HOW TO STOP COVID-19 USING MATHEMATICS

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COVID-19 MODELLING GROUP

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Stanford University


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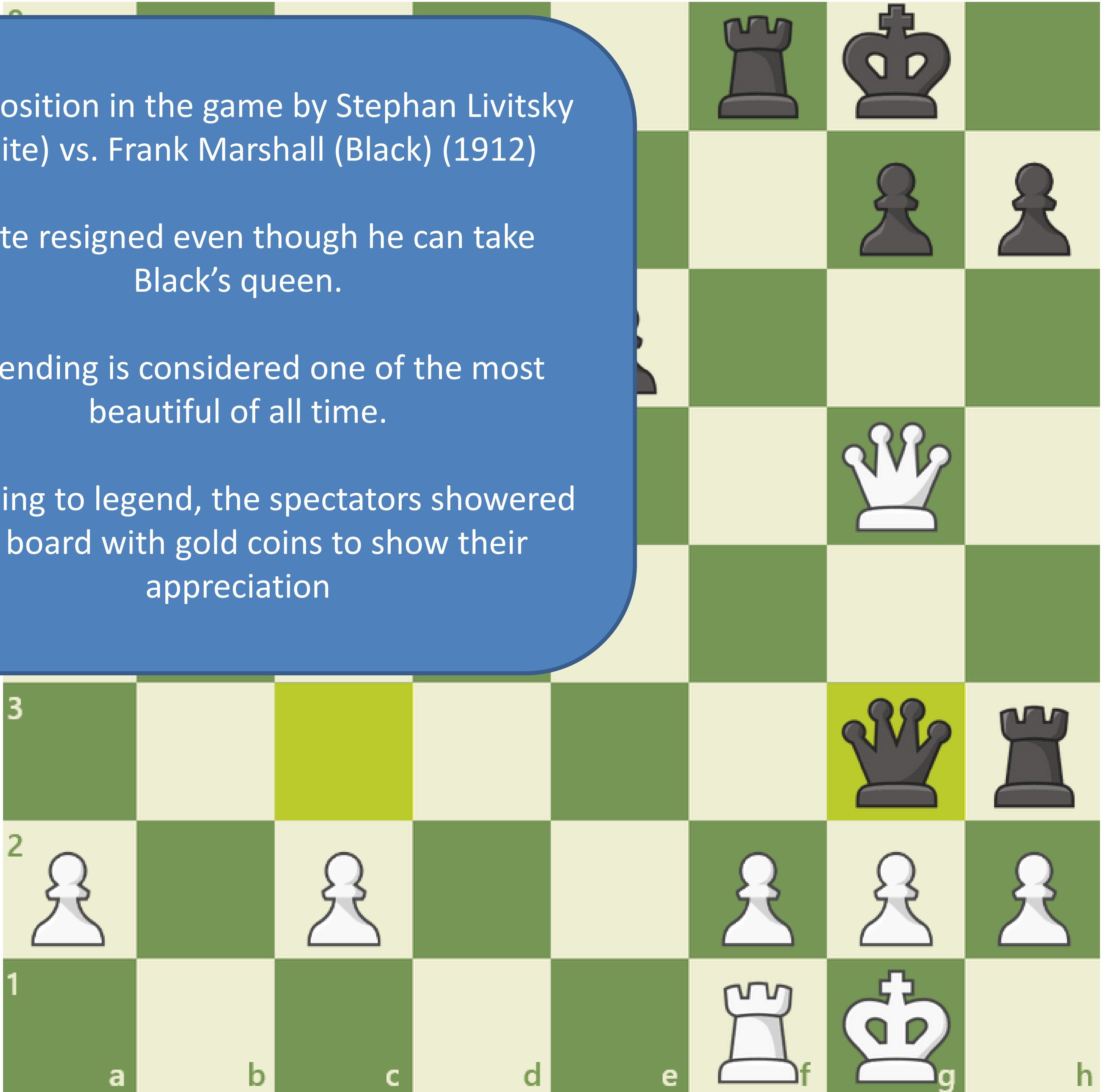

Final position in the game by Stephan Livitsky (White) vs. Frank Marshall (Black) (1912)

White resigned even though he can take Black’s queen.

This ending is considered one of the most beautiful of all time.

According to legend, the spectators showered the board with gold coins to show their appreciation

Legend of the invention of chess

- As a reward for creating chess, a king promised to give the inventor
  - 1 grain of rice for the 1st square (day 1)
  - 2 grains of rice for the 2nd square (day 2)
  - 2 X 2 grains of rice for the 3rd square (day 3)
  - 2 X 2 X 2 grains of rice for the 4th square (day 4)
  - 2 X 2 X 2 X 2 grains of rice for the 5th square (day 5)
  -
  -
  - ??? grains of rice for the 64th square (day 64)

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  - 2 X 2 X 2 grains of rice for the 4th square (day 4)
  - 2 X 2 X 2 X 2 grains of rice for the 5th square (day 5)
  - By day 5 the inventor has 1 + 2 + 4 + 8 + 16 = 31 grains
  - This is $2^5 - 1$ grains of rice.
  - On day N the inventor has $2^N - 1$

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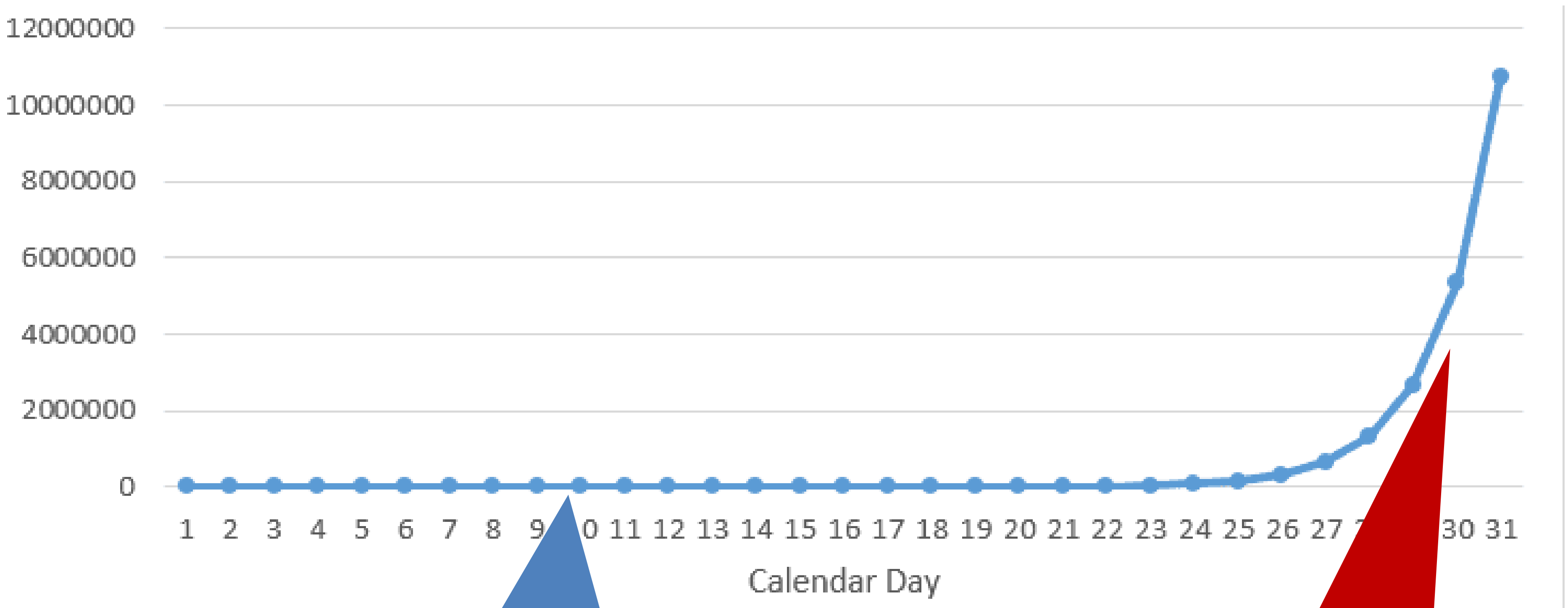
  - On day N the inventor has $2^N – 1$ grains of rice

  - By day 15 the inventor has about 32000 grains of rice
    - This is about a pound of rice and is worth a few dollars
  - By day 20 the inventor has about a million grains of rice
    - This is worth about $50
  - By day 36, the inventor has several million dollars of rice
  - By around day 50, the inventor has more rice than is produced in a year!

Legend of the invention of chess



Slow start

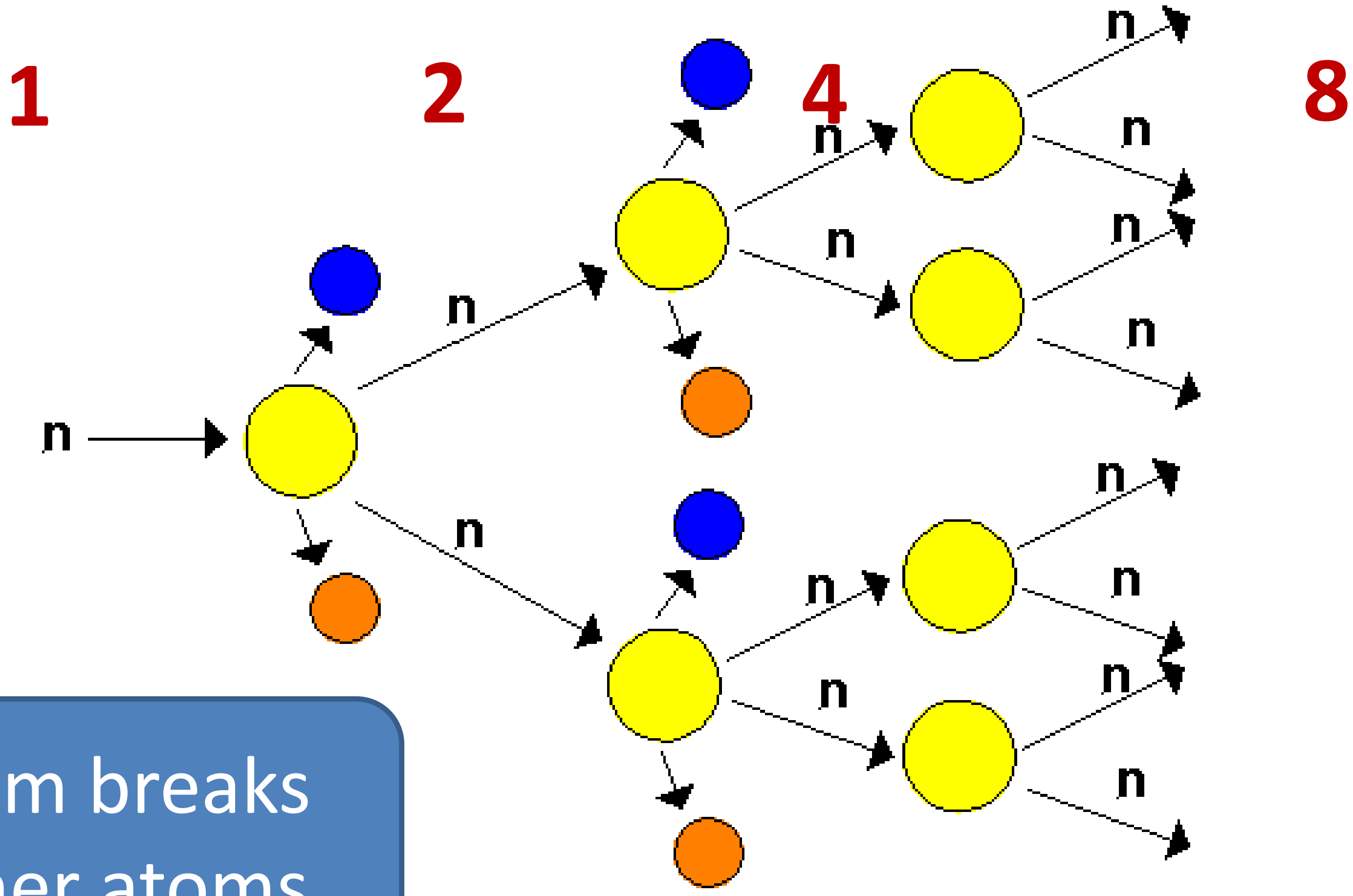
Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

