SAND2020-6501PE

EPIDEMIOLOGY MODELING OF THE COVID-19 PANDEMIC

June 30, 2020

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COVID-19 IN THE NEWS AND PUBLICATIONS

Forecast (reported on March 16) : Imperial College COVID-19 Response Team Published
[Ferguson, 2020]

- An unmitigated epidemic is forecasted to result in 2.2M deaths in the U.S.

Stay-at-Home Orders

Forecast (reported on March 31) : White House Briefing
https://www.whitehouse.gov/briefings-statements/remarks-president-trump-vice-president-pence-members-coronavirus-task-force-press-briefing-15/ [Dr. Birx]

- With social distancing in place the forecasted death toll in the U.S. will be 100—200K

Mandated Facial Masks in Public

June 20 : CDC Daily Updates of Totals by Week and State
(Provisional Death Counts for Coronavirus Disease 2019 (COVID-19))
https://www.cdc.gov/nchs/nvss/vsrr/covid19/index.htm

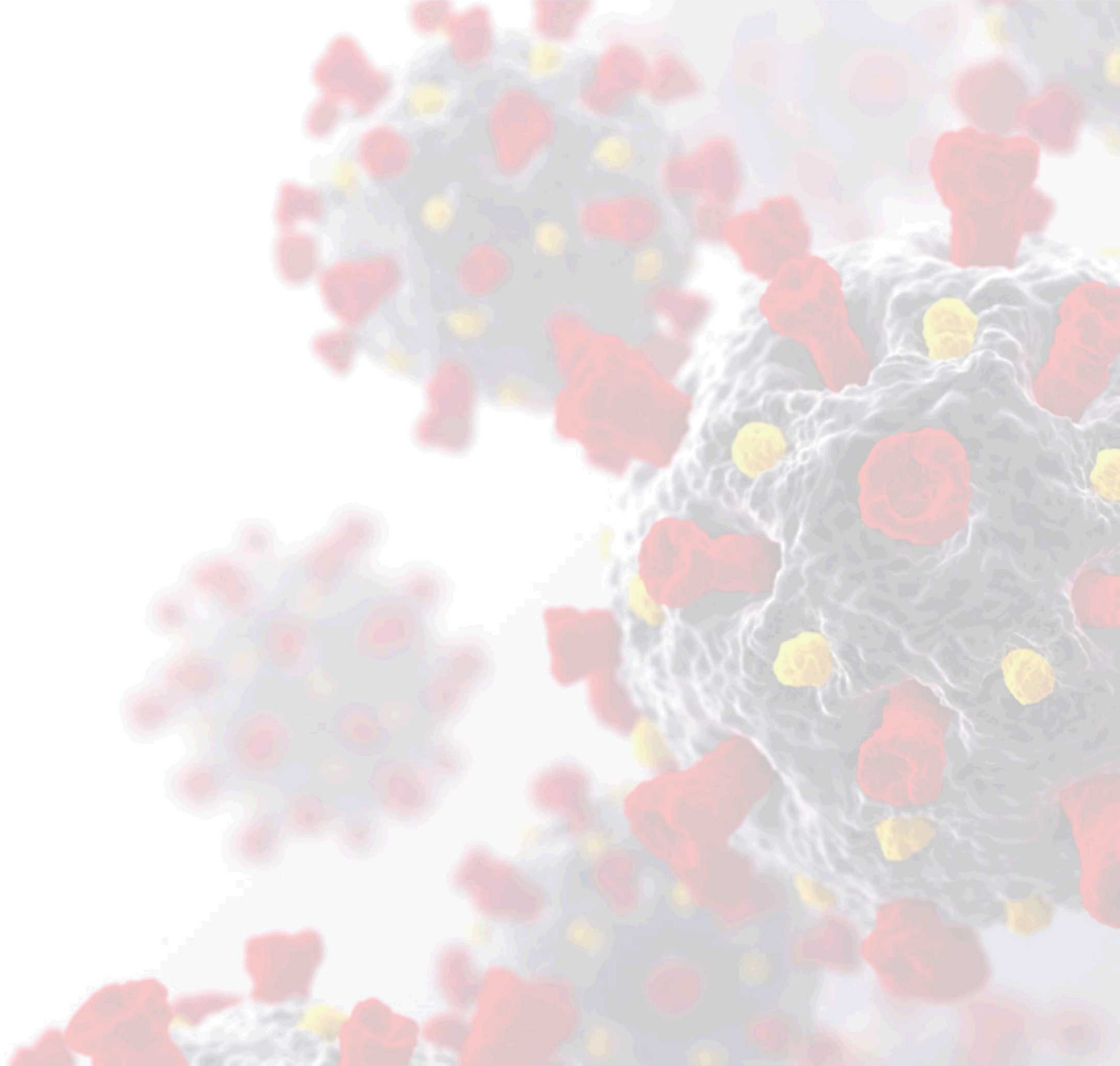
- The reported number of COVID-19 deaths is ~106K in the U.S.

States Start Opening Back Up

Forecast for October 1 (reported on June 23) :
Institute for Heath Metrics and Evaluation (IHME) at University of Washington
https://covid19.healthdata.org/united-states-of-america

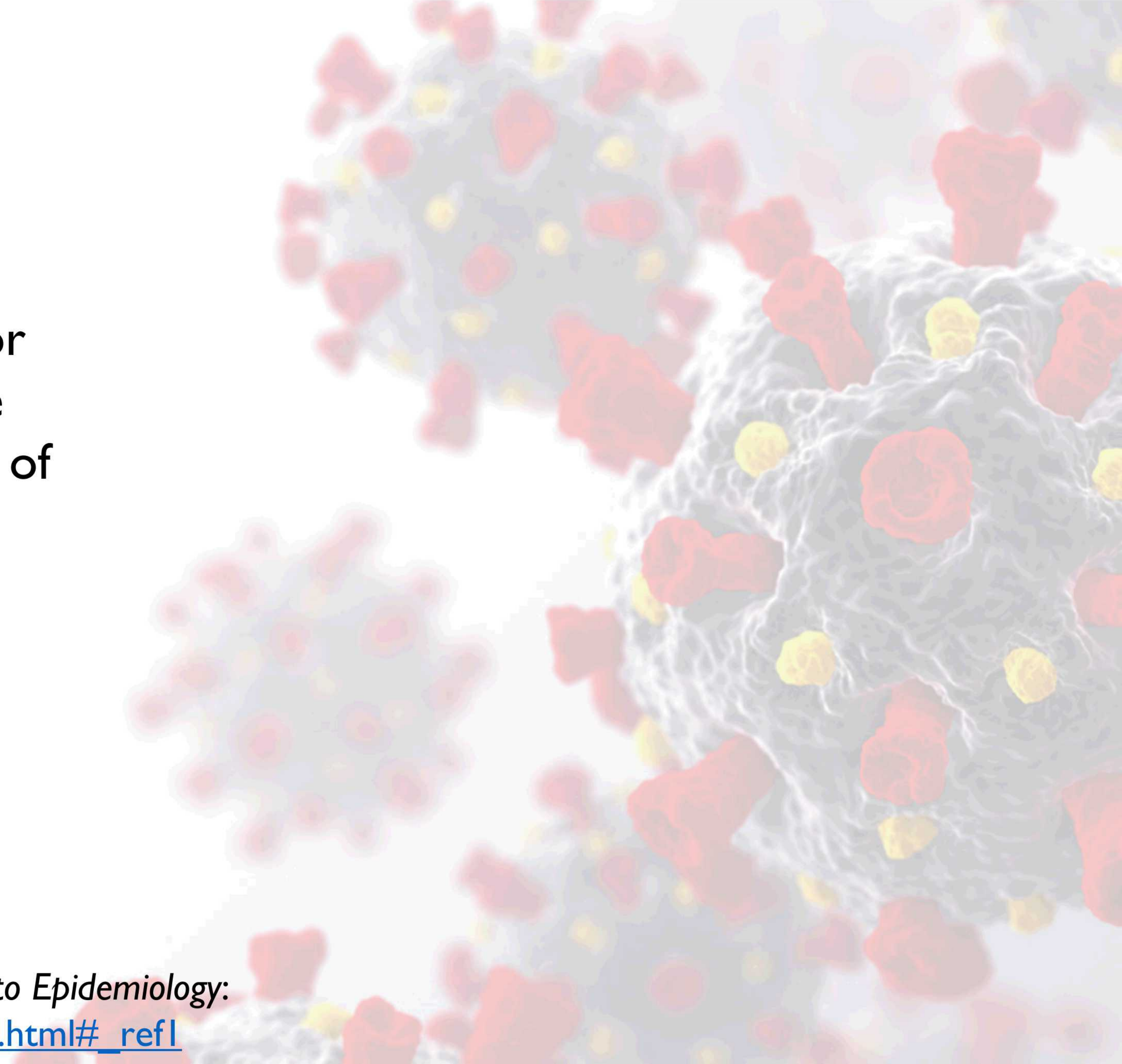
- Assuming social distancing is relaxed, there will be 170K-270K deaths in the U.S.

OUTLINE



- INTRO TO EPIDEMIOLOGY
- MEDICAL RESOURCE UTILIZATION
- EPI MODELING PARADIGMS
- MODELING MITIGATION STRATEGIES

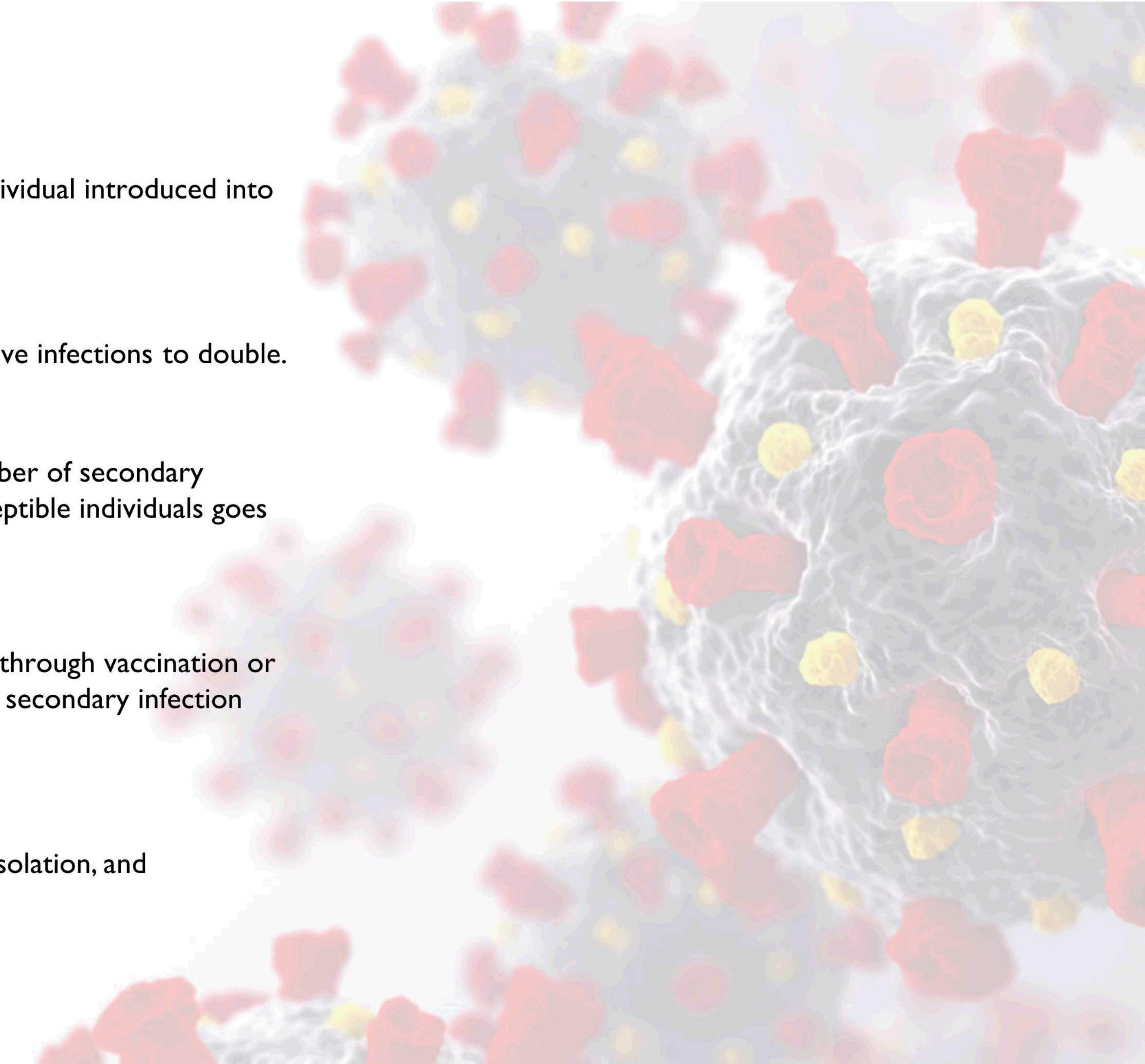
EPIDEMIOLOGY



The study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems [Last, 2001]

For more details, please reference the CDC's *Introduction to Epidemiology*: https://www.cdc.gov/csels/dsepd/ss1978/Lesson1/Section1.html#_ref1

EPIDEMIOLOGY NOMENCLATURE



Basic Reproduction Number, R_0

The expected number of infections from one infected individual introduced into a population of 100% susceptible individuals.

