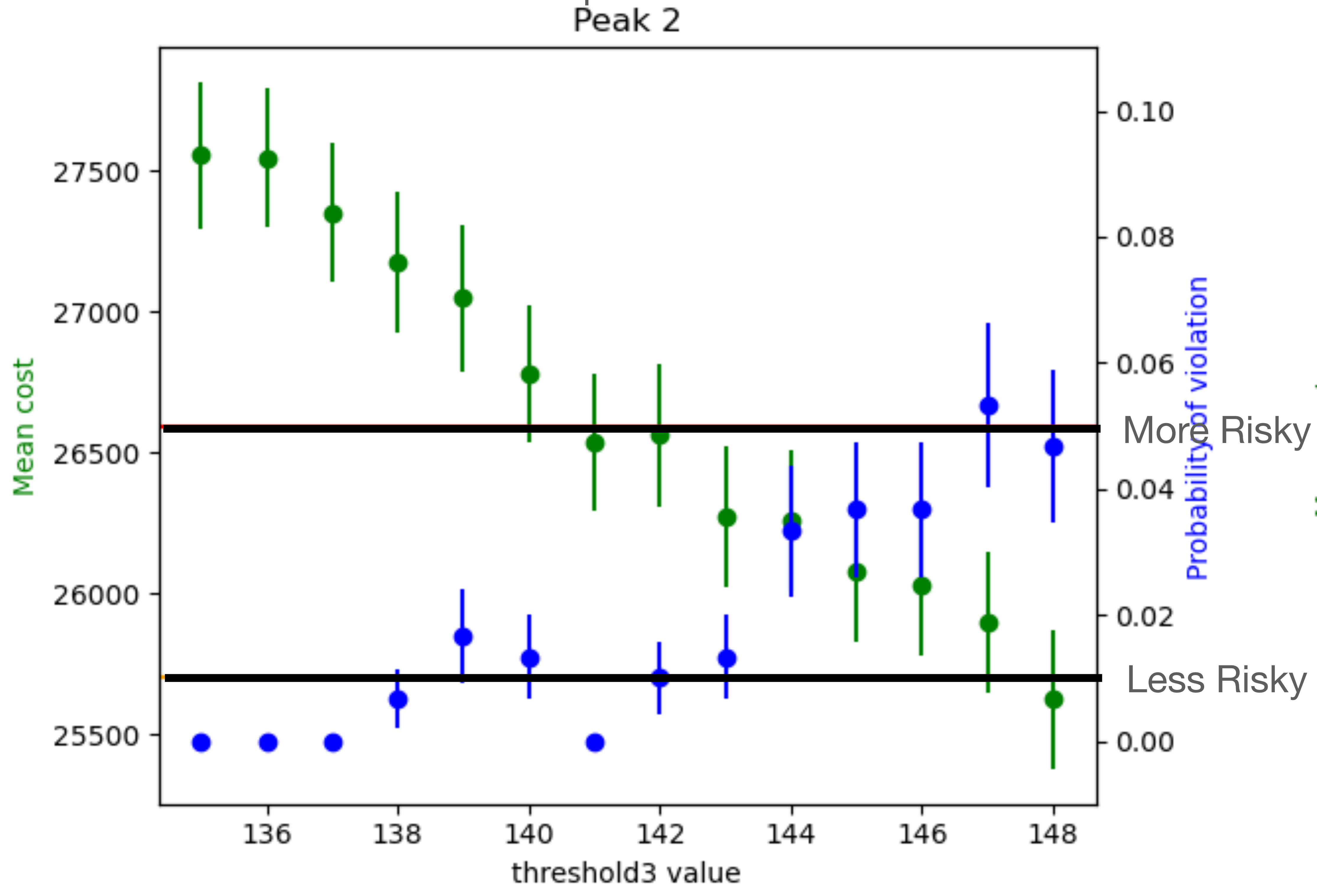
Observation: The larger the threshold3 value is, the larger the probability of ICU violation is.
Wastewater policy generally incurs less socioeconomic cost.