Nuclear fission

- Uranium 235 is an unstable atom
- A neutron colliding with it will cause it to break apart
- When it breaks, it will produce 2 or 3 other neutrons
  - On average each atom that splits produces 2.4 neutrons
- These neutrons can collide with other Uranium 235 atoms to produce more neutrons

An uncontrolled chain reaction



1 atom breaks
2 other atoms

Uncontrolled chain reaction

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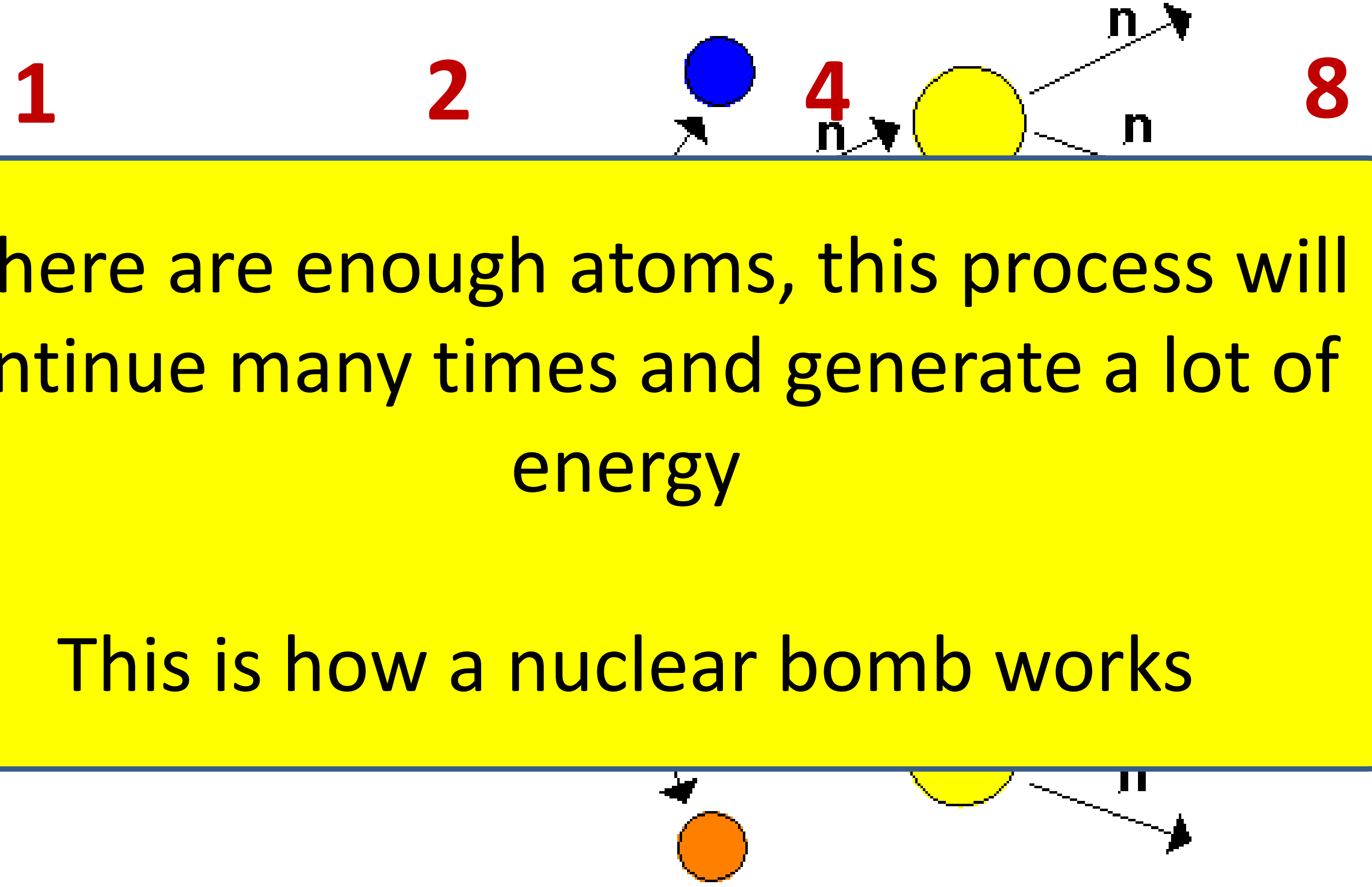
An uncontrolled chain reaction



If there are enough atoms, this process will continue many times and generate a lot of energy

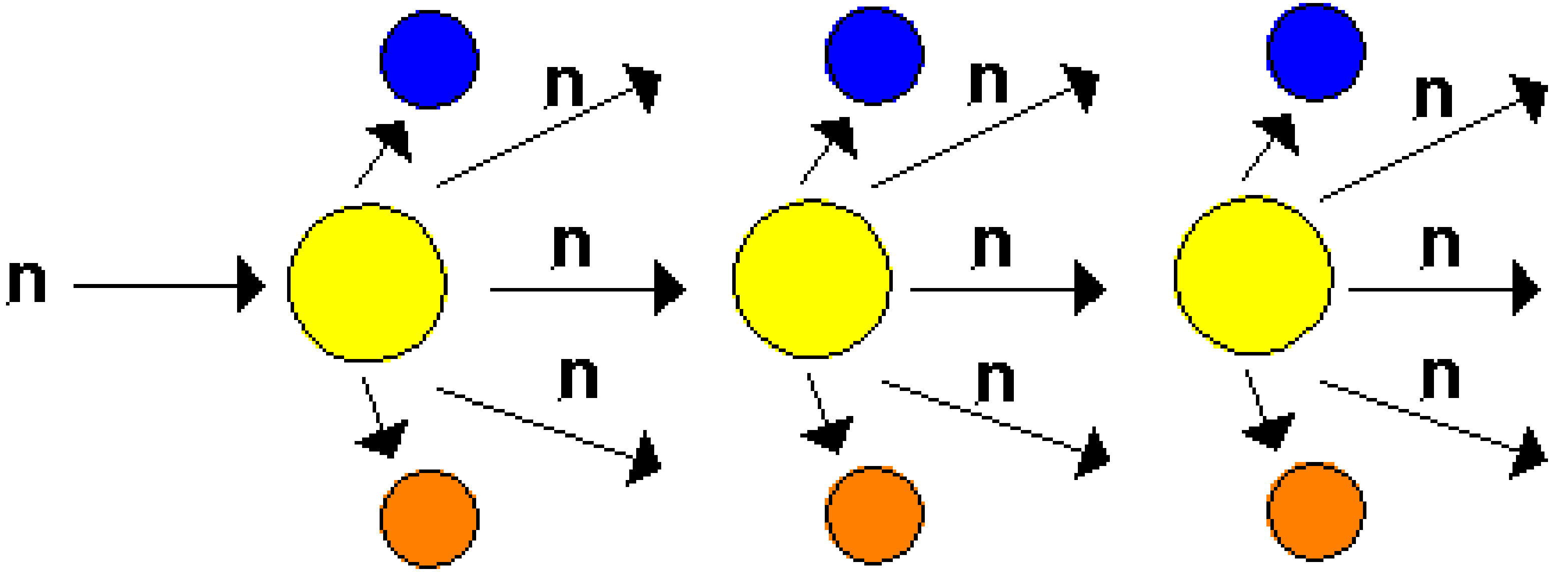
This is how a nuclear bomb works

Uncontrolled chain reaction

https://populationeducation.org/exponential-growth-and-doubling-time/

A critical chain reaction

1 1 1 1

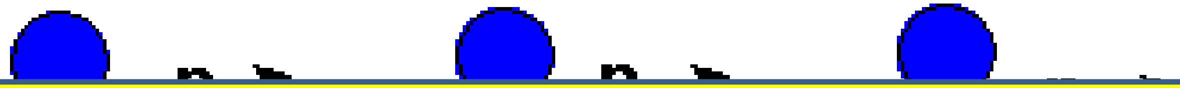


Controlled nuclear chain reaction (only 1 neutron from each fission goes on to produce another fission)

https://populationeducation.org/exponential-growth-and-doubling-time/

A critical chain reaction

1 1 1 1



If there are not enough atoms, or something absorbs some of the neutrons produced, the reaction does not grow but just keeps going generating energy

This is how a nuclear reactor works

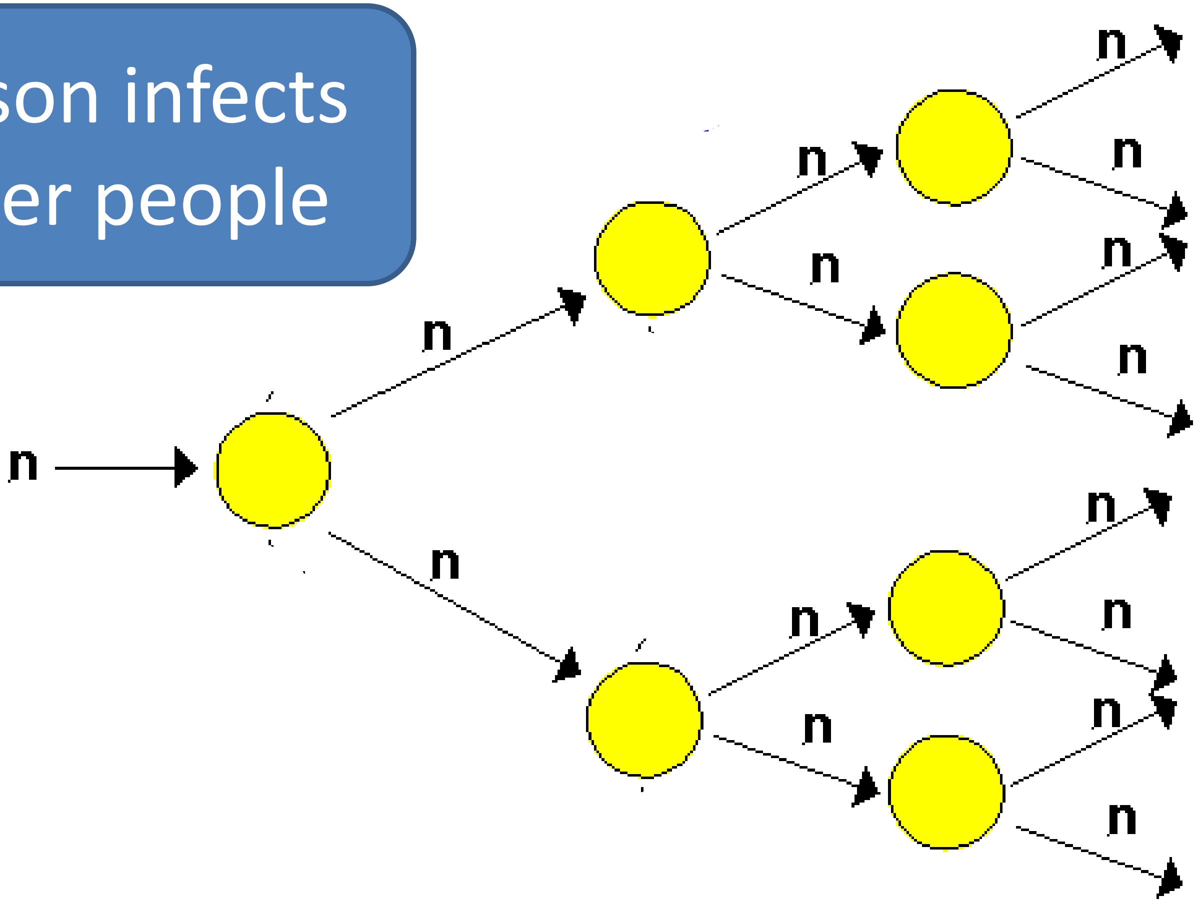
(only) 1 neutron from each fission goes on to produce another fission)

https://populationeducation.org/exponential-growth-and-doubling-time/

COVID-19 is a biological atomic bomb

An uncontrolled chain reaction

1 person infects
2 other people

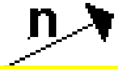


Uncontrolled chain reaction

https://populationeducation.org/exponential-growth-and-doubling-time/

An uncontrolled chain reaction

1 person infects
2



This is an epidemic.