Doubling Time, T_d

The expected amount of time for the number of cumulative infections to double.

Replacement Number, R

After the early stages of an epidemic has passed, the number of secondary infections is expected to go down as the number of susceptible individuals goes down.

Herd Immunity

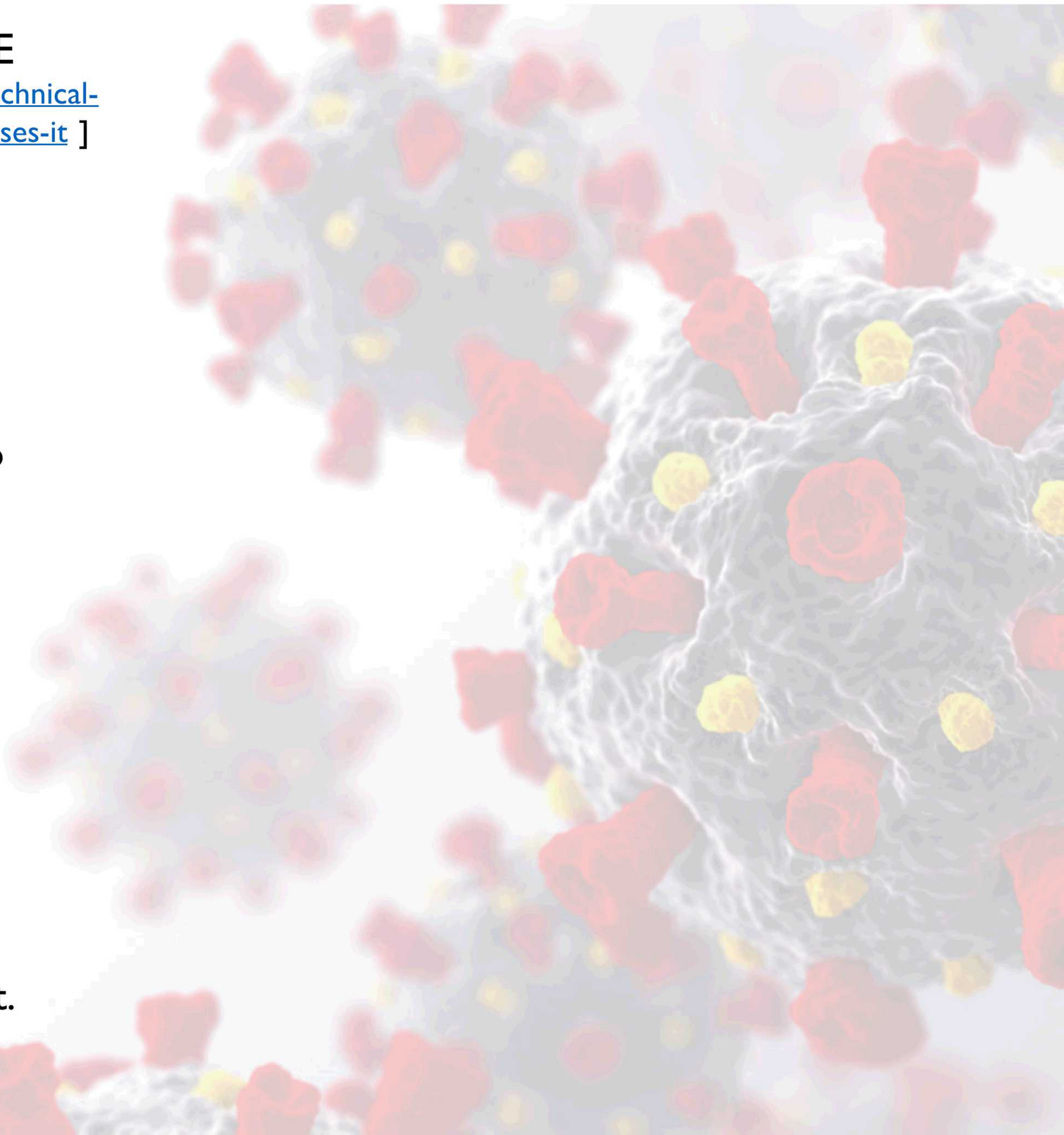
Implies the susceptible population is small enough, either through vaccination or immunity due to infection and recovery, that the effective secondary infection rate tends toward 0.

Non-Medical Interventions (NMI)

Social distancing, business & school closures, face masks, isolation, and quarantine.

THE COVID-19 PANDEMIC NOMENCLATURE

[WHO, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it]



Virus:

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

Viruses are named based on their genetic structure to facilitate the development of diagnostic tests, vaccines and medicines.

Pathology

Disease:

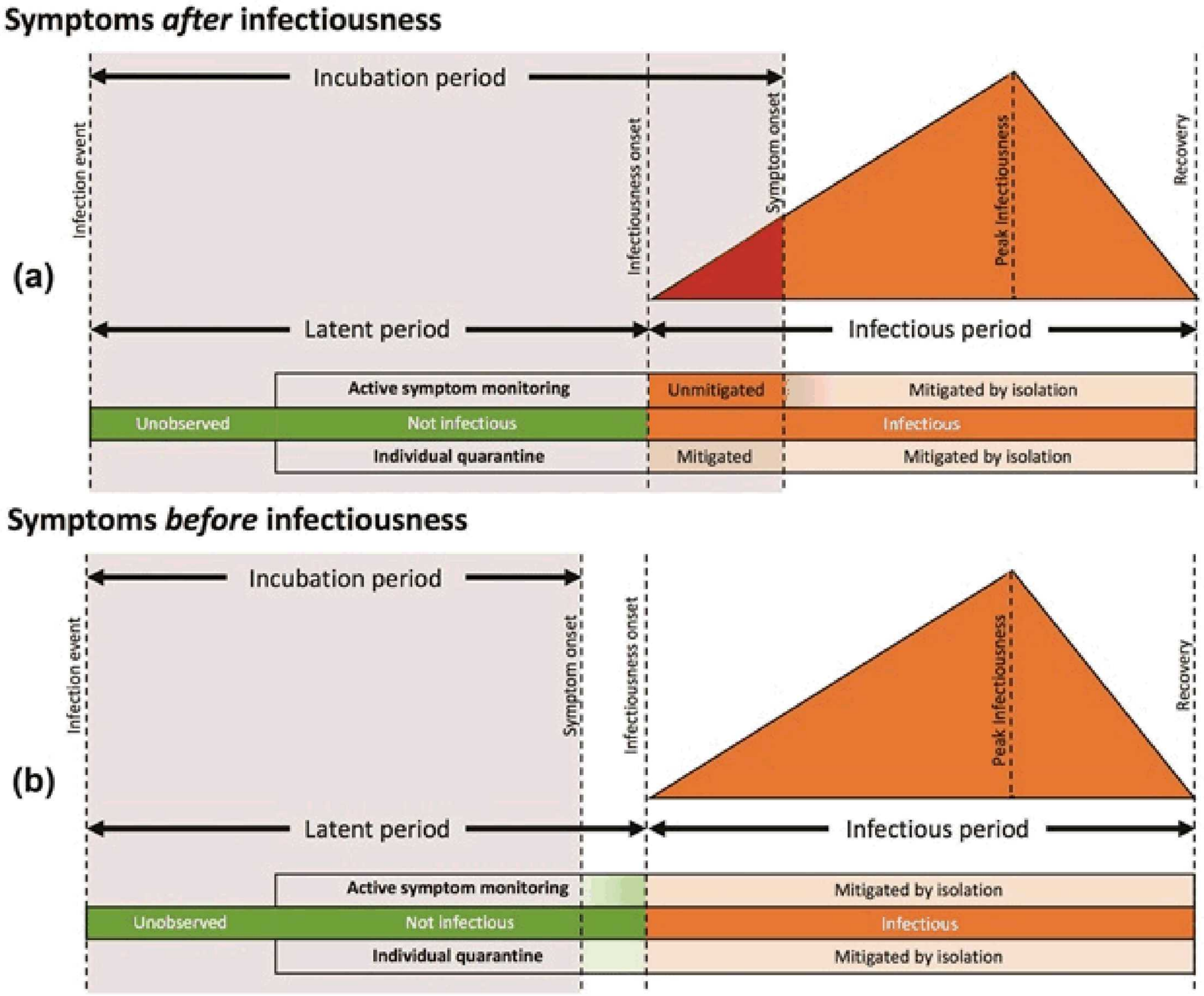
COronaVIrus Disease, 2019 (COVID-19)

Diseases are named to enable discussion on disease prevent, spread, transmissibility, severity and treatment.

Epidemiology

TIMELINE OF INFECTION AND TERMINOLOGY

[Childs, 2020]



COVID-19

Follows timeline (a)

Infectiousness onset occurring 2-3 days before Symptom onset.

The Peak Infectiousness occurring more closely aligned with the Infectiousness onset