Second Surge of COVID-19

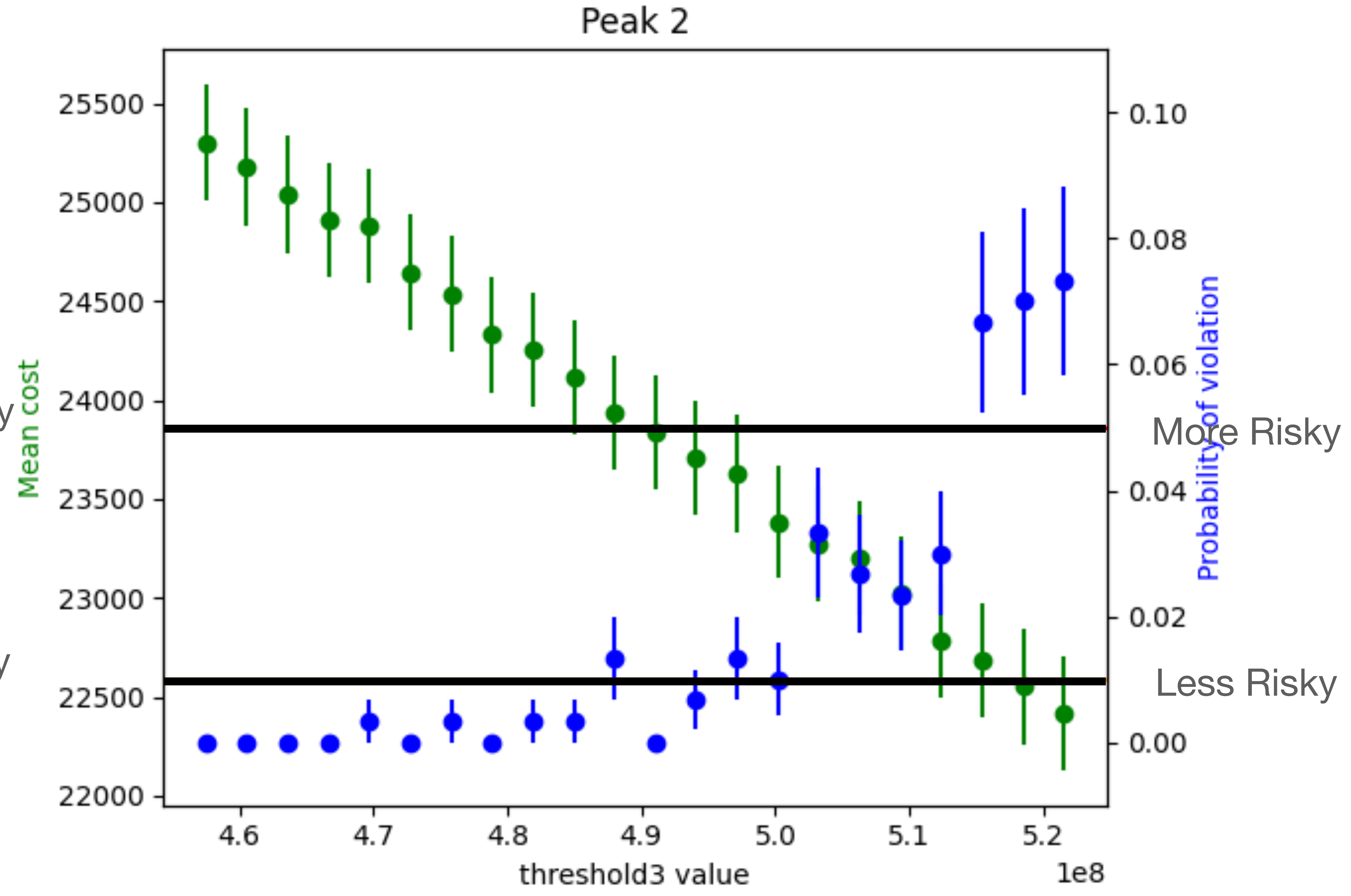
Time Span: from 10/8/2020 to 3/13/2021



Critical Stat: Hospital Admissions



Critical Stat: Wastewater Viral Load



Evaluation Performance Summary

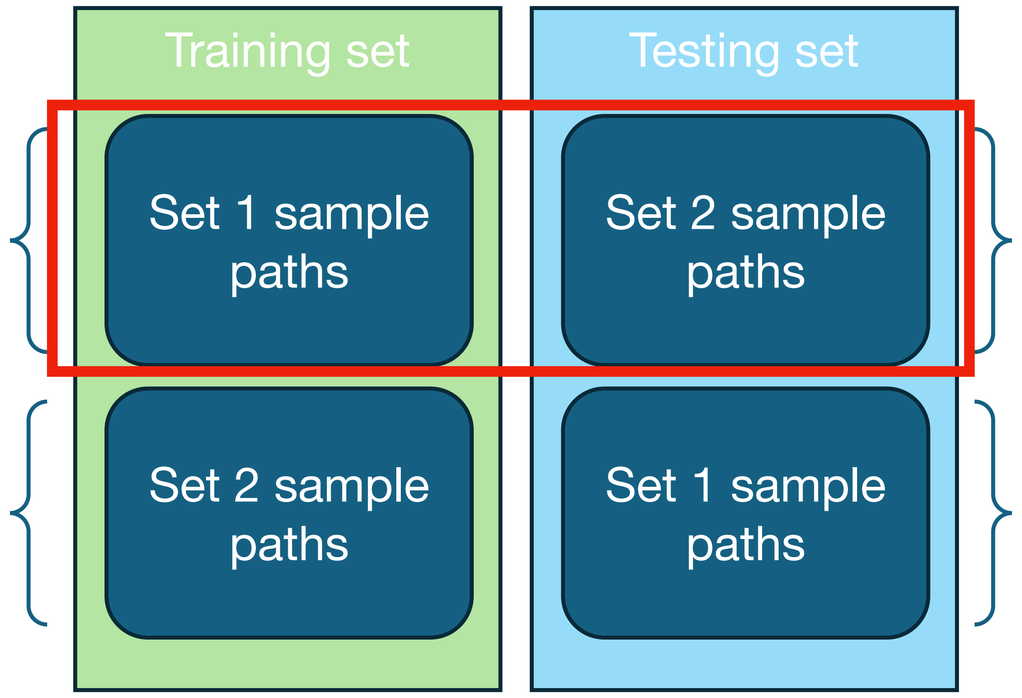
Low risk: Prob(ICU capacity is violated) $\leq$ 1%

Medium risk: Prob(ICU capacity is violated) $\leq$ 5%

	Less Risky Policy				More Risky Policy			
	First Peak		Second Peak		First Peak		Second Peak	
	Viral Load	Hospital Admission	Viral Load	Hospital Admission	Viral Load	Hospital Admission	Viral Load	Hospital Admission
Median cost [90% PI]	50.6K [46K-64.1K]	65K [51.5K-78.5K]	23.7K [15.6K-30.9K]	27.3K [21K-34.5K]	49.7K [45.2K-62.3K]	60.5K [49.7K-74.5K]	22.8K [15.6K-30K]	26.4K [18.3K-30.9K]
Median days in red stage [90% PI]	34 [29-49]	50 [35-63]	9 [0-17]	13 [6-18]	33 [28-47]	45 [33-61]	8 [0-16]	12 [3-17]
Probability ICU demand exceeds capacity	0.0%	0.7%	1.0%	0.7%	2.7%	4.7%	3.7%	3.0%
Median peak ICU demand	862.0	833.0	500.0	482.0	888.0	852.0	526.0	500.0
95th percentile of peak ICU demand	919.0	926.0	545.0	540.0	943.0	943.0	567.0	561.0
Median peak hospitalizations	3982.0	3517.0	2290.0	2233.0	4076.0	3624.0	2378.0	2311.0
95th percentile peak hospitalizations	4155.0	3880.0	2540.0	2536.0	4263.0	3989.0	2640.0	2632.0