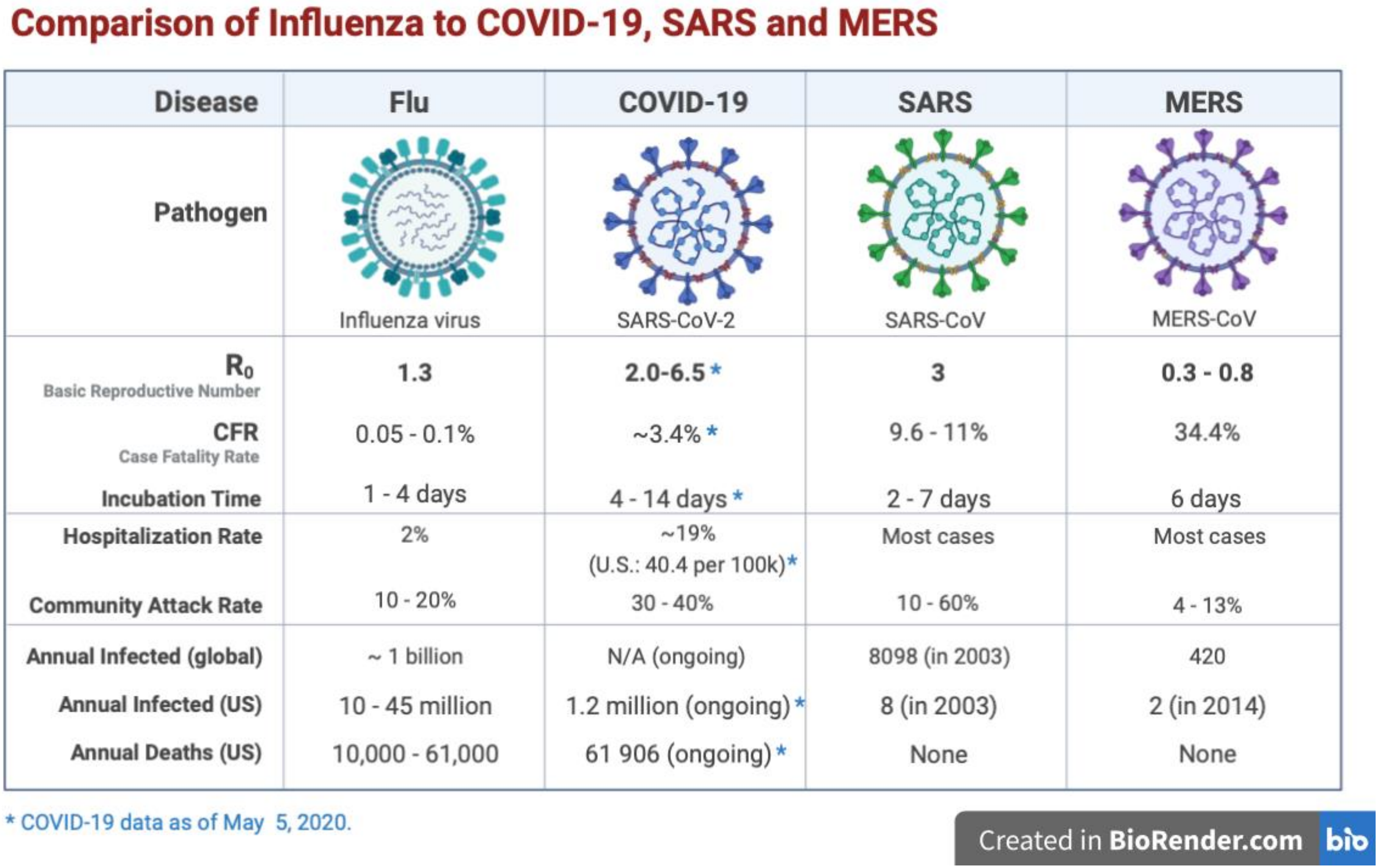
The number of infected people keeps growing.

Because each person infects 2 others, we say that the reproduction number of the epidemic is

R = 2

https://populationeducation.org/exponential-growth-and-doubling-time/

Why the COVID-19 panic?



Comparison of Influenza to COVID-19, SARS and MERS

Disease	Flu	COVID-19	SARS	MERS
Pathogen	Influenza virus	SARS-CoV-2	SARS-CoV	MERS-CoV
R_0 Basic Reproductive Number	1.3	2.0-6.5 *	3	0.3 - 0.8
CFR Case Fatality Rate	0.05 - 0.1%	~3.4% *	9.6 - 11%	34.4%
Incubation Time	1 - 4 days	4 - 14 days *	2 - 7 days	6 days
Hospitalization Rate	2%	~19% (U.S.: 40.4 per 100k)*	Most cases	Most cases
Community Attack Rate	10 - 20%	30 - 40%	10 - 60%	4 - 13%
Annual Infected (global)	~ 1 billion	N/A (ongoing)	8098 (in 2003)	420
Annual Infected (US)	10 - 45 million	1.2 million (ongoing) *	8 (in 2003)	2 (in 2014)
Annual Deaths (US)	10,000 - 61,000	61 906 (ongoing) *	None	None

* COVID-19 data as of May 5, 2020.

Created in **BioRender.com** bio

CDC. COVIDView Week 17, ending April 25, 2020

Sanche et al., EID. 26(7) early release 2020

CDC. Disease Burden of Influenza. May 5, 2020

WHO MERS Situation Update, Nov., 2019

WHO/CDS/CSR/GAR/2003.11

WHO Coronavirus disease (COVID-19) Situation Report 106

Jessica Brinkworth

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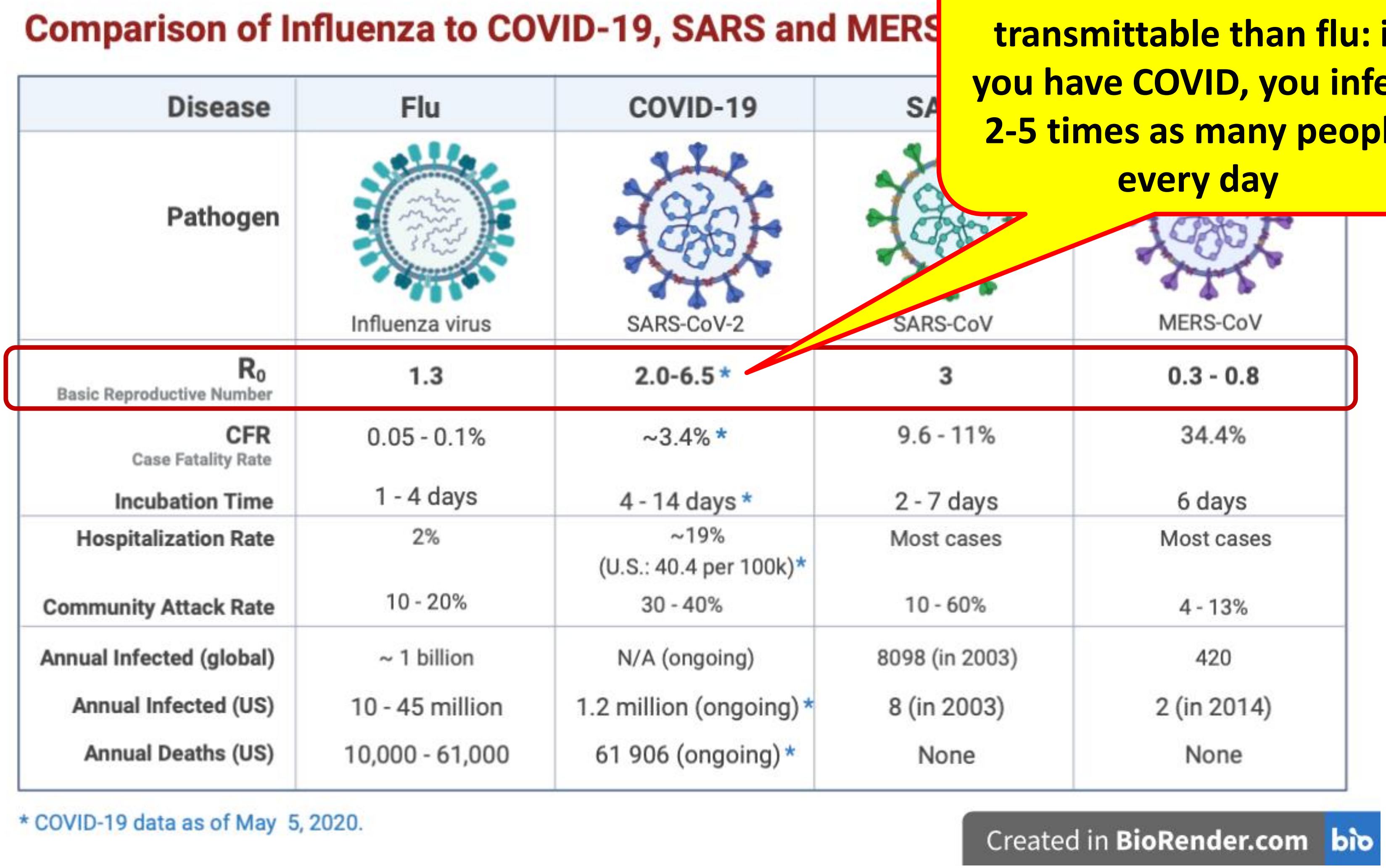