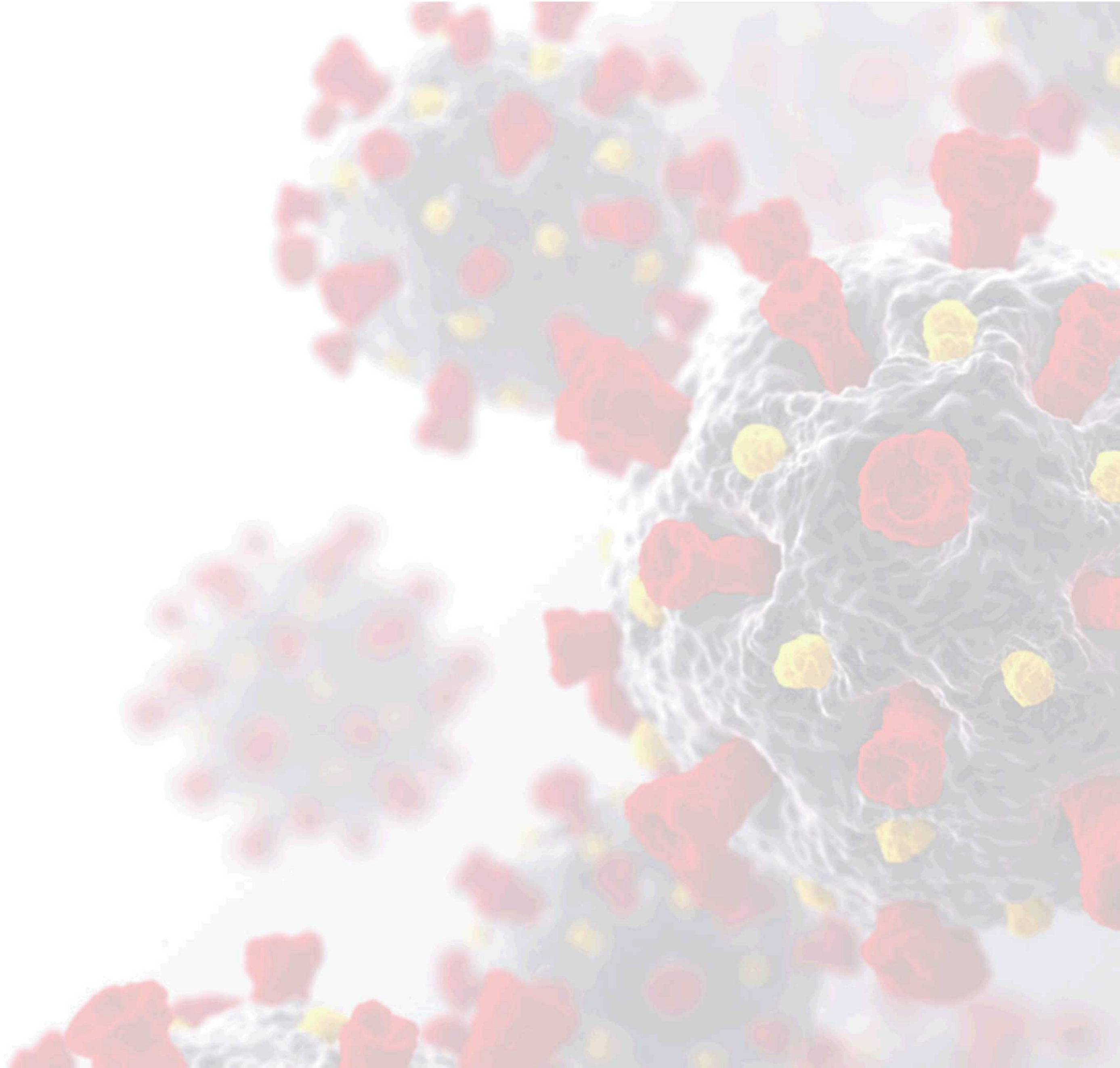
OUTLINE

INTRO TO EPIDEMIOLOGY

MEDICAL RESOURCE UTILIZATION

EPI MODELING PARADIGMS

MODELING MITIGATION STRATEGIES

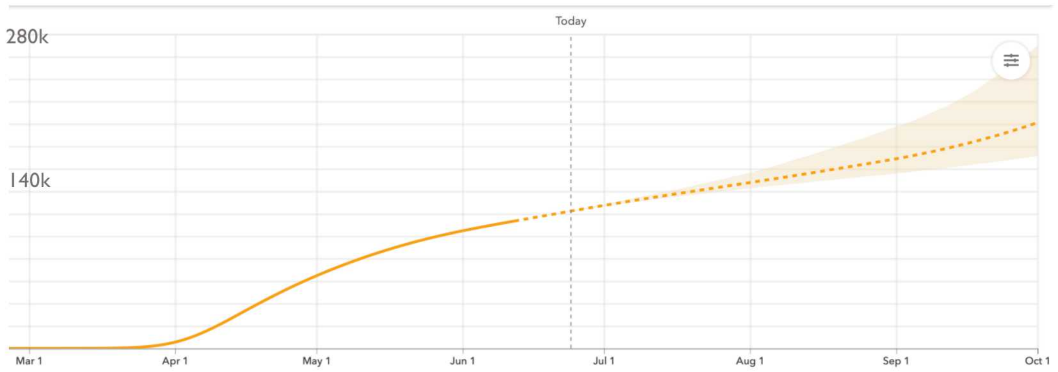


UNIVERSITY OF WASHINGTON: INSTITUTE FOR HEALTH METRICS AND EVALUATION

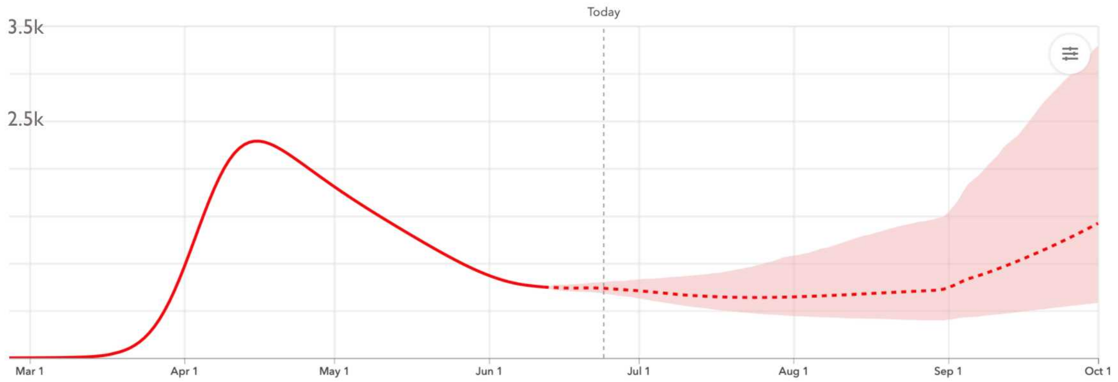
https://covid19.healthdata.org/united-states-of-america (June 24, 2020)

United States Forecasts

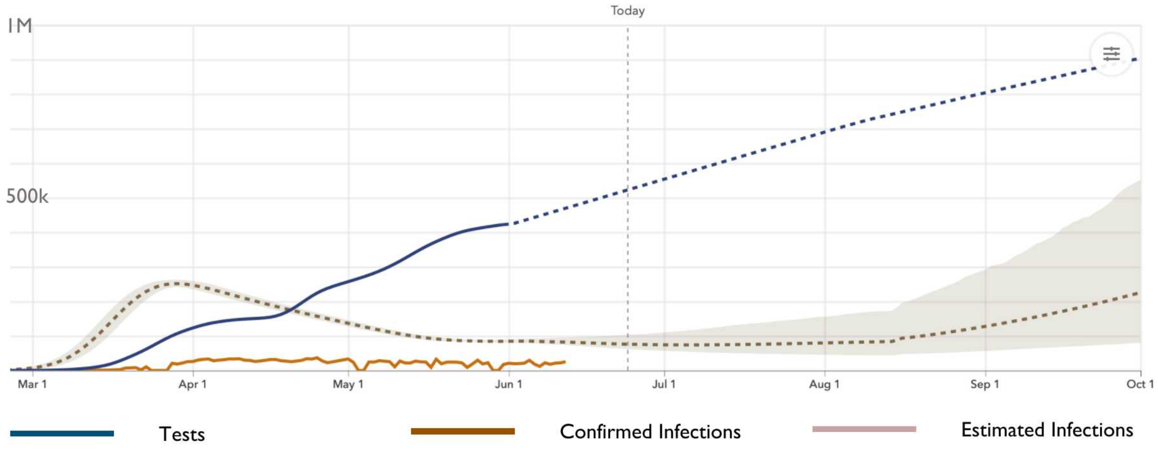
Cumulative COVID-19 Deaths



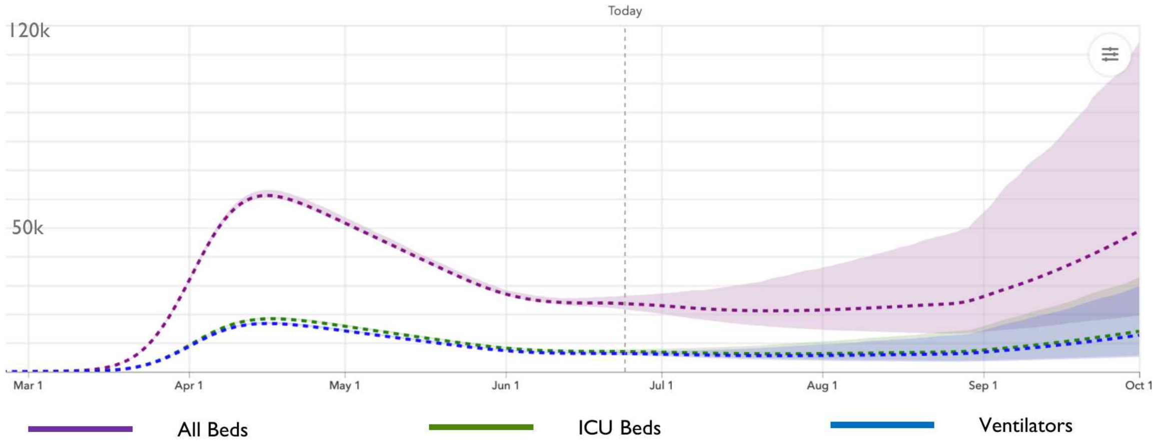
Daily COVID-19 Deaths



Daily Testing and New Cases



Medical Resource Utilization



DETAILED SURGE MODELING OF MEDICAL RESOURCE DEMANDS

Goal

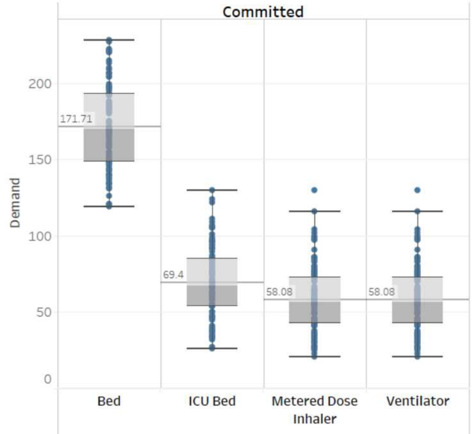
- Calculate resource demands for treating COVID-19 patients based on disease spread projections from epi models
- Anticipate possible times and locations of medical resource shortfalls throughout the pandemic

Approach

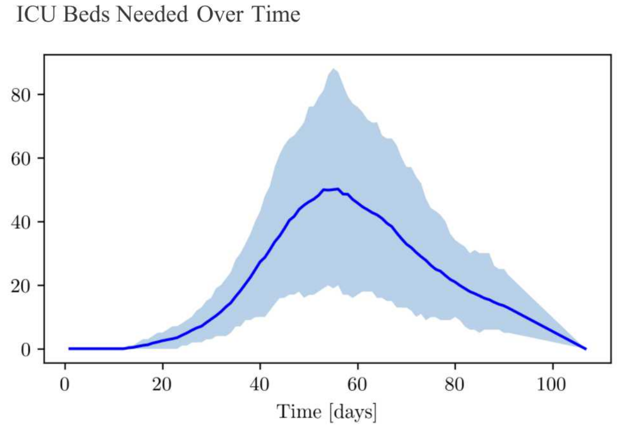
- Use discrete event mathematical model to track patient progress through a hospital treatment system
- Incorporate uncertainty in patient treatment pathways and ranges of resource use per patient to provide risk indicators
- Inputs are patient arrival stream projections from epidemiological models at varying spatial or temporal scales

Results

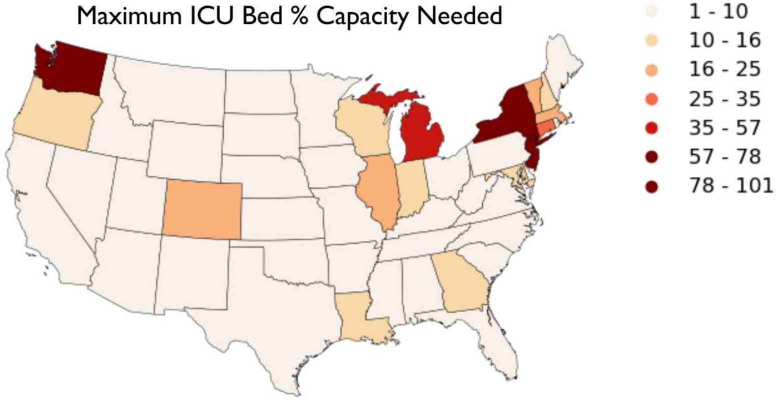
Maximum number of resource needs with a range of uncertainty



Resource needs over time with a range of uncertainty



State or county risk indicators



DETAILED ANALYSIS FOR INDIVIDUAL LOCATIONS

Compare maximum resource demand across different epi models and different scenarios