ICU Capacity: 950 | ICU Capacity: 570 | ICU Capacity: 950 | ICU Capacity: 570

Cross Validation Experiment I



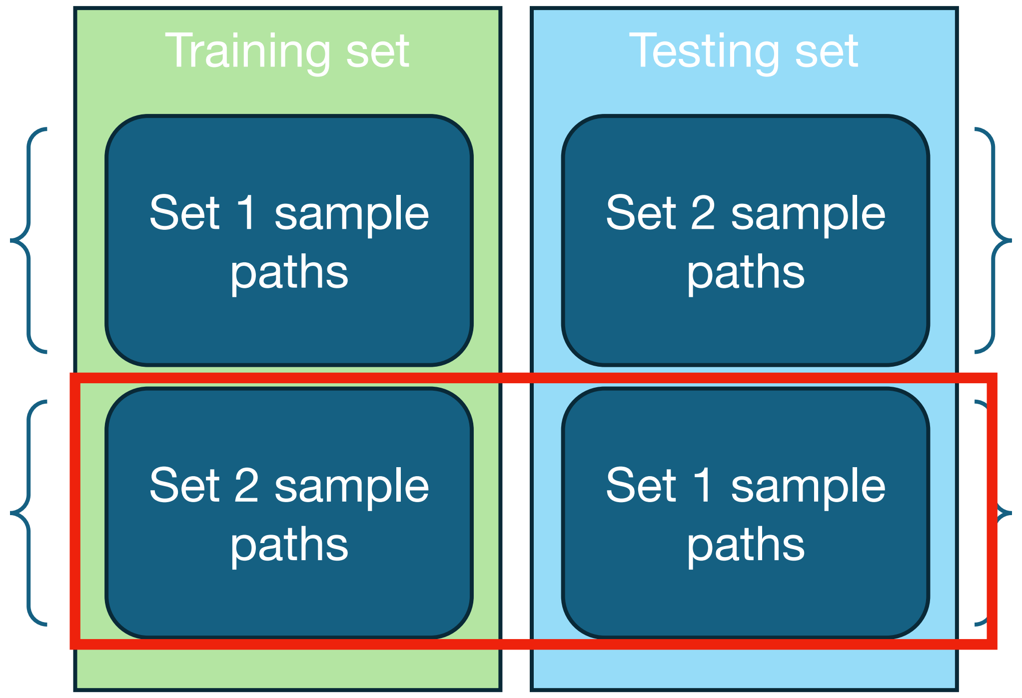
Evaluation Performance Summary

Low risk: Prob(ICU capacity is violated) $\lesssim 1\%$ | Medium risk: Prob(ICU capacity is violated) $\lesssim 5\%$

	Less Risky Policy				More Risky Policy			
	First Peak		Second Peak		First Peak		Second Peak	
	Viral Load	Hospital Admission	Viral Load	Hospital Admission	Viral Load	Hospital Admission	Viral Load	Hospital Admission
Median cost [90% PI]	51.5K [45.2K-63.2K]	65K [52.3K-79K]	23.7K [15.6K-30K]	27.3K [21K-33.6K]	50.6K [45.2K-61.4K]	61.4K [50.5K-75.8K]	22.8K [15.6K-29.1K]	26.4K [18.2K-31.8K]
Median days in red stage [90% PI]	35 [28-48]	50 [36-66]	9 [0-16]	13 [6-20]	34 [28-46]	46 [33-62]	8 [0-15]	12 [3-18]
Probability ICU demand exceeds capacity	2.3%	2.7%	0.7%	0.7%	4.0%	5.3%	3.7%	2.3%
Median peak ICU demand	869.0	828.0	502.0	480.0	886.0	849.0	527.0	502.0
95th percentile of peak ICU demand	935.0	927.0	542.0	539.0	947.0	955.0	566.0	555.0
Median peak hospitalizations	4019.0	3534.0	2333.0	2289.0	4076.0	3616.0	2401.0	2300.0
95th percentile peak hospitalizations	4197.0	3879.0	2533.0	2486.0	4278.0	3984.0	2647.0	2609.0