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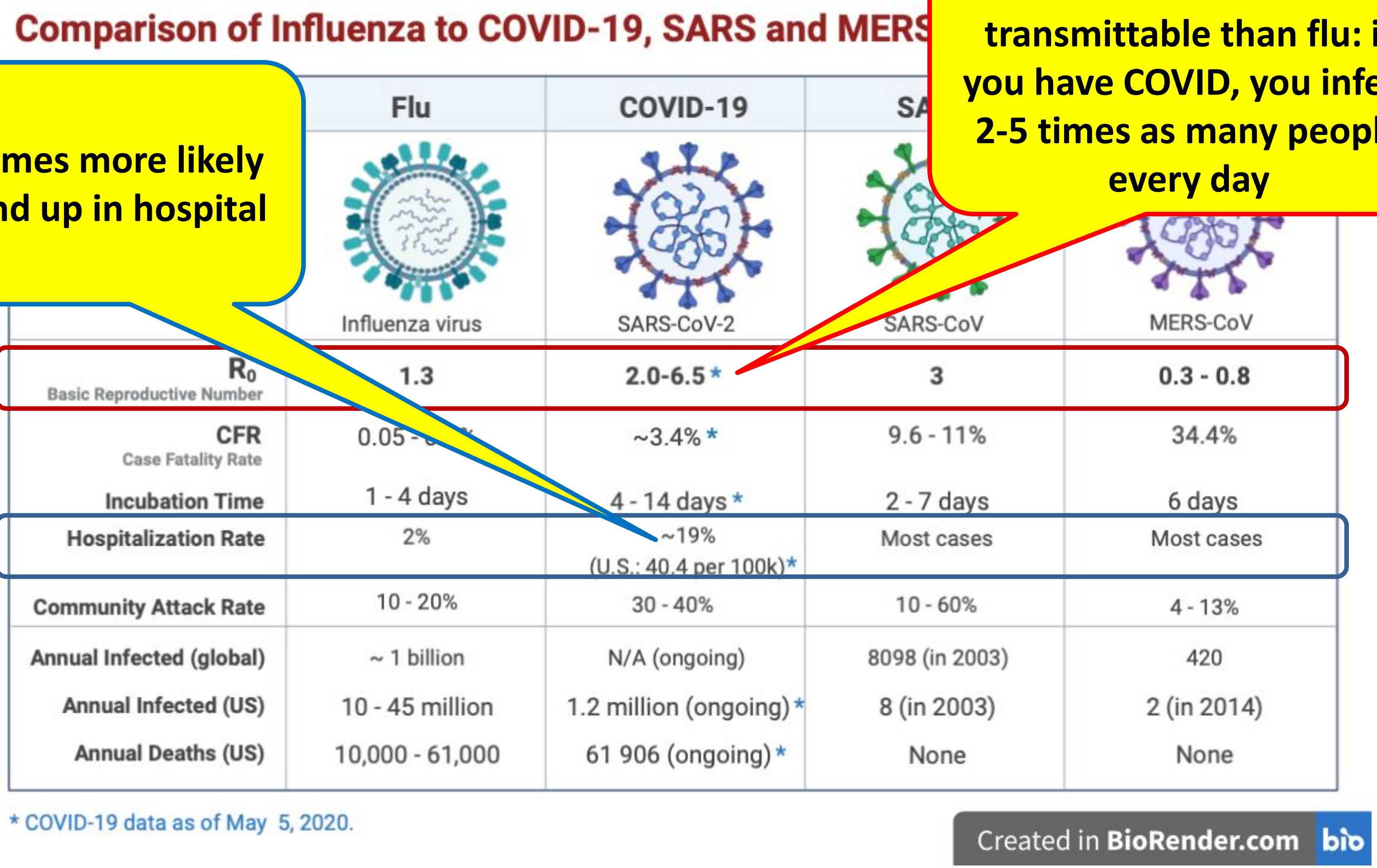

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10 times more likely to end up in hospital

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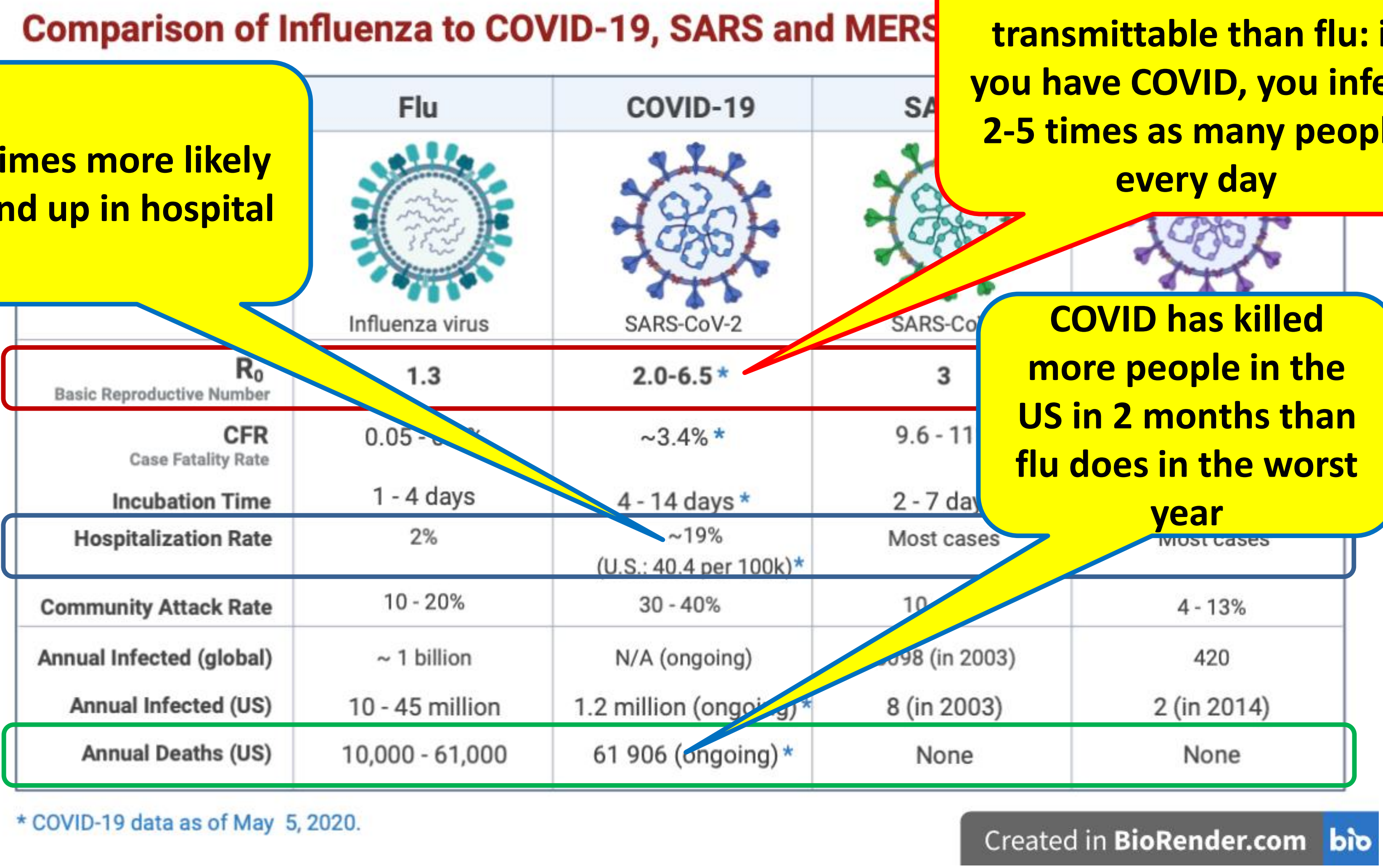

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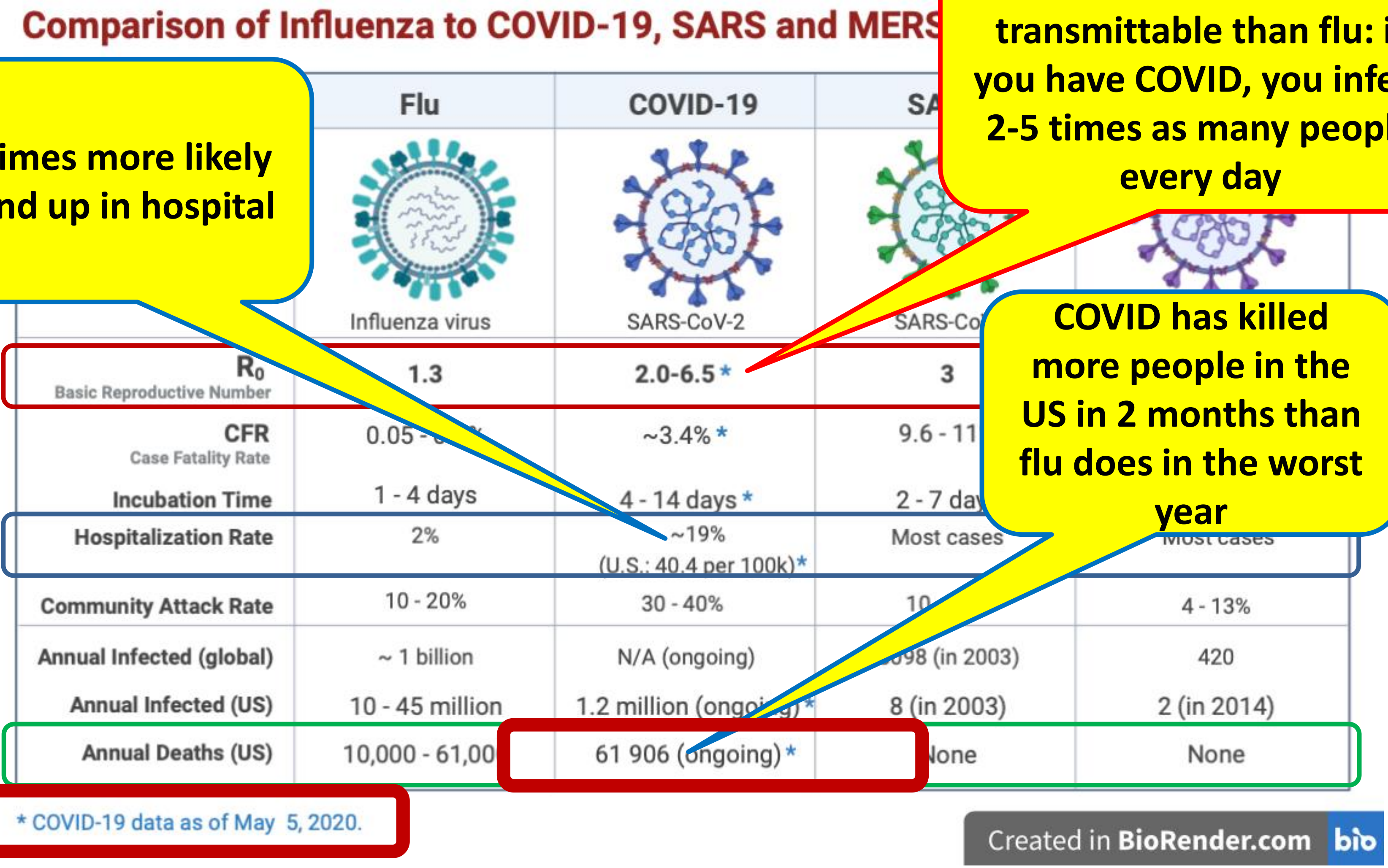

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Comparison ... Influenza to COV... 9, SARS ... ERS

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10 times more likely to end up in ho

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ID has killed le in the S in 2 months than does in the worst year

Two weeks later: we are above 94,000 deaths!!