Inputs

Local

IHME

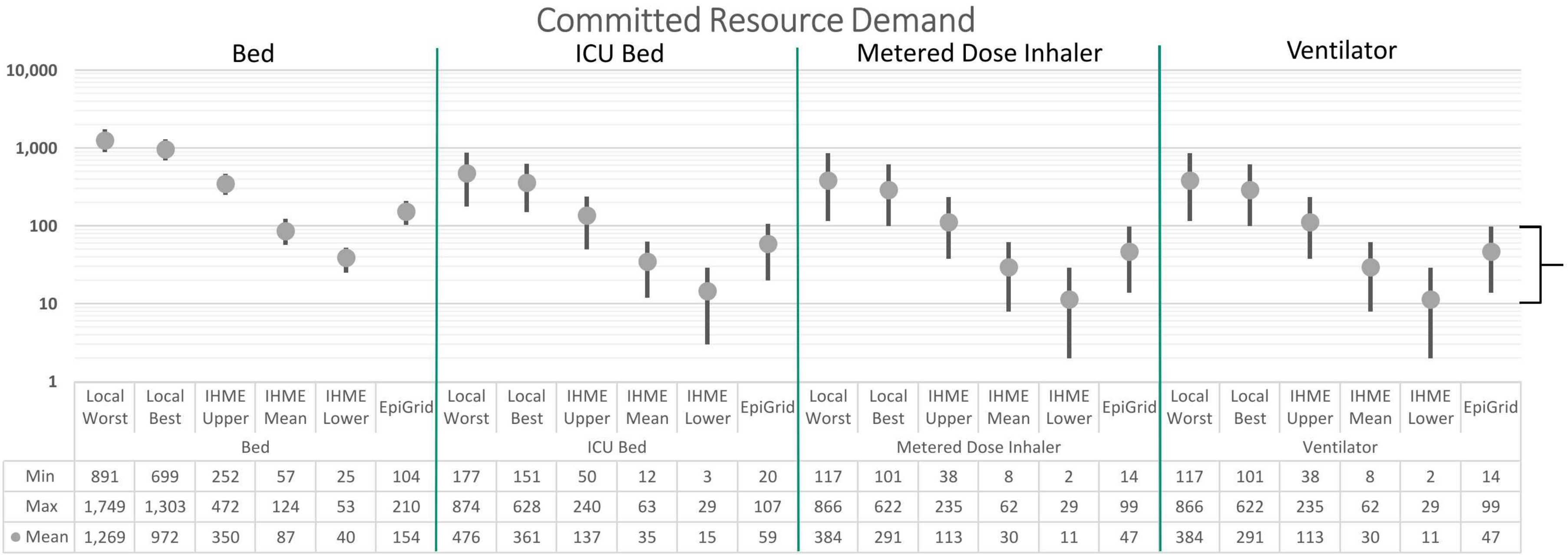
EpiGrid

Outputs

Committed Resources Need Over Time

Consumable Resources Need Over Time

Practitioner Need Over Time



	Local Worst	Local Best	IHME Upper	IHME Mean	IHME Lower	EpiGrid	Local Worst	Local Best	IHME Upper	IHME Mean	IHME Lower	EpiGrid	Local Worst	Local Best	IHME Upper	IHME Mean	IHME Lower	EpiGrid	Local Worst	Local Best	IHME Upper	IHME Mean	IHME Lower	EpiGrid
	Bed						ICU Bed						Metered Dose Inhaler						Ventilator					
Min	891	699	252	57	25	104	177	151	50	12	3	20	117	101	38	8	2	14	117	101	38	8	2	14
Max	1,749	1,303	472	124	53	210	874	628	240	63	29	107	866	622	235	62	29	99	866	622	235	62	29	99
● Mean	1,269	972	350	87	40	154	476	361	137	35	15	59	384	291	113	30	11	47	384	291	113	30	11	47

Ranges in demand are dictated by uncertainties in parameters (e.g., probability the patient goes into the ICU, needs a ventilator, length of stay)

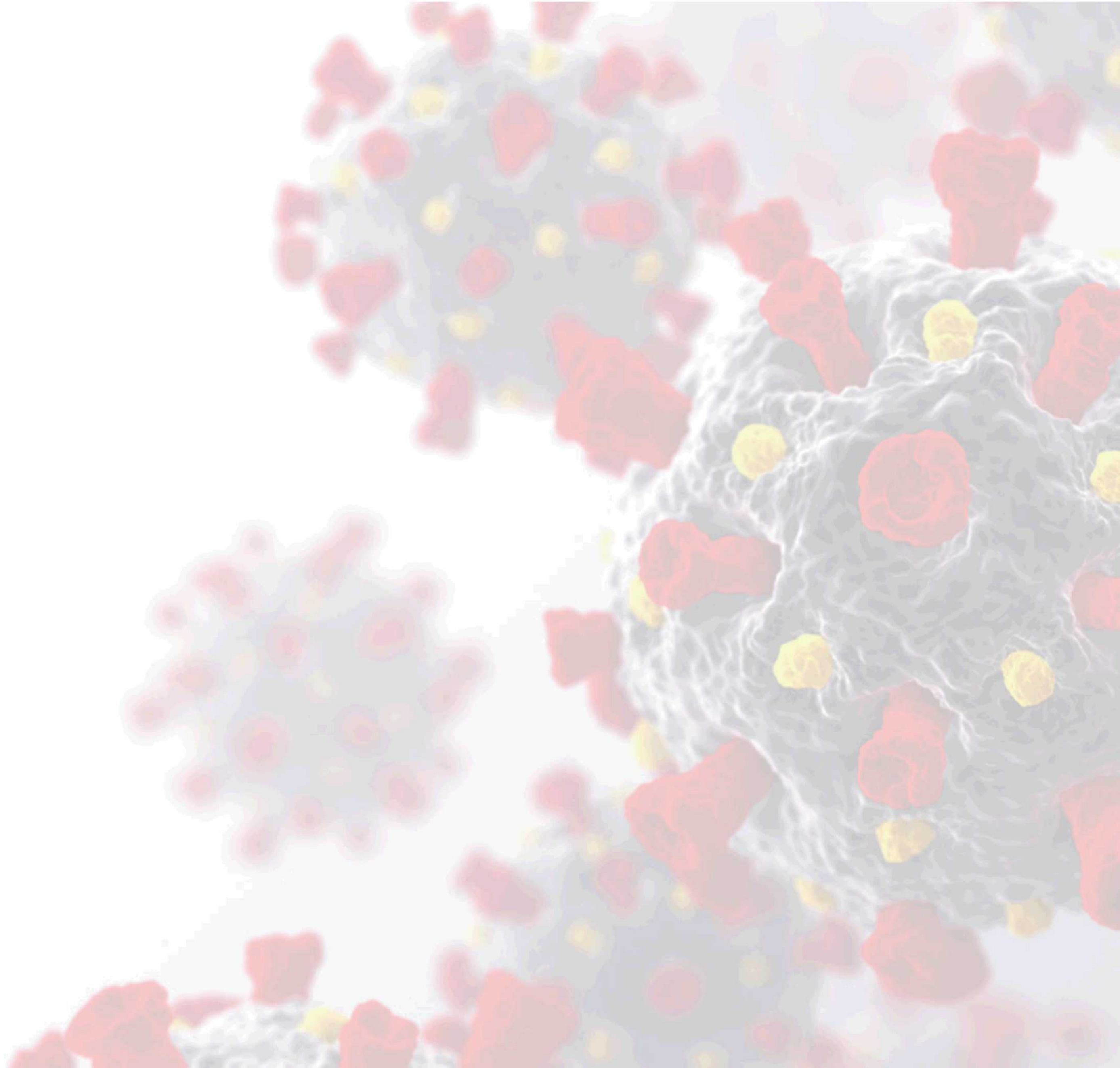
OUTLINE

INTRO TO EPIDEMIOLOGY

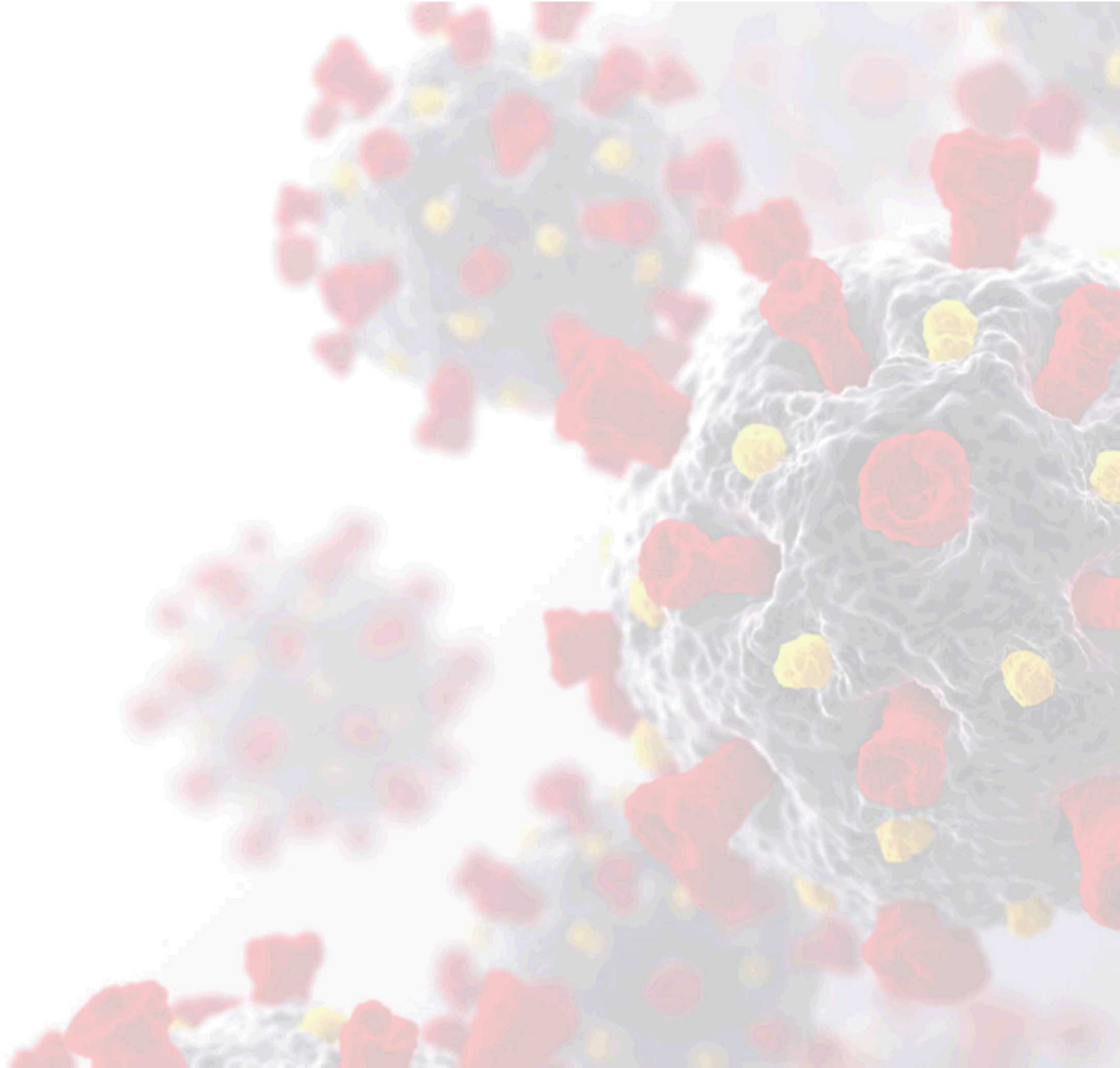
MEDICAL RESOURCE UTILIZATION

EPI MODELING PARADIGMS

MODELING MITIGATION STRATEGIES



VARIETY OF MODELING PARADIGMS



Limited Range Forecasts:

- Exponential Growth
- Bayesian Methods

Mid-Late Stage:

- Compartmental Models (SIR, SEIR, ect.)