ICU Capacity: 950 | ICU Capacity: 570 | ICU Capacity: 950 | ICU Capacity: 570

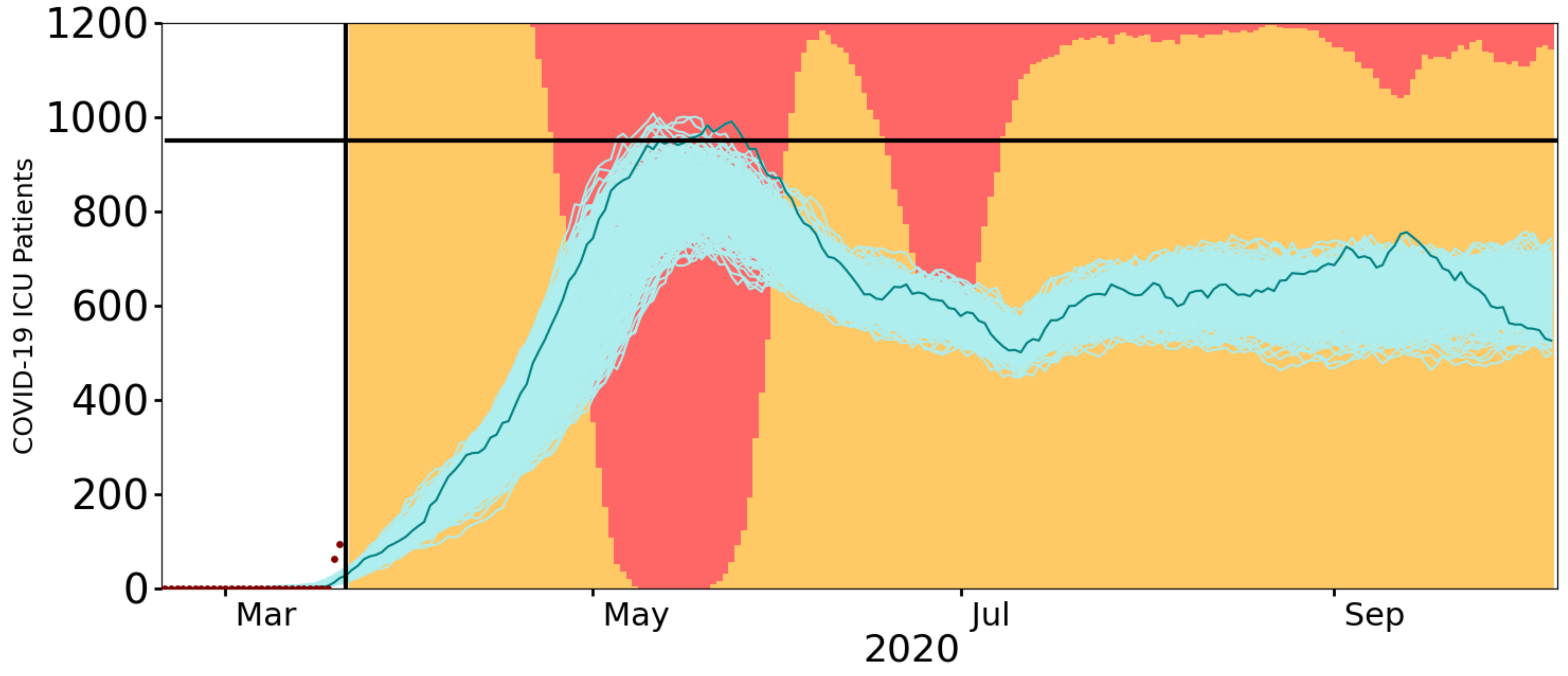
Cross Validation Experiment II



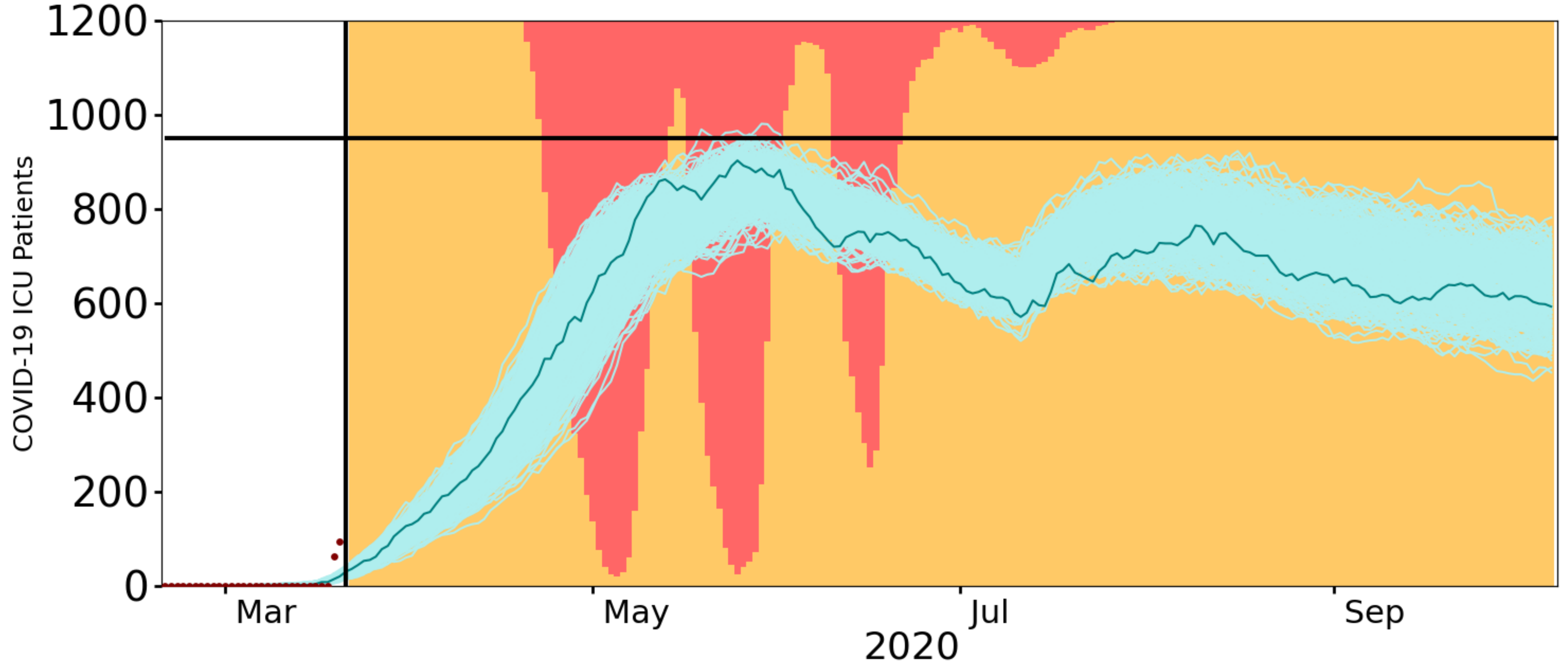
Takeaway from wastewater policy: ICU capacity is protected with less socioeconomic cost.