CDC. COVIDView Week 17, ending April 25, 2020

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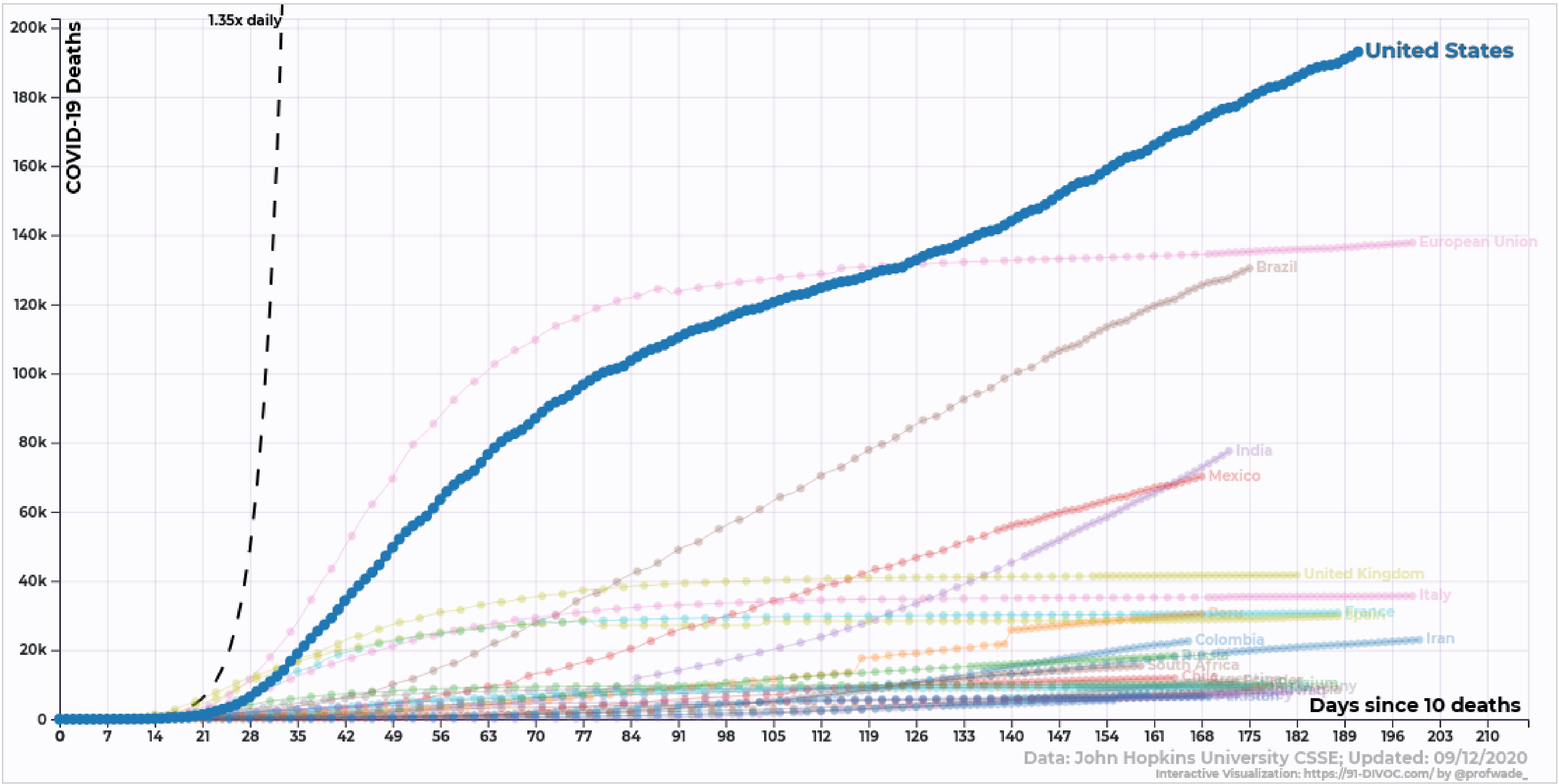
TODAY

Deaths from COVID-19



Data: John Hopkins University CSSE; Updated: 09/12/2020

Interactive Visualization: https://91-DIVOC.com/ by @profwade_

Visualization by UIUC CS Professor **Wade Fagen-Ulmschneider**

History

Our backgrounds

- During last 20 years or so, interdisciplinary physics has become a major field.
  - Our background is in using statistical reasoning to solve problems in physics (e.g. how huge numbers of atoms can self-organize into phases like solid, magnet, superconductors, …).
  - We use these same methods to analyse ecosystems that evolve, including the behavior of populations of biological organisms, mostly viruses and bacteria, but also genes, and even honeybees!
  - We work primarily at the University of Illinois Carl R. Woese Institute for Genomic Biology
- The mathematical modeling used in ecology is also the foundation of mathematical modeling in epidemiology.
  - This is why it was easy for us to quickly pivot from our regular research to COVID-19 modeling

During March and April, testing was inadequate to track COVID-19 in Illinois …

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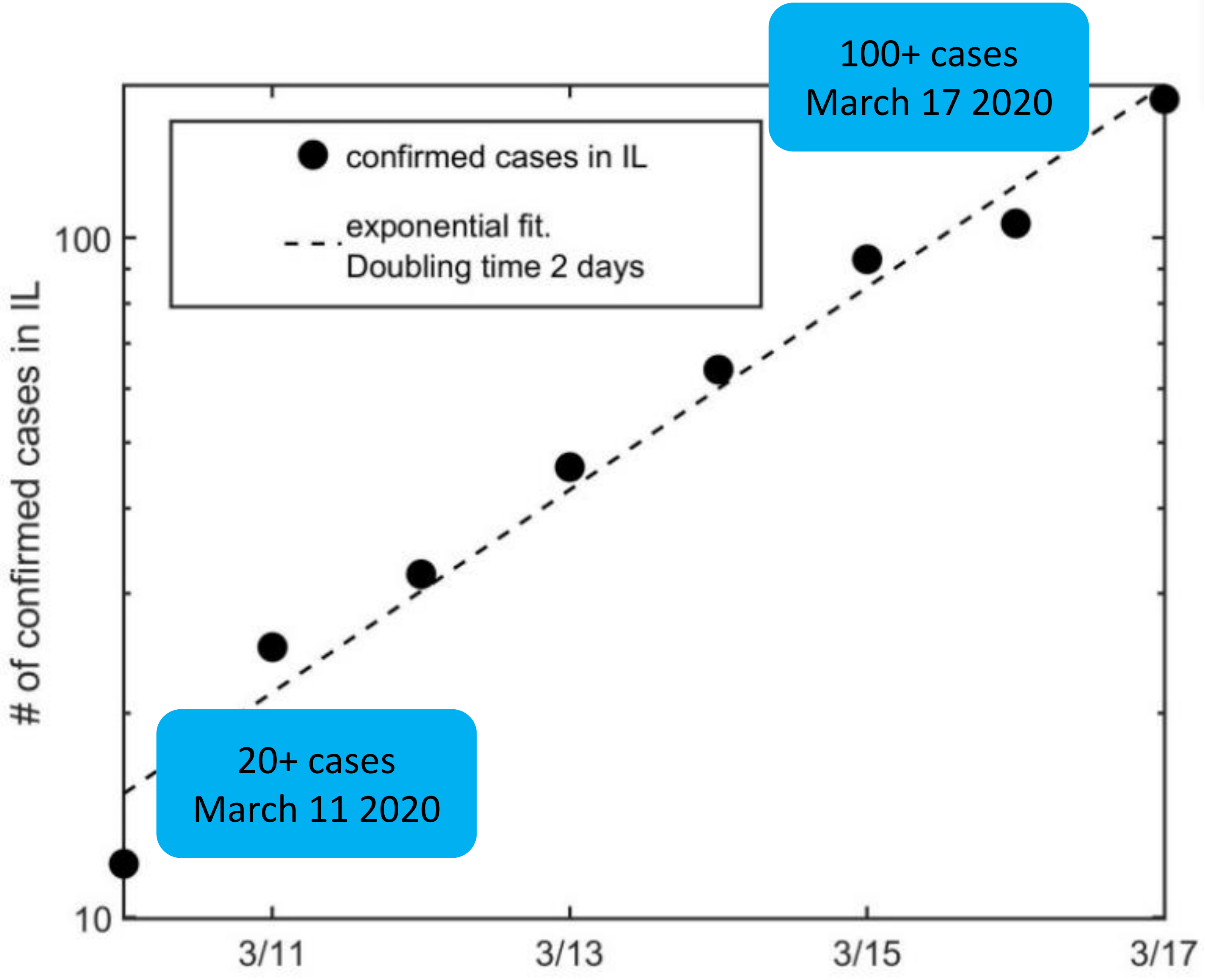
… The only way to see the disease was through mathematics

Even though the number of reported cases was only about 100, we could predict the dramatic effect of a pre-emptive stay-at-home order

Even though the number of reported cases was only about 100, we could predict the dramatic effect of a pre-emptive stay-at-home order

And the State had a lockdown starting a few days later. Why?