Early-Late Stage:

- Self-Exciting Point Process (Branching-Process)

EXPONENTIAL GROWTH

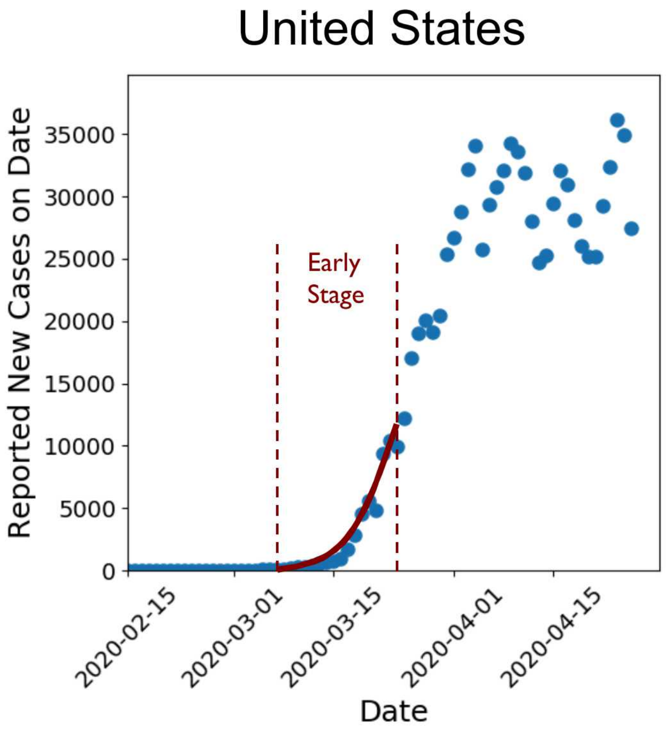
[Bertozzi, 2020]

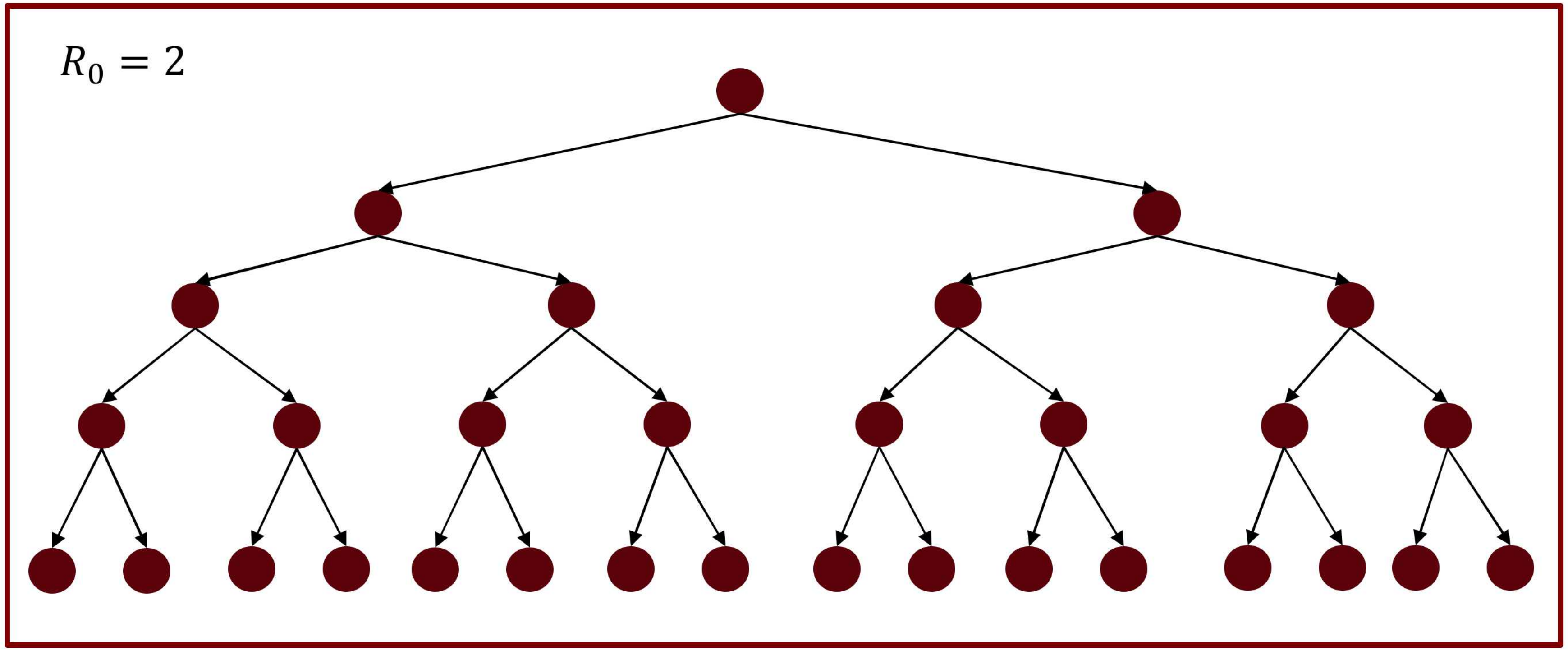
As an early stage model, these models are typically used to derive the secondary infection rate, R_0, for an emerging epidemic.

$$I(t) = I_0 e^{R_0 t}$$

$$T_d = \ln(2)\,/R_0$$

$$R_0 = \ln(2)\,/T_d$$

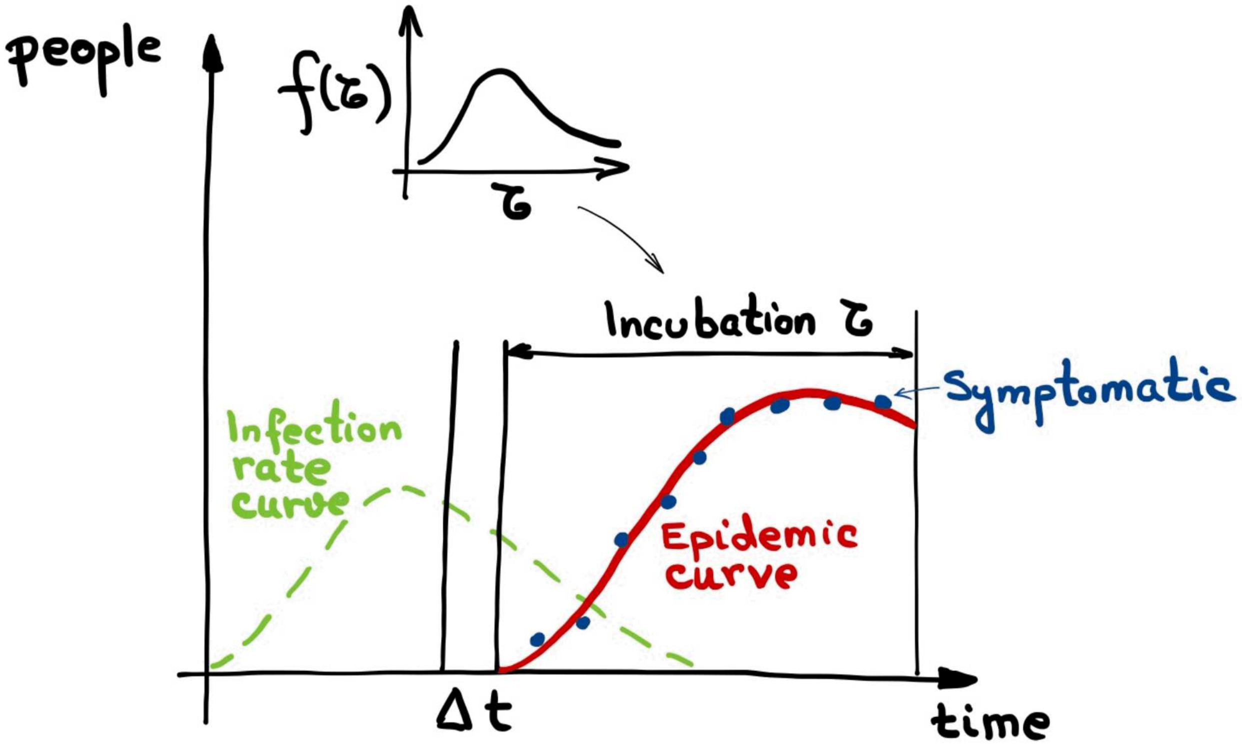




BAYESIAN MODEL: COVID-19 MODELING AND BAYESIAN FORECAST (COMBO)

[Safta, 2011]

From observable reported new cases, Bayesian models infer the infection rate curve then push forward a predictive epidemic curve.



- Infection Rate curve modeled as a Gamma distribution with unknown shape (k) and scale (θ) parameters

$$\mathrm{InfR}(t - t_0) \sim \Gamma(k, 1/\theta)$$

- The incubation rate is modeled using a log-normal distribution with parameters based on published results [Lauer, 2020]

$$\mathrm{IncR} \sim \mathrm{Lognormal}(\mu(\xi_1), \sigma(\xi_2)^2)$$

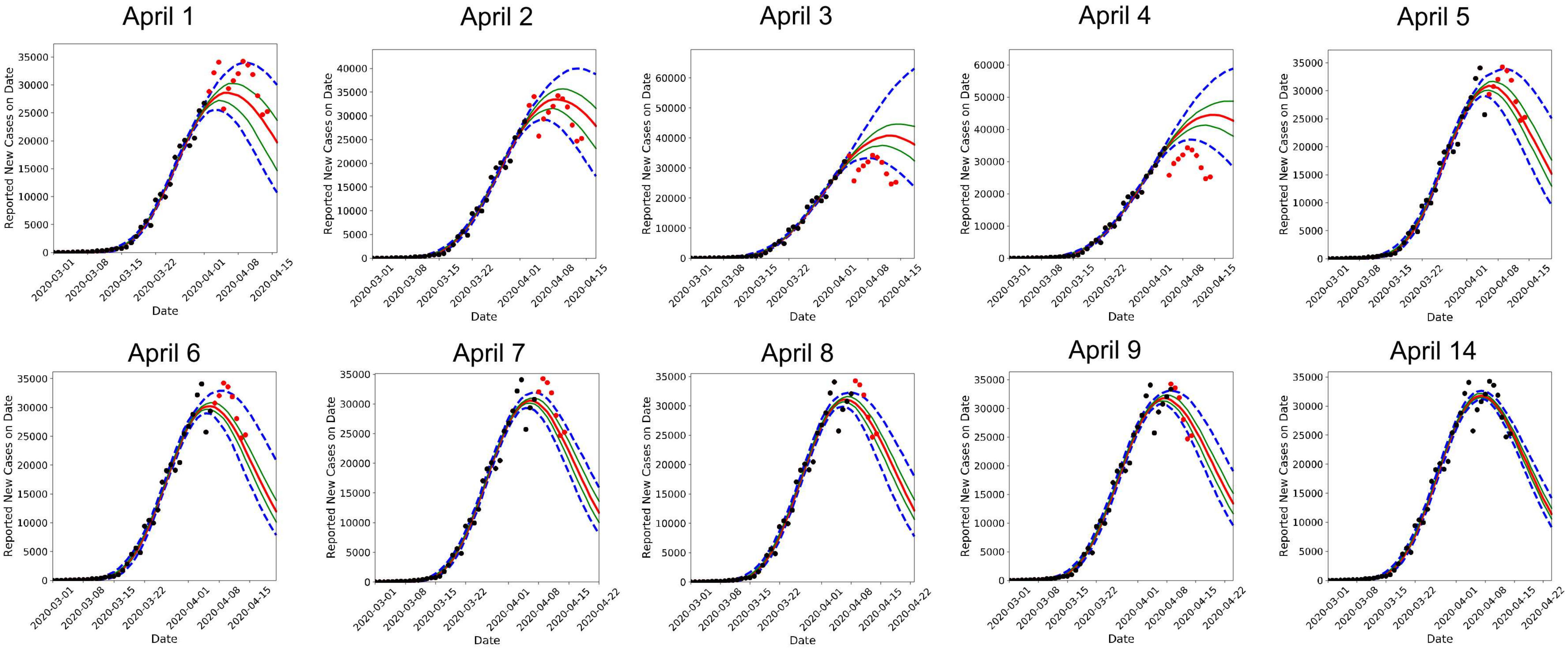
$$\mu = 1.504 \ldots 1.755$$

$$\sigma = 0.271 \ldots 0.542$$

BAYESIAN MODEL: COVID-19 MODELING AND BAYESIAN FORECAST (COMBO)

[Safta, 2011]

U.S. Forecasts over time, learning the bend in the curve



- Black symbols show data used for model inference and to generate forecasts
- Red symbols display data observed after the forecast was produced

COMPARTMENTAL MODELS

[Hethcote, 2000]

Susceptible-Exposed-Infected-Recovered

System of ordinary differential equations (ODEs):

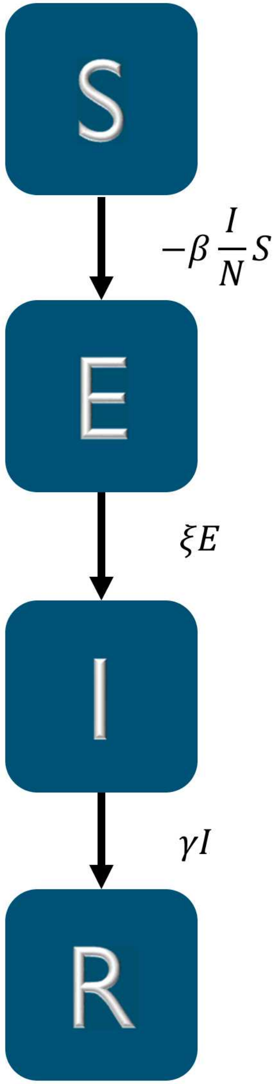
$$\dot{S} = -\beta \frac{I}{N} S$$
$$\dot{E} = \beta \frac{I}{N} S - \xi E$$
$$\dot{I} = \xi E - \gamma I$$
$$\dot{R} = \gamma I$$

Force of Infection Function: $\beta \frac{I}{N}$

Average Incubation Period: $\frac{1}{\xi}$

Average Infectious Period: $\frac{1}{\gamma}$

Model $R_0 = \beta \frac{1}{\gamma}$



$$N = S + E + I + R$$

COMPARTMENTAL MODELS

[Hethcote, 2000]

Susceptible-Exposed-Infected-Recovered
Explicitly add a parameter for average number of contacts.