ICU Projection

Hospitalization Policy



Wastewater Policy



Takeaways of wastewater policy:

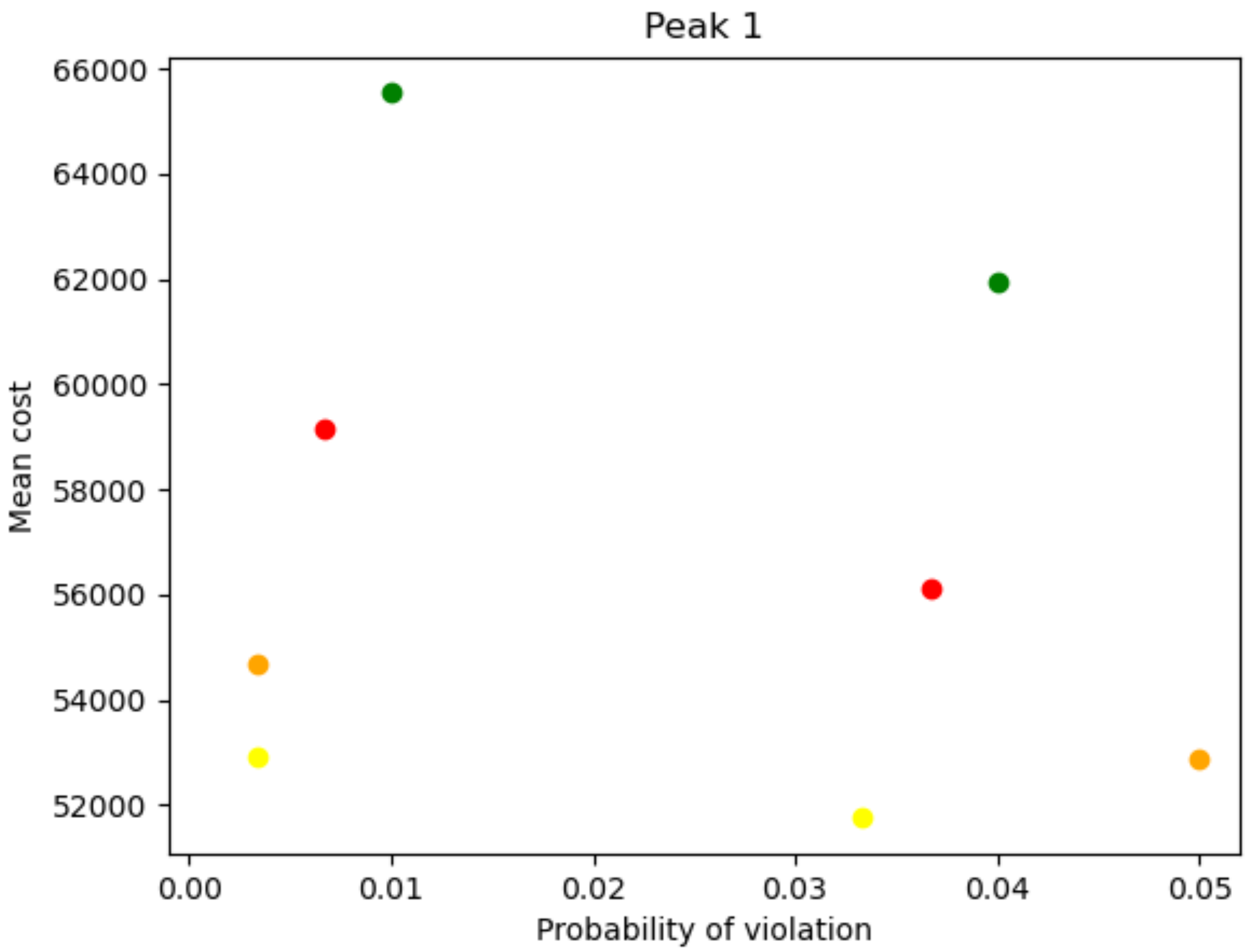
- There are fewer days in red stage.
- Width of the wastewater cloud is narrower around the peak, which is due to the upstream sampling (in the SEIR-V model).