Rapid growth of COVID-19 in Illinois

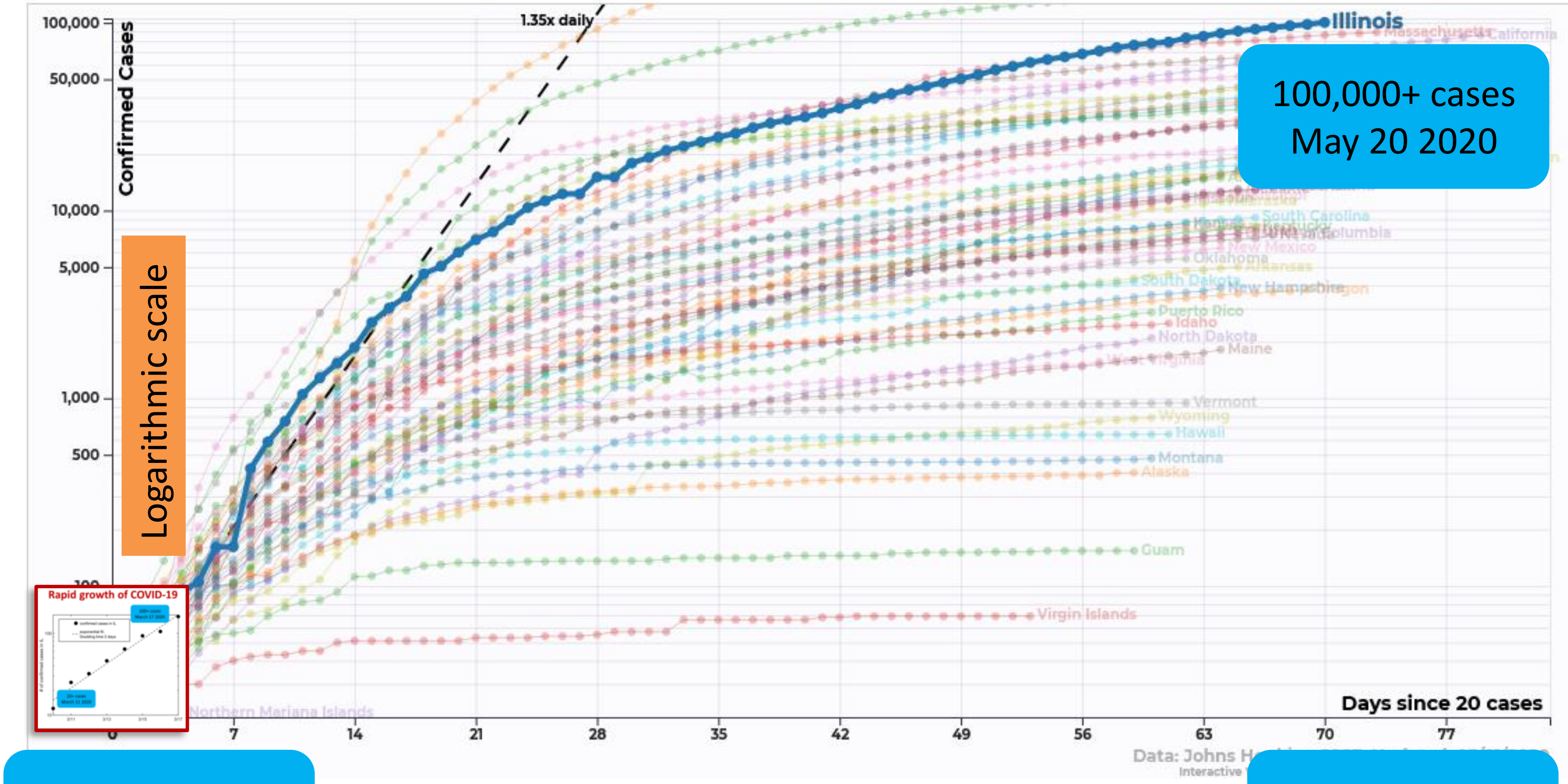


100+ cases
March 17 2020

20+ cases
March 11 2020

Rapid growth of COVID-19 in Illinois

Confirmed COVID-19 Cases by US States/Territories



Logarithmic scale

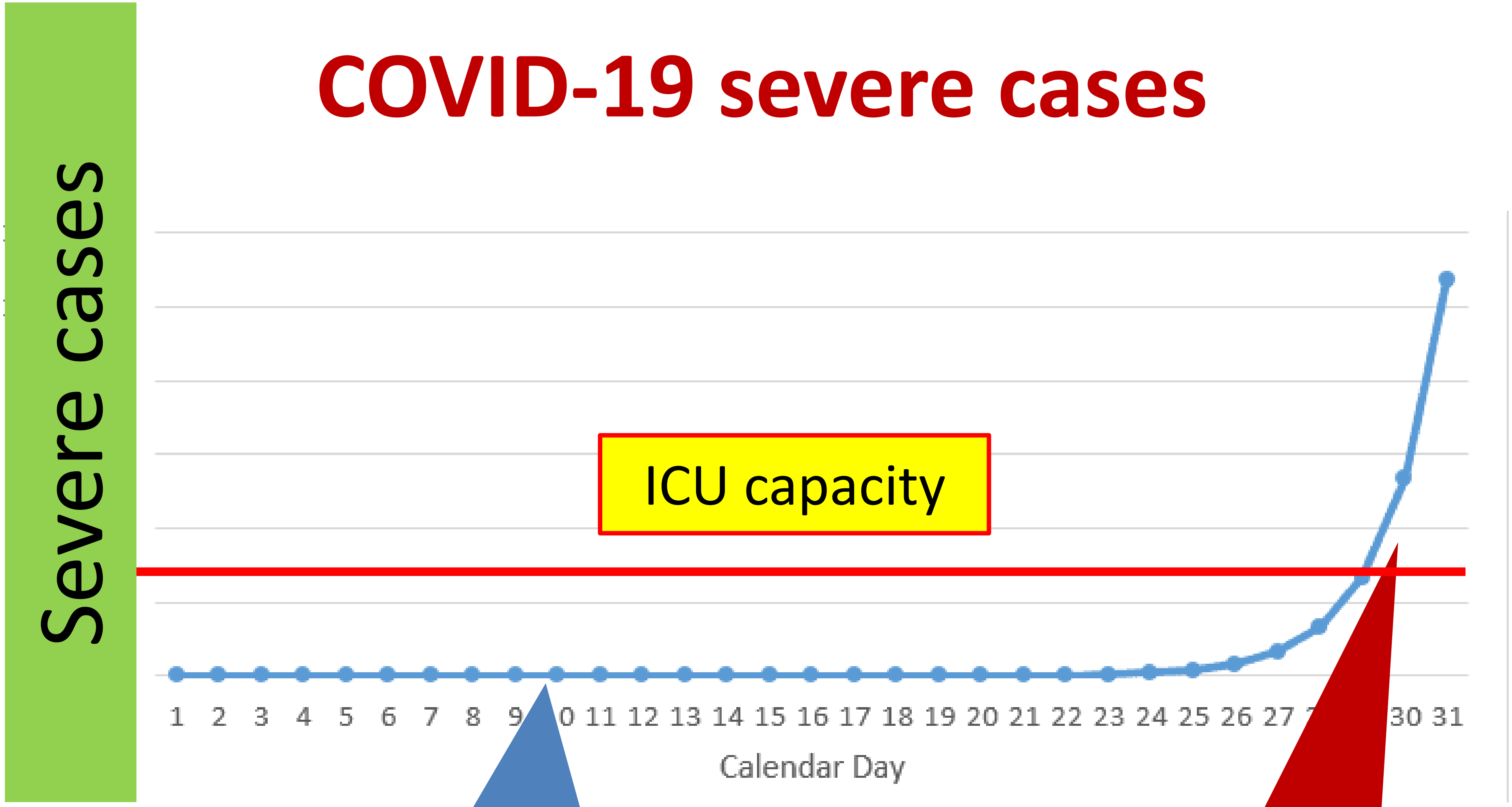
100,000+ cases
May 20 2020

20+ cases
March 11 2020

May 20 2020

91-divoc.com

COVID-19 severe cases



Slow start

Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

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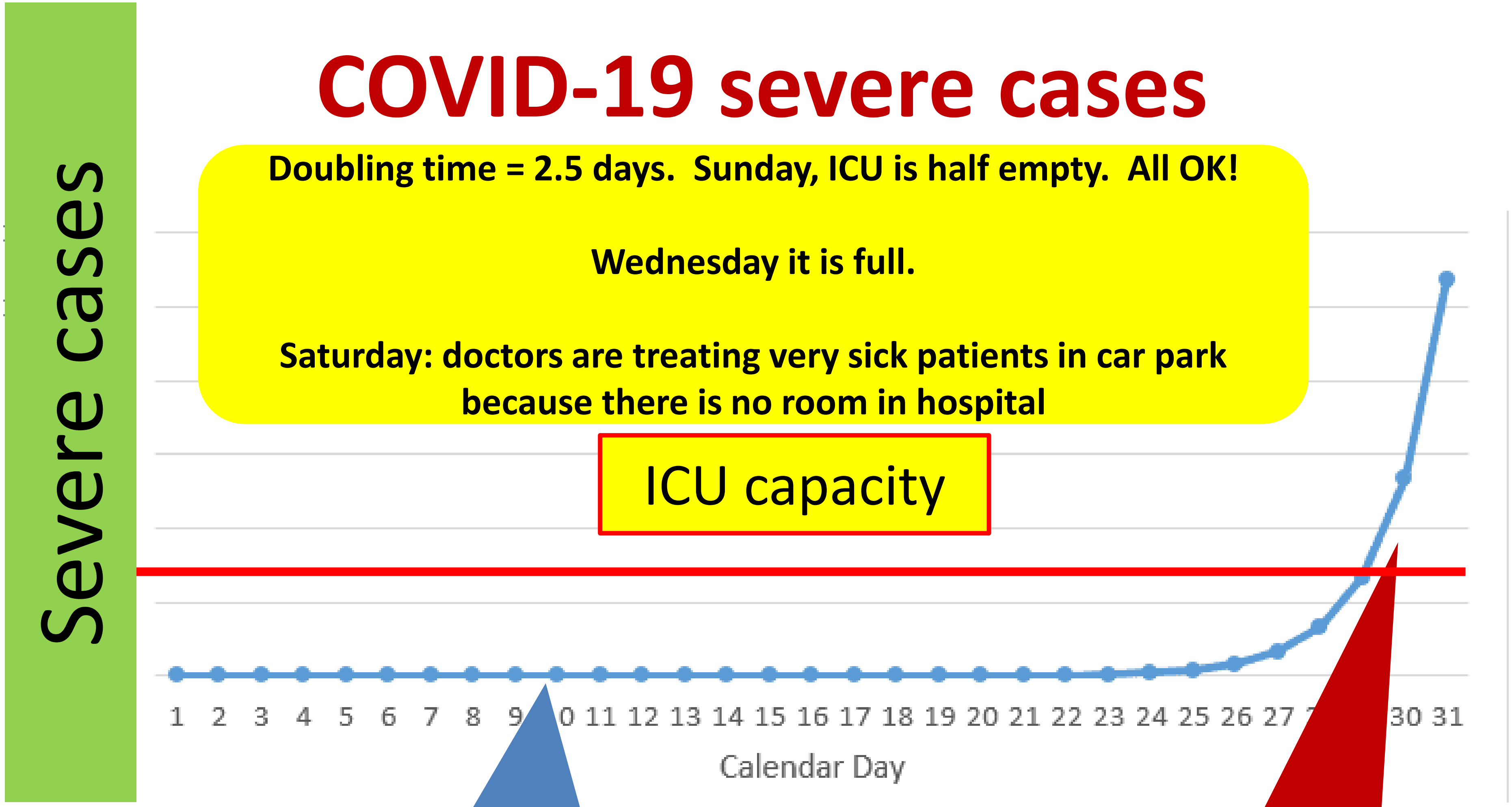

Doubling time = 2.5 days. Sunday, ICU is half empty. All OK!

Wednesday it is full.

Saturday: doctors are treating very sick patients in car park because there is no room in hospital

ICU capacity

Slow start

Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

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Window of Opportunity for Mitigation to Prevent Overflow of ICU capacity in Chicago by COVID-19

Sergei Maslov and Nigel Goldenfeld

Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana-Champaign

March 18 2020

Please note: this is a working document and has not been submitted for journal publication. It is planned that a later version of this document will be submitted for peer-reviewed publication, but in the interests of sharing information during a rapidly changing epidemic landscape, we are making this early version available.

Executive Summary

We estimate the growth in demand for ICU beds in Chicago during the emerging COVID-19 epidemic, using state-of-the-art computer simulations calibrated for the SARS-CoV-2 virus. The questions we address are these:

(1) Will the ICU capacity in Chicago be exceeded, and if so by how much?

(2) Can strong mitigation strategies, such as lockdown or shelter in place order, prevent the overflow of capacity?

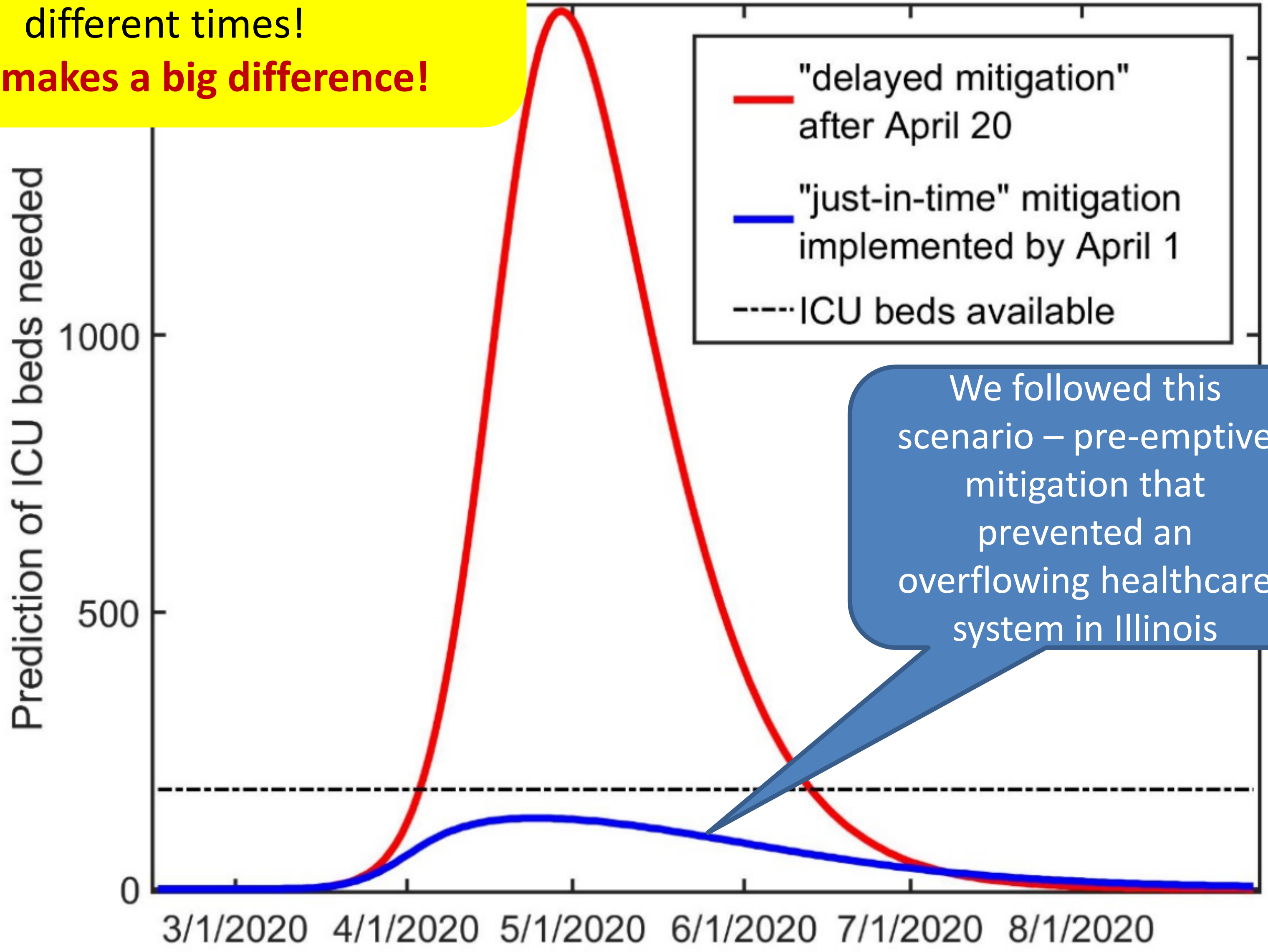
(3) When should such strategies be implemented?