System of ordinary differential equations (ODEs):

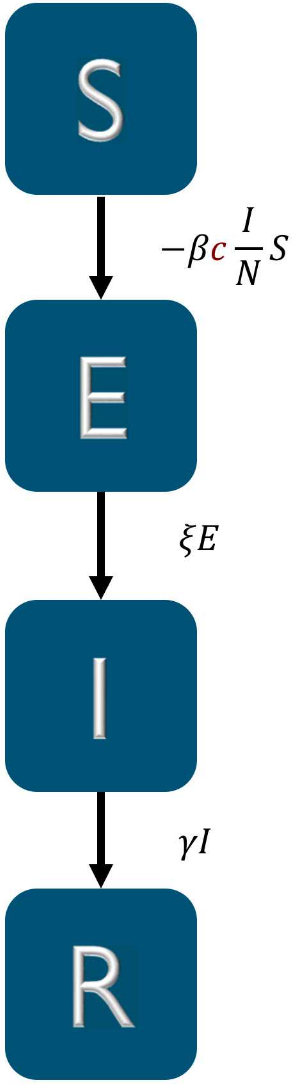
$$\dot{S} = -\beta c \frac{I}{N} S$$
$$\dot{E} = \beta c \frac{I}{N} S - \xi E$$
$$\dot{I} = \xi E - \gamma I$$
$$\dot{R} = \gamma I$$

Force of Infection Function: $\beta c \frac{I}{N}$

Average Incubation Period: $\frac{1}{\xi}$

Average Infectious Period: $\frac{1}{\gamma}$

Model $R_0 = \beta c \frac{1}{\gamma}$



$$N = S + E + I + R$$

COMPARTMENTAL MODELS

[Hethcote, 2000]

Susceptible-Exposed-Infected(Asymptomatic)-Infected(Symptomatic)-Recovered
Explicitly add a parameter for average number of contacts.

System of ordinary differential equations (ODEs):

$$\dot{S} = -\beta c \frac{A+I}{N} S$$

$$\dot{E} = \beta c \frac{A+I}{N} S - \xi E$$

$$\dot{A} = f_a \xi E - \gamma_A A$$

$$\dot{I} = (1 - f_a)\xi E - \gamma_I I$$

$$\dot{R} = \gamma_A A + \gamma_I I$$

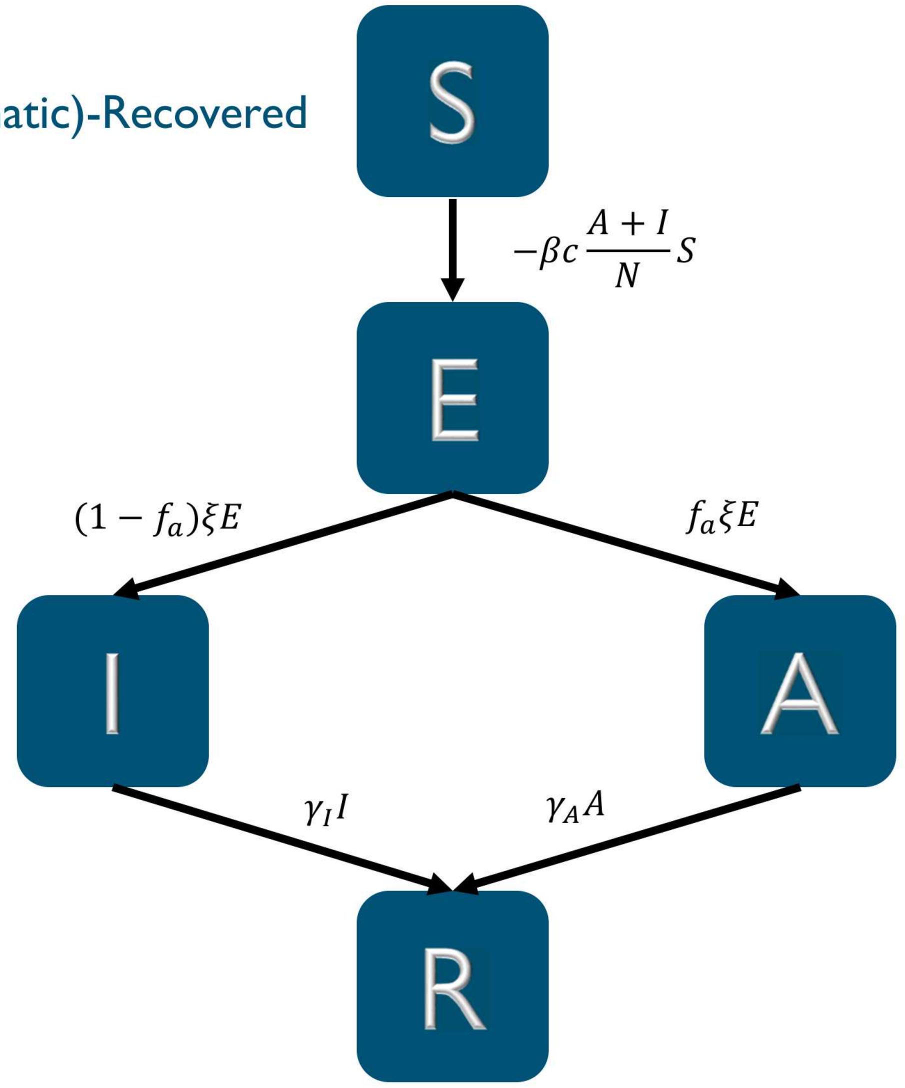
Force of Infection Function: $\beta c \frac{A+I}{N}$

Average Incubation Period: $\frac{1}{\xi}$

Average Infectious Period: $½\left(\frac{1}{\gamma_A} + \frac{1}{\gamma_I}\right)$

Proportion of infections that are Asymptomatic: f_a

Model $R_0 = \beta c \left(½\left(\frac{1}{\gamma_A} + \frac{1}{\gamma_I}\right)\right)$

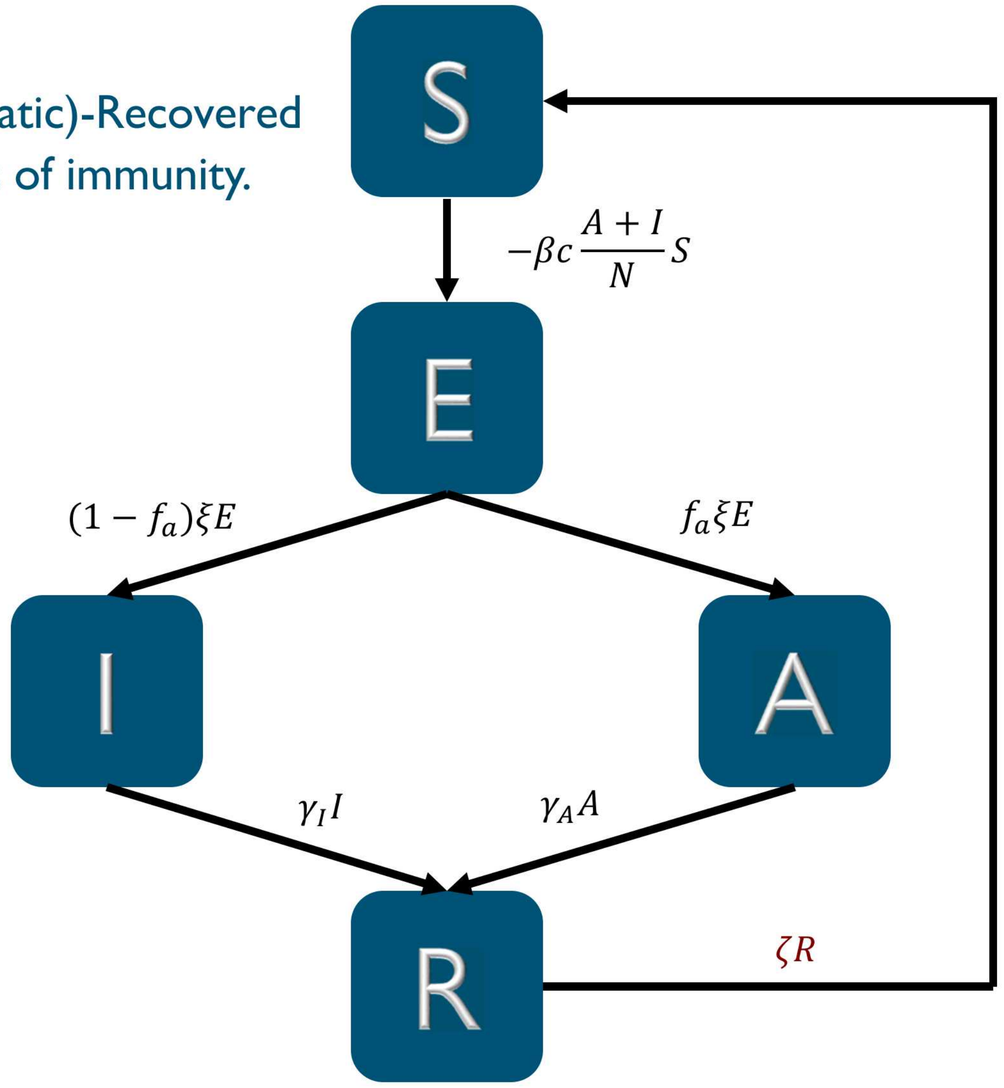


$$N = S + E + A + I + R$$

COMPARTMENTAL MODELS

[Hethcote, 2000]

Susceptible-Exposed-Infected(Asymptomatic)-Infected(Symptomatic)-Recovered
Explicitly add a parameter for average number of contacts & loss of immunity.