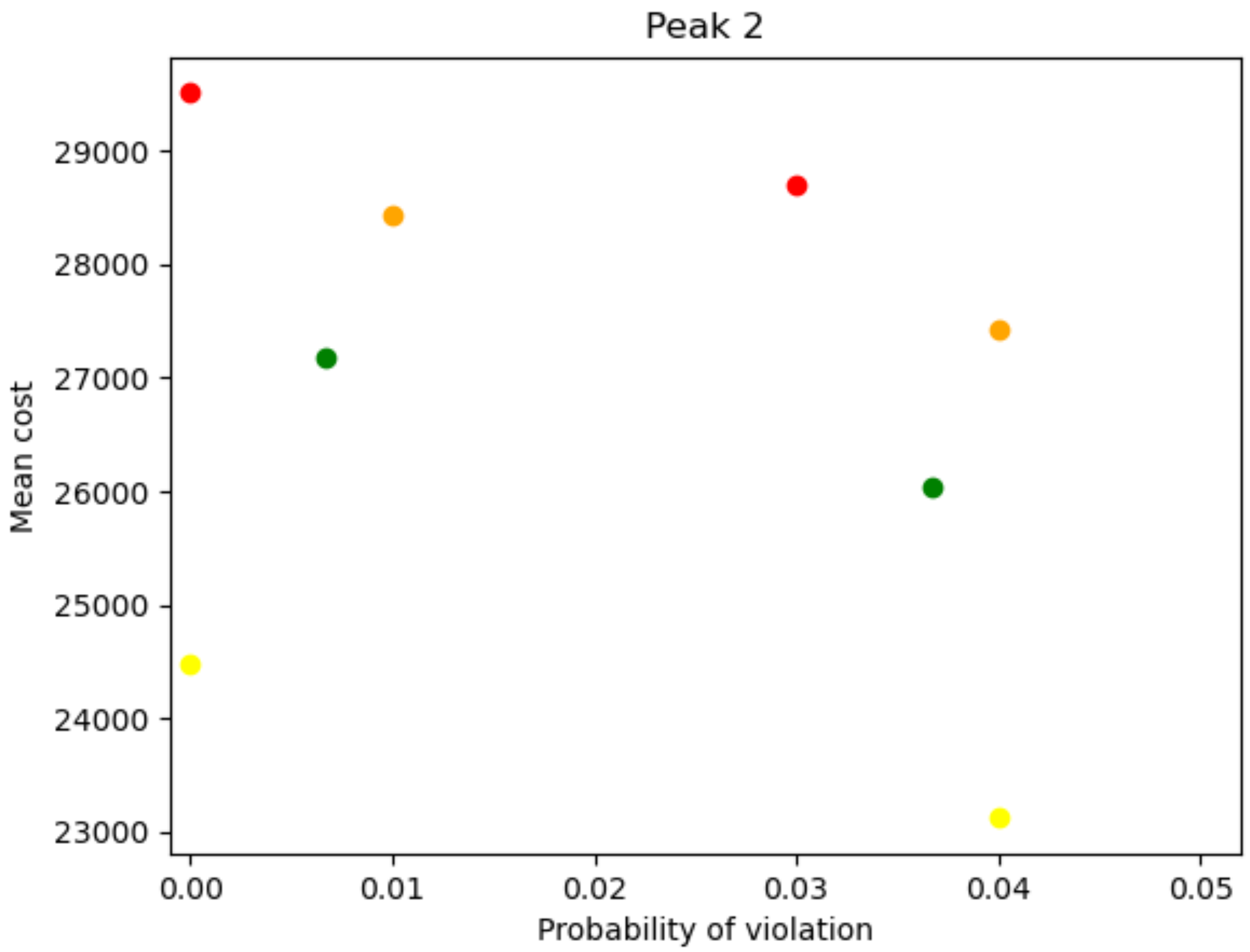
7-day moving average of COVID hospital admission

VS

7-day moving average of SARS-Cov-2 RNA viral load in wastewater with **various collection frequency**

Various Collection Frequency



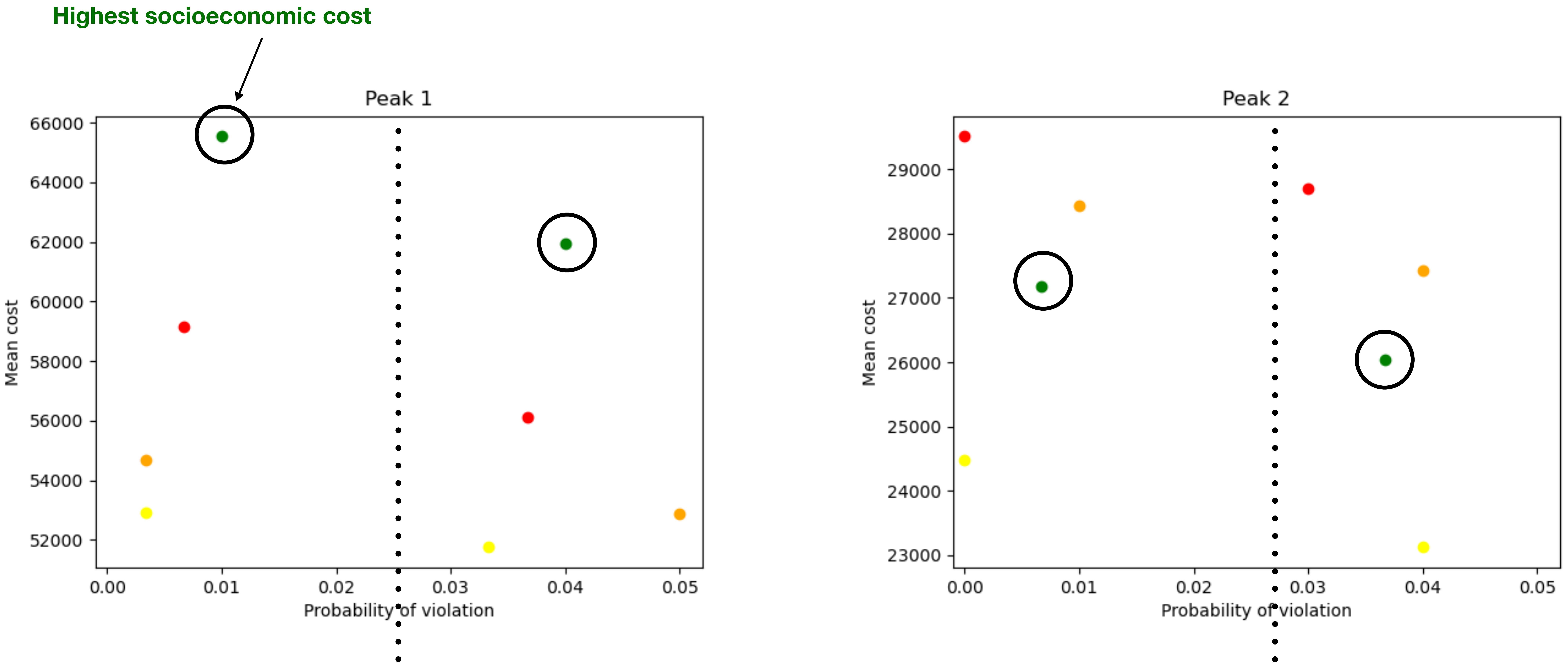


Prob(ICU Violation) $\leq 1\,\%$	Prob(ICU Violation) $\leq 5\,\%$

Prob(ICU Violation) $\leq 1\,\%$	Prob(ICU Violation) $\leq 5\,\%$

Various Collection Frequency

- sampling frequency: everyday (admission)
- sampling frequency: once a week
- sampling frequency: twice a week
- sampling frequency: three times a week