Our answers are as follows:

(1) The ICU capacity may be exceeded by a large amount, probably by a factor of ten.

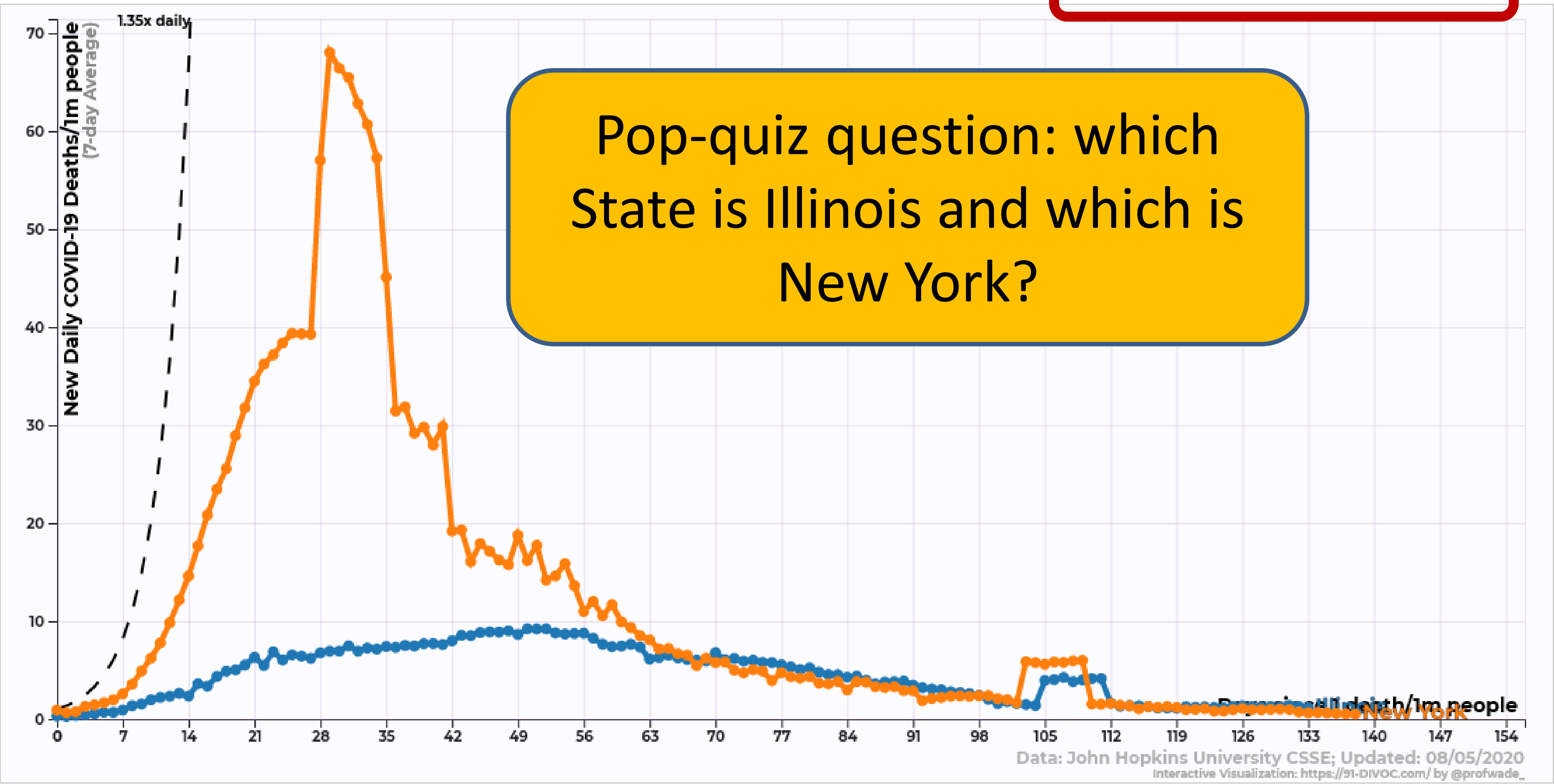
Two identical mitigation scenarios for Chicago but implemented at different times!

Early makes a big difference!



We followed this scenario – pre-emptive mitigation that prevented an overflowing healthcare system in Illinois

New Deaths from COVID-19 per Day by US States/Territories, normalized by population

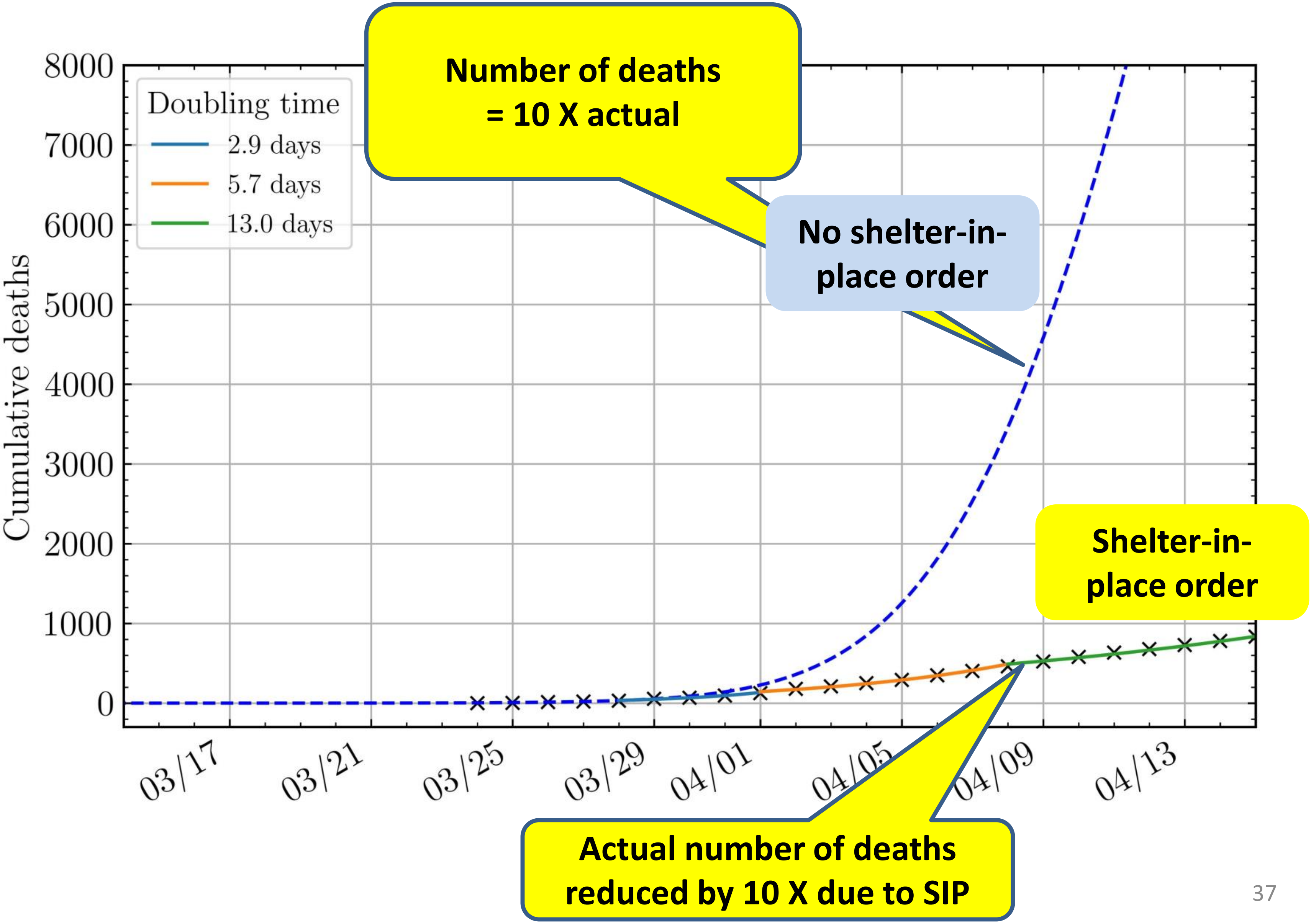


Pop-quiz question: which State is Illinois and which is New York?

Data: John Hopkins University CSSE; Updated: 08/05/2020
Interactive Visualization: https://91-DIVOC.com/ by @profwade_

Visualization by UIUC CS Professor **Wade Fagen-Ulmschneider**

Social distancing saves lives



Number of deaths = 10 X actual

No shelter-in-place order

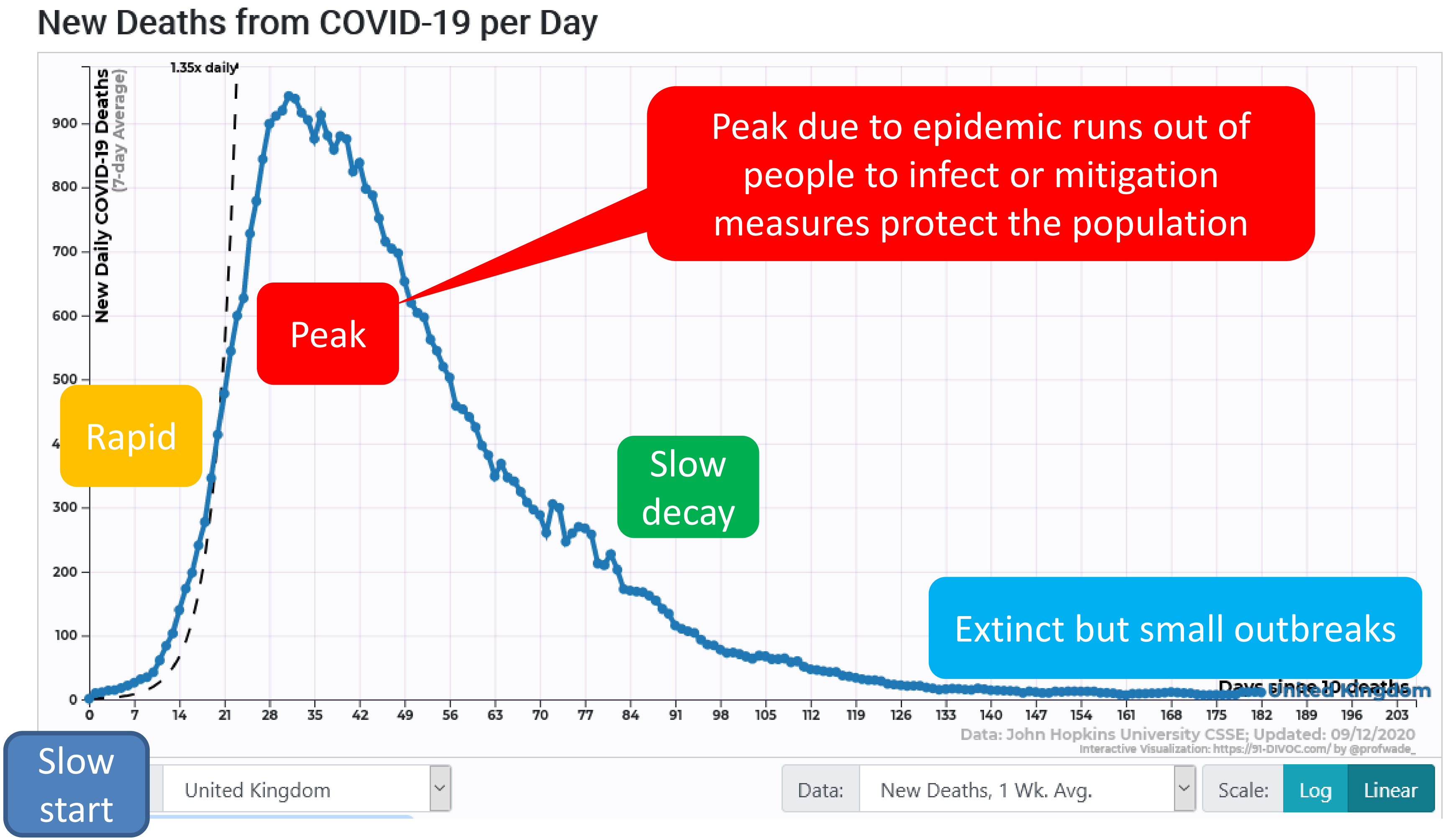
Shelter-in-place order

Actual number of deaths reduced by 10 X due to SIP

To beat the exponential …

- Reduce the reproduction number R
  - Break the chain of transmission
- The strategies have been known for centuries
  - Isolate infected people
  - Quarantine anyone they may have already infected by contact tracing
  - Good hygiene and social distancing
  - Wear masks for airborne diseases
- If necessary, lockdown populations to get the cases down to a number manageable by contact tracing