System of ordinary differential equations (ODEs):

$$\dot{S} = -\beta c\frac{A+I}{N}S + \zeta R$$
$$\dot{E} = \beta c\frac{A+I}{N}S - \xi E$$
$$\dot{A} = f_a\xi E - \gamma_A A$$
$$\dot{I} = (1-f_a)\xi E - \gamma_I I$$
$$\dot{R} = \gamma_A A + \gamma_I I - \zeta R$$

For COVID-19 secondary infections are possible. Accounting for the potential loss on immunity has been deemed important.

$$N = S + E + A + I + R$$

COMPARTMENTAL MODELS

[Hethcote, 2000]

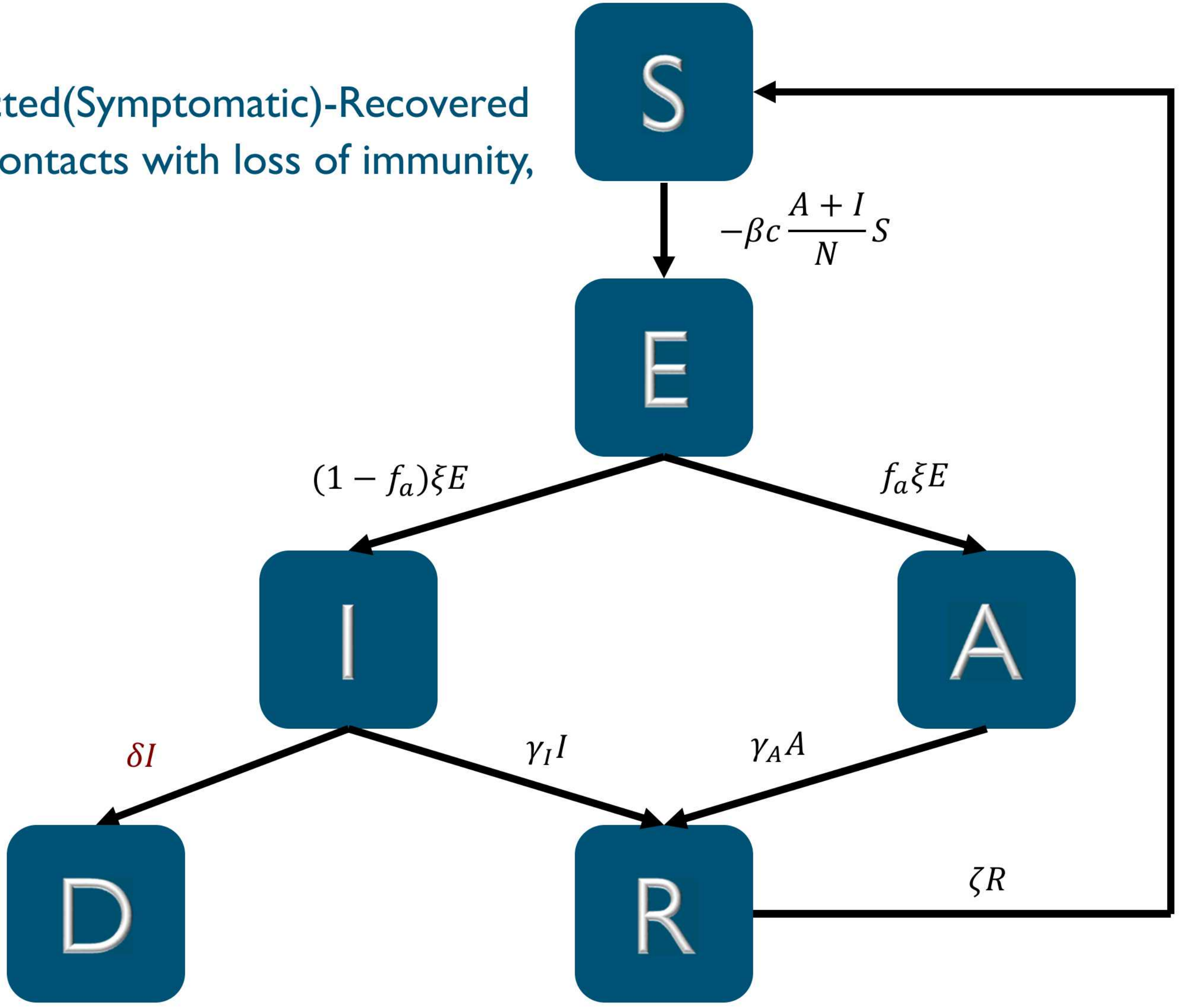
Susceptible-Exposed-Infected(Asymptomatic)-Infected(Symptomatic)-Recovered

Explicitly add a parameter for average number of contacts with loss of immunity, and disease related deaths.

System of ordinary differential equations (ODEs):

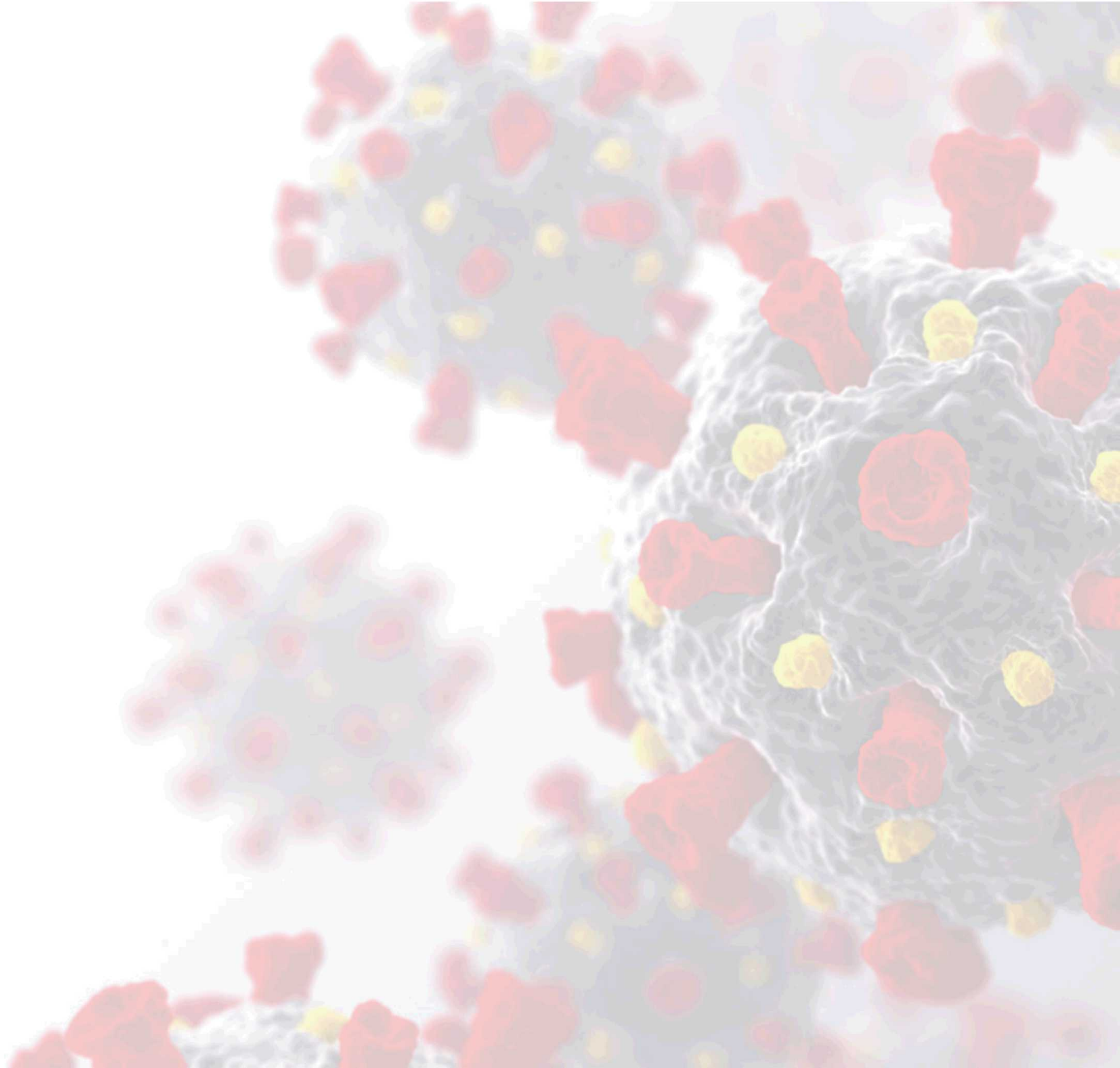
$$\dot{S} = -\beta c \frac{A+I}{N} S + \zeta R$$
$$\dot{E} = \beta c \frac{A+I}{N} S - \xi E$$
$$\dot{A} = f_a \xi E - \gamma_A A$$
$$\dot{I} = (1 - f_a)\xi E - \gamma_I I - \delta I$$
$$\dot{R} = \gamma_A A + \gamma_I I - \zeta R$$
$$\dot{D} = \delta I$$

For COVID-19 Compartmental Epi Modeling: the death state, D, is essential to calibration of the model parameters.



$$N = S + E + A + I + R$$

OUTLINE



INTRO TO EPIDEMIOLOGY

EPI MODELING PARADIGMS

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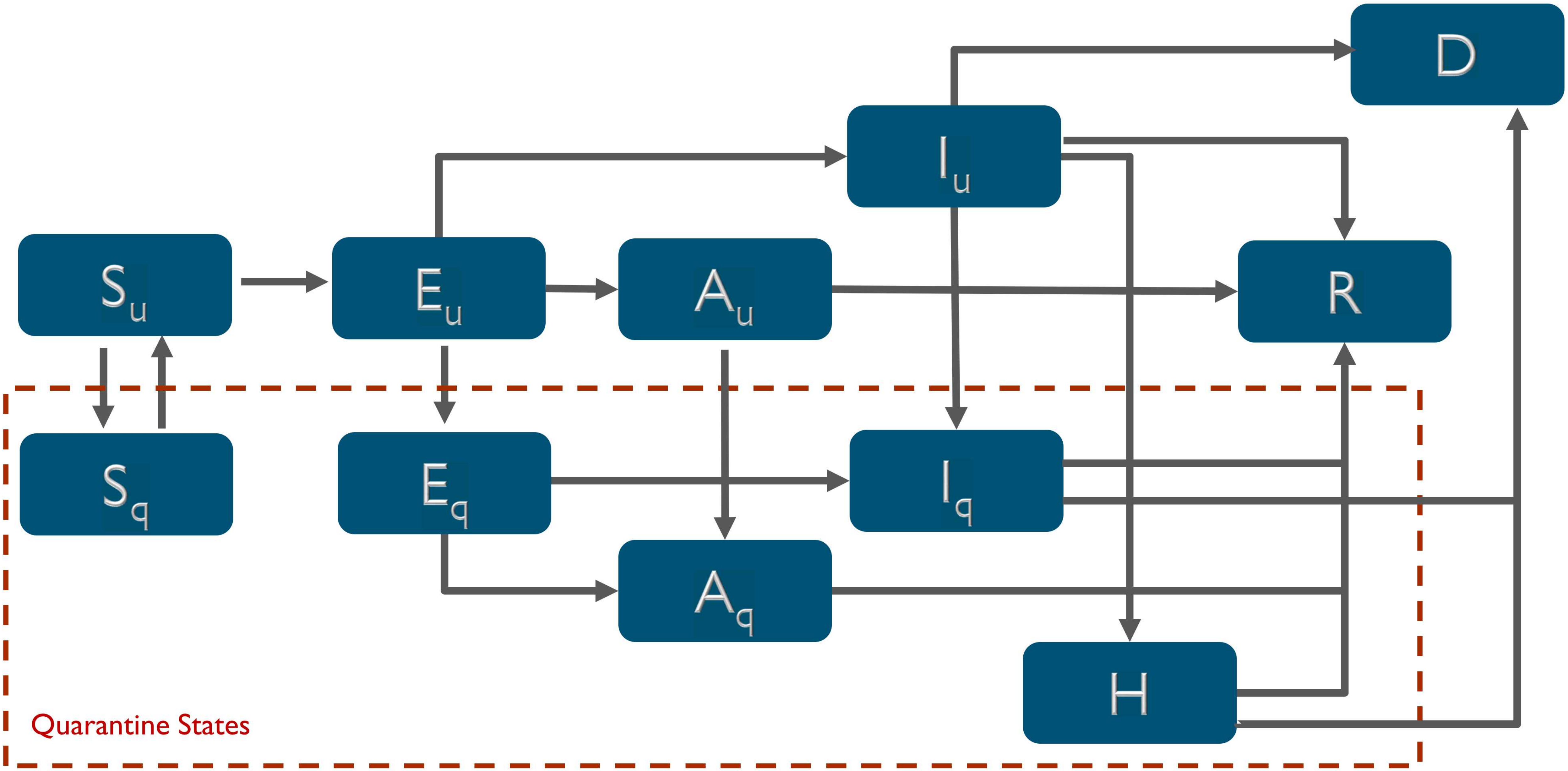
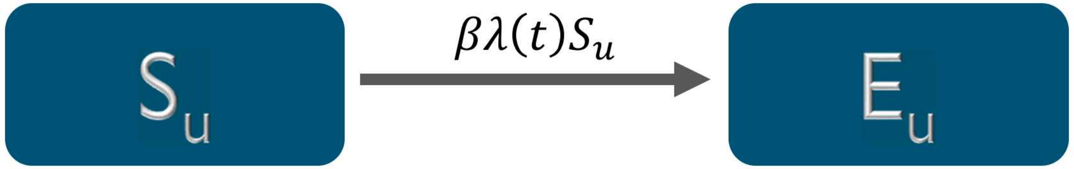
COMPARTMENTAL MODEL: QUARANTINE STATES