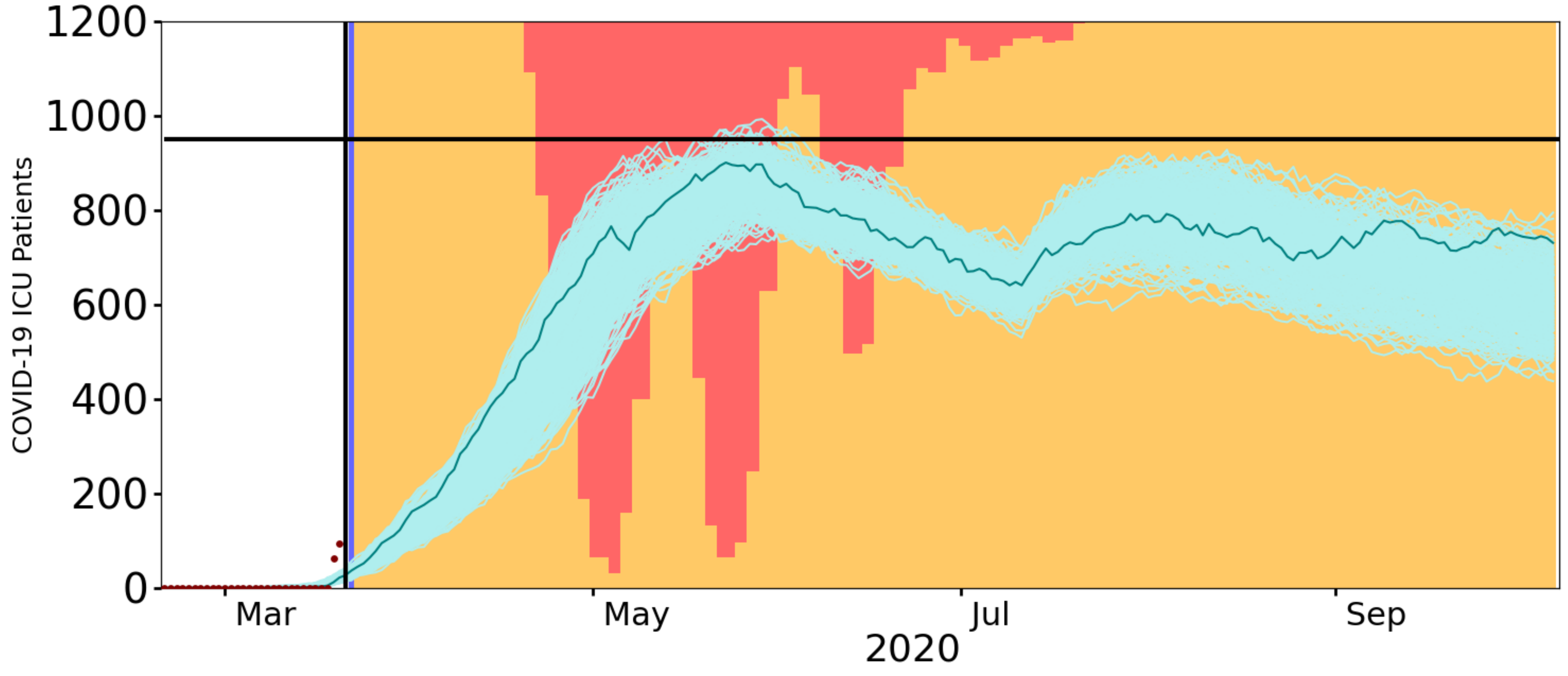


Prob(ICU Violation) $\leq 1\,\%$ | Prob(ICU Violation) $\leq 5\,\%$

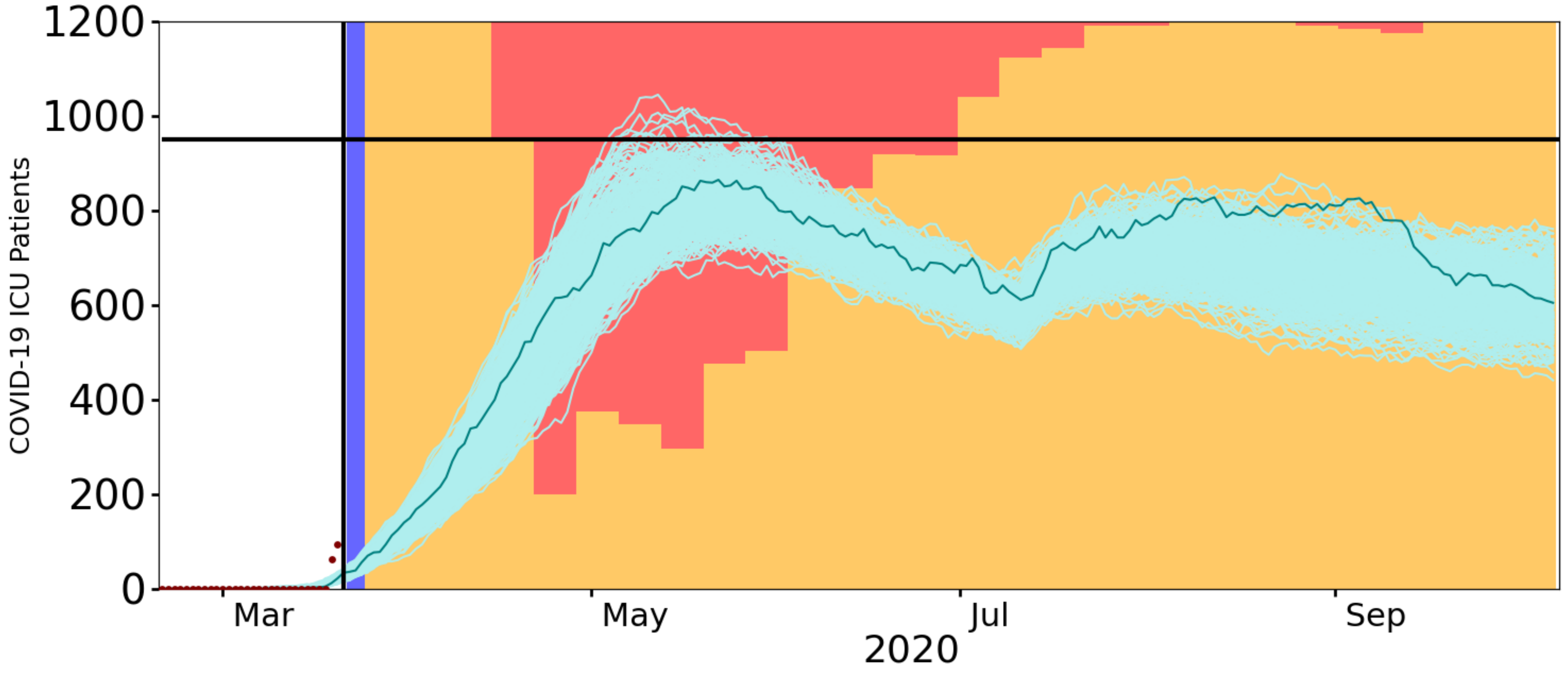
Prob(ICU Violation) $\leq 1\,\%$ | Prob(ICU Violation) $\leq 5\,\%$