FORCE OF INFECTION
ACCOUNTING FOR FACE MASKS AND EFFECTIVENESS OF QUARANTINE



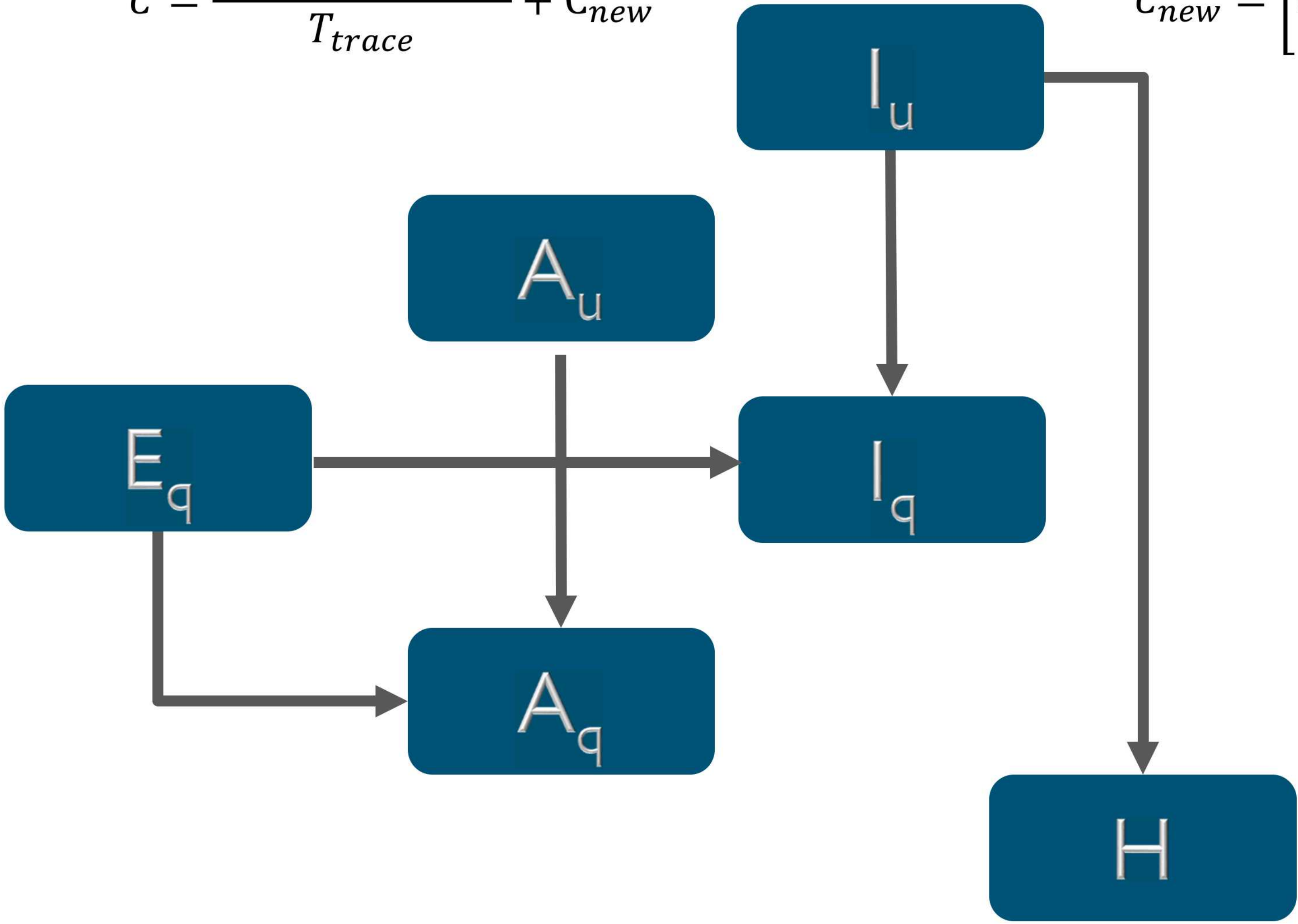
$$\lambda(t) = \frac{\kappa(1-\varepsilon p)(\eta_E E_u + \eta_A A_u + I_u + (1-\theta_q)(\eta_E E_q + \eta_A A_q + I_q + \eta_H H))}{N}$$

$$N = S_u + S_q + E_u + E_q + A_u + A_q + I_u + I_q + H + R$$

κ	Average number of contacts
ε	Effectiveness of face masks
p	Probability an interaction is protected by a face mask
η_*	Relative infectivity of individual in disease state *
θ_q	Effectiveness of Quarantine

COMPARTMENTAL MODEL:
RANDOM TESTING AND CONTACT TRACING INITIATES NEW CONTACTS TO TRACE

$$\dot{C} = \frac{-\min(C, N_{trace})}{T_{trace}} + C_{new}$$

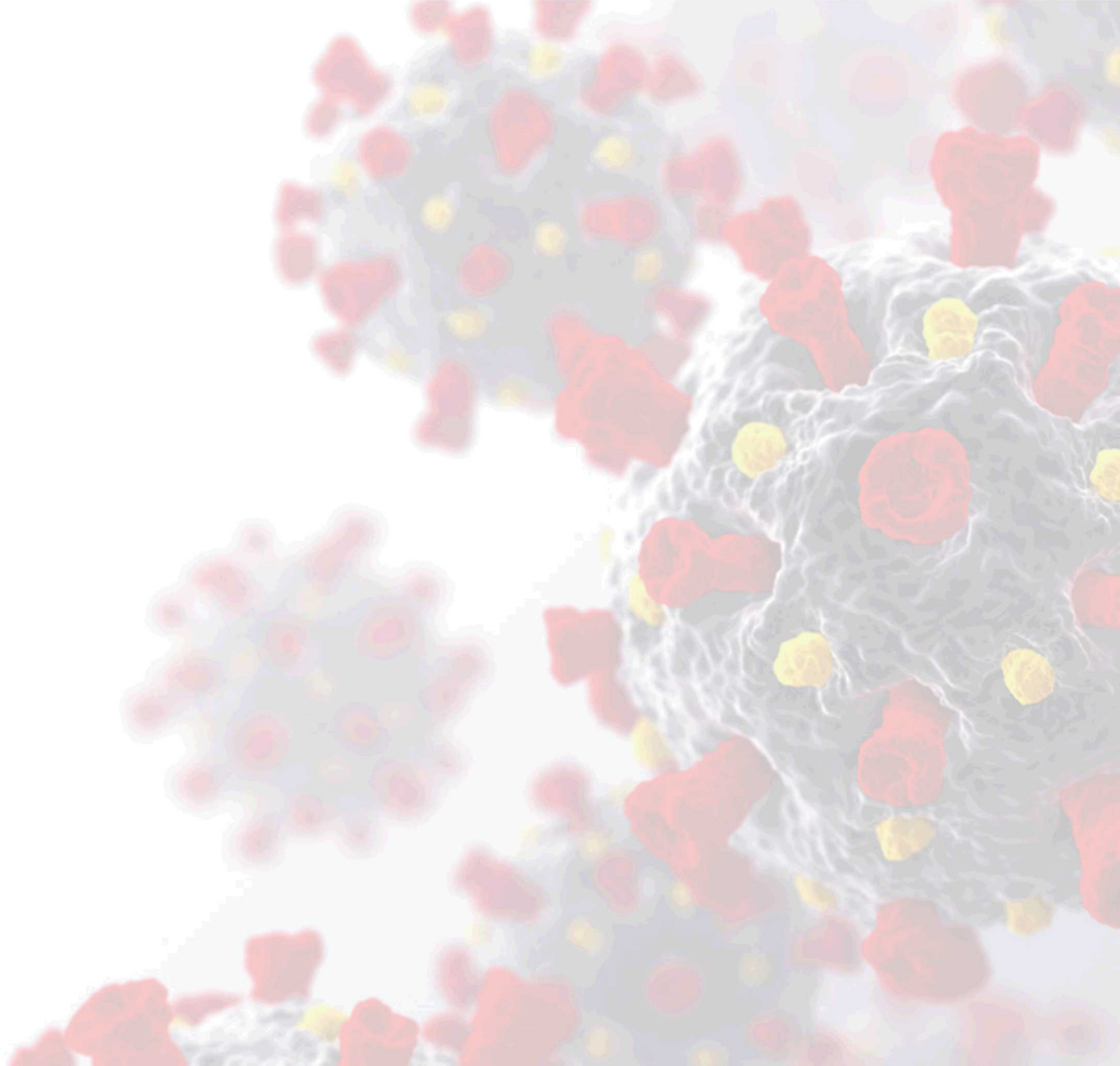


$$C_{new} = \left[d\phi_{\kappa}\kappa T_I \left[1 - \frac{C}{N}\right]\right] * \left[\tau_{E_q} E_q + q_{rA}(t) + q_{rI}(t) + q_{tA}(t) + q_{tI}(t) + \tau_{I_u H} I_u\right]$$

κ	Average number of contacts
d	Dispersion of contact
ϕ_{κ}	Likelihood a contact is recalled
T_I	Average amount of infectious time before identified as COVID-19 positive
τ_{*}	Rate of transmission out of population *
q_{r*}	Rate of random testing
q_{t*}	Rate of contact tracing
N_{trace}	Maximum number of concurrent contact tracing
T_{trace}	Time for contact tracing system to engage each contact

Thank You!

Any Questions?



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BACKUP

EPIDEMIC VS ENDEMIC COMPARTMENTAL MODELS

Epidemic

$$\frac{dS}{dt} = -\beta \frac{cI}{N} S$$

$$\frac{dE}{dt} = \beta \frac{cI}{N} S - \xi E$$

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

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

Endemic

$$\frac{dS}{dt} = bS - \beta \frac{cI}{N} S - dS$$

$$\frac{dE}{dt} = \beta \frac{cI}{N} S - (\xi + d)E$$

$$\frac{dI}{dt} = \xi E - (\gamma + d)I$$

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

b: birth rate
d: non-disease related death rate,

AGE STRUCTURED COMPARTMENTAL MODELS

Homogeneous SEIR (endemic ODE)

$$\frac{dS}{dt} = bS - \beta\frac{cI}{N}S - dS$$

$$\frac{dE}{dt} = \beta\frac{cI}{N}S - (\xi + d)E$$

$$\frac{dI}{dt} = \xi E - (\gamma + d)I$$

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

Heterogeneous SEIR (age structured endemic PDE)

$$\frac{\partial S}{\partial a} + \frac{\partial S}{\partial t} = -(\lambda(a,t) + d(a))S$$

$$\frac{\partial E}{\partial a} + \frac{\partial E}{\partial t} = \lambda(a,t)S - (\xi + d(a))E$$

$$\frac{\partial I}{\partial a} + \frac{\partial I}{\partial t} = \xi E - (\gamma + d(a))I$$

$$\frac{\partial R}{\partial a} + \frac{\partial R}{\partial t} = \gamma I - \mathrm{d(a)R}$$

With:

$$\lambda(a,t) = \frac{\int_0^\infty b(a)\,\tilde{b}(\tilde{a})I(\tilde{a},t)d\tilde{a}}{\int_0^\infty U(\tilde{a},t)d\tilde{a}}$$

$U(a,t)$: age distribution of the total population

$d(a)$: age-specific non-disease related death rate

b: birth rate, β: infectivity, c: # of contacts, d: non-disease related death rate,
ξ: reciprocal incubation window, γ: reciprocal infectious window