ICU Projection

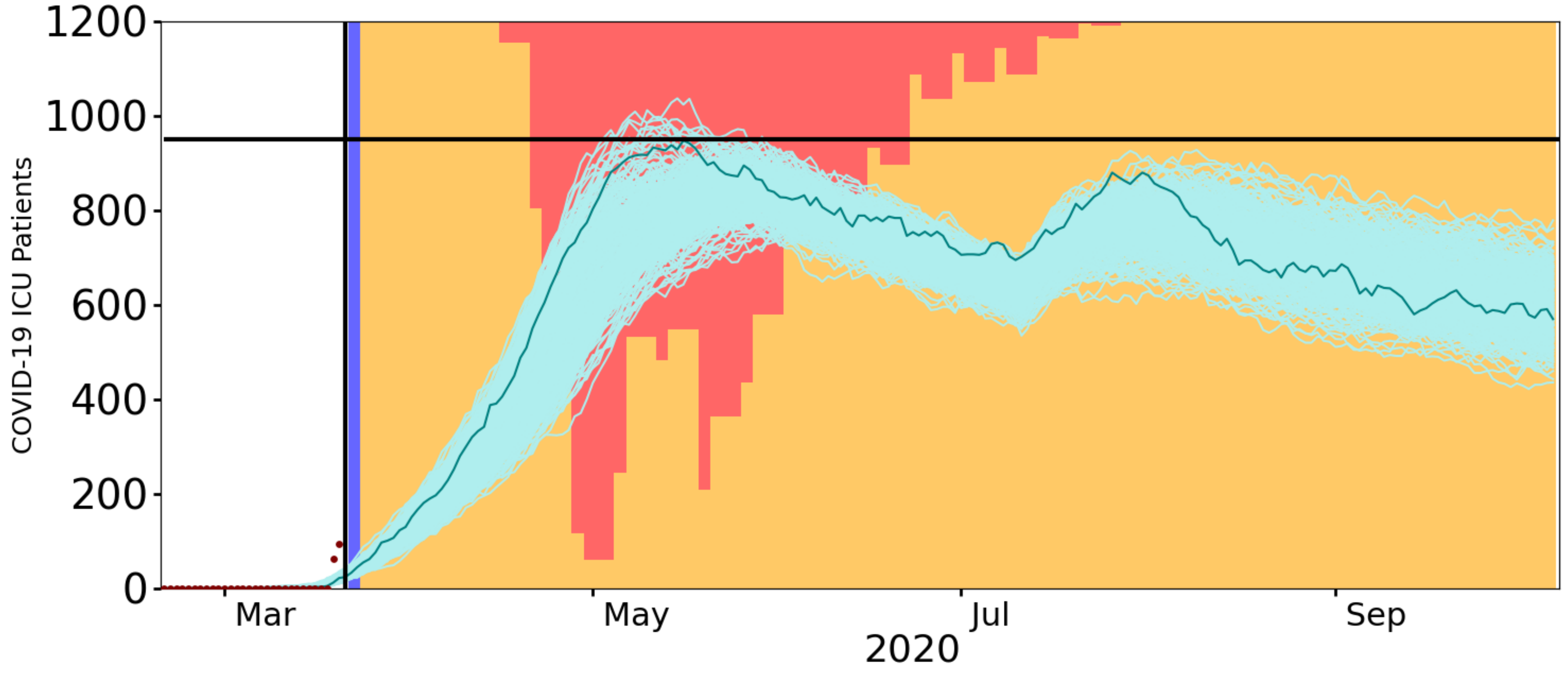
3 times a week



Once a week



Twice a week



Takeaway:
Decreasing sample collection frequency may increase socioeconomic cost.

Summary & Future Work

- We design a staged-alert system guided by the wastewater signal.
- We perform a retrospective analysis to compare wastewater policy and hospitalization policy.
- This framework shows great potential in guiding upstream sampling (e.g., ramp up sample collection or lab report based on the indicated stage)
- Future work includes
  - ✦ Using finer grid and lager sample paths to obtain more accurate policy (i.e., thresholds)
  - ✦ Using data degradation to mimic the noise in the streaming data
  - ✦ Designing a staged-alert system guided by the **hybrid** signals
  - ✦ Designing an adaptive staged-alert system that is able to track the evolution of the virus.