The stages of an epidemic



New Deaths from COVID-19 per Day

Data: John Hopkins University CSSE; Updated: 09/12/2020

Interactive Visualization: https://91-DIVOC.com/ by @profwade_

United Kingdom

Data: New Deaths, 1 Wk. Avg.

Scale: Log Linear

Peak due to epidemic runs out of people to infect or mitigation measures protect the population

Peak

Rapid

Slow decay

Extinct but small outbreaks

Slow start

Visualization by UIUC CS Professor **Wade Fagen-Ulmschneider**

Epidemiology is not rocket science – it’s harder!

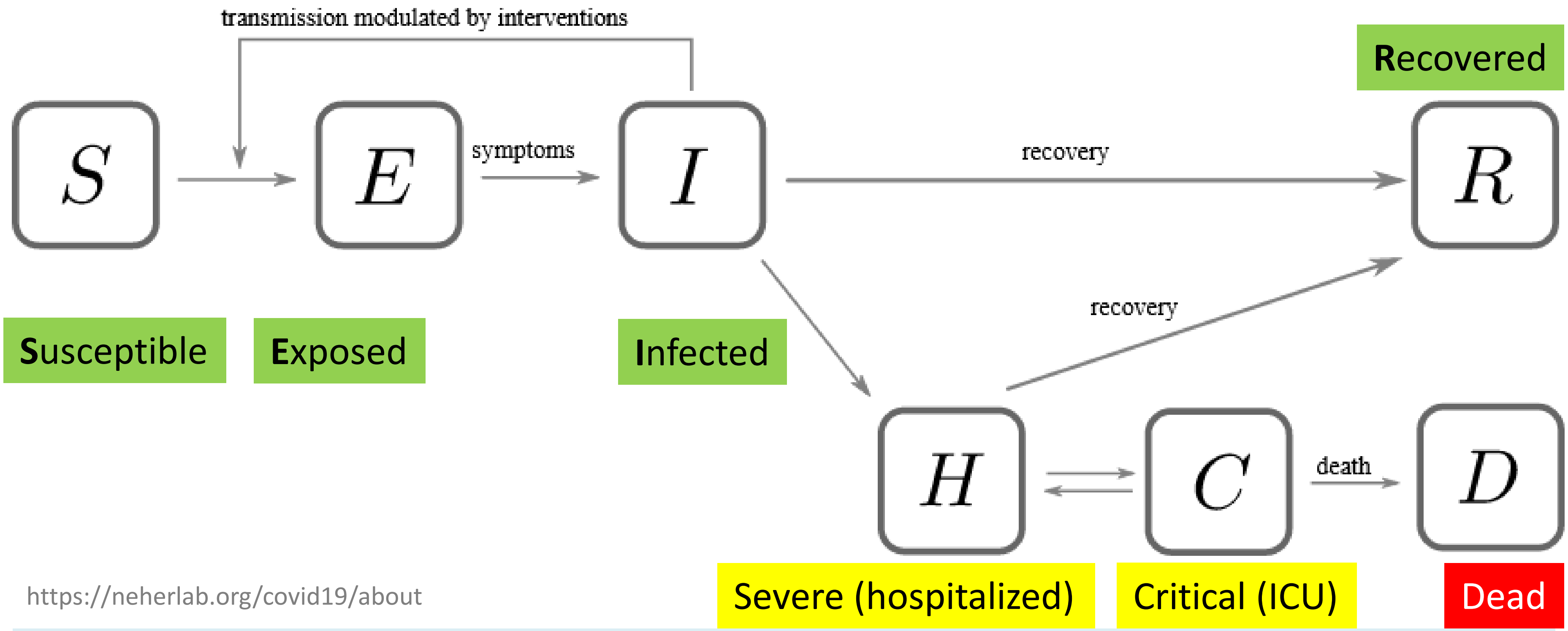
People’s behavior can change the predictions for better or for worse

Epidemiology is not rocket science – it is harder

- If you hear that the epidemic is growing dangerously in your area, you go out and get food
  - Hunker down and slow your social interactions.
  - This makes R get smaller
- If you hear that the epidemic is hardly present in your area, or that there are excellent public health measures to protect you …
  - The government opens indoor dining, gyms, bars
  - You go and have parties
  - This makes R get bigger
  - **And the cycle of infection starts again**
  - **Slow then rapid growth**

Computational epidemiology

Our Methods as of 3/2020: SEIR model



https://neherlab.org/covid19/about

- Parameters in SEIR model are rates of
  - Transmission, symptoms, hospitalization, criticality, death
  - Intervention included by modifying transmission rate
  - Seasonal forcing
  - Age-dependent severity and rates of transition between compartments from China data

- We initially used a code made available by Lab of Richard Neher (Basel University), but rapidly developed improved modeling including stochastic simulations, probability distribution of epidemic parameters, calibration tools.
- Unlike curve-fitting models, our models follow the time course and process of the epidemic using standard techniques in the academic literature.

Modeling is two parts

- Model calibration
  - **The equations of the epidemic** need to know what the starting condition is
  - The equations of the epidemic **need certain parameters** that describe the disease transmission
  - One needs **good data** to estimate parameters. We get ours from IDPH through Data Use Agreement
  - We use a **sophisticated process** of estimating these parameters using a high dimensional model fitting algorithm known as Markov Chain Monte Carlo
  - We need **supercomputers** to do this, because we have to try many combinations of parameters and see which have the highest statistical support
- Forward simulation
  - Once these parameters are known, together with their ranges, we can **run the equations forward in time**.
  - We **estimate uncertainties** due to fitting of parameters

Timeline

- Mid-March: Our activities were mostly model development and making estimates for hospitals in Illinois: Carle Hospital, Rush University Hospital, and we were in touch with others.
  - Communication with Champaign-Urbana Public Health Department
  - Modeling support for Grainger College of Engineering group making ventilators

- March 18 2020: We alert Governor Pritzker of a “Window of Opportunity” to avoid a New York style health care disaster

- March 20 2020: Shelter-in-Place order issued. Illinois was the first State to issue such an order <u>pre-emptively</u>.

- March 26 2020: Governor Pritzker convenes a group of modelers to work with his staff and the Illinois Department of Public Health
  - UIUC, University of Chicago, Northwestern University and Argonne National Laboratory

What we do

- Our models require hospital utilization and other epidemic data that is not in the public domain
  - Close collaboration with Illinois Department of Public Health is essential!
- Work with IDPH to design appropriate metrics to track COVID-19 in Illinois
- Make forecasts of the epidemic Statewide and for the different regions
- Respond to requests from the Governor’s office or IDPH for modeling predictions and simulate policy as it is announced (if possible)

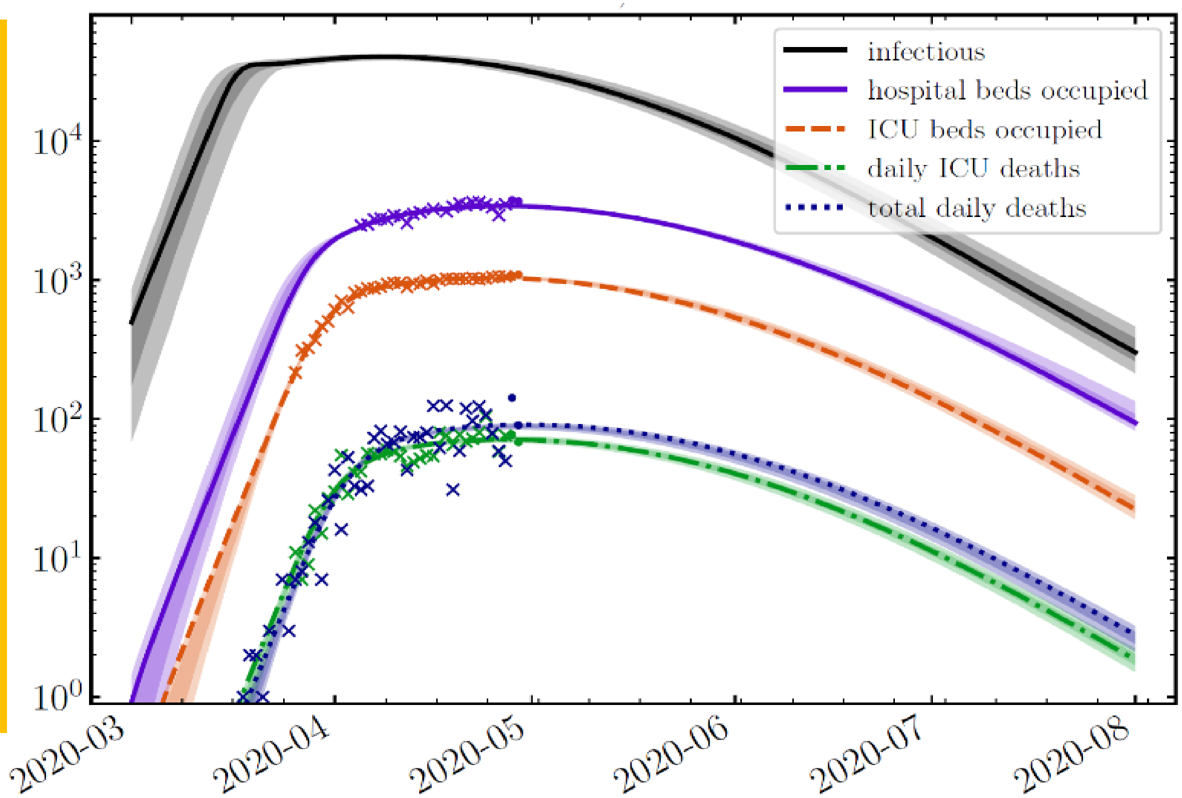
Role

- The 3 university groups independently attempt to develop their models and to make predictions of the epidemic.
  - The independence is important. We do not have time to do peer review of scientific work, a process that takes a year or more.

- The goal of convening these groups is to achieve a consensus understanding and a converging description of the epidemic
  - Analogous to getting a "second opinion" if you need a serious medical procedure

Trajectory of COVID-19 in Illinois

Our model is calibrated using **hospital** and **ICU** room occupancy and **deaths** both in and out of hospitals



Prediction from May 7, 2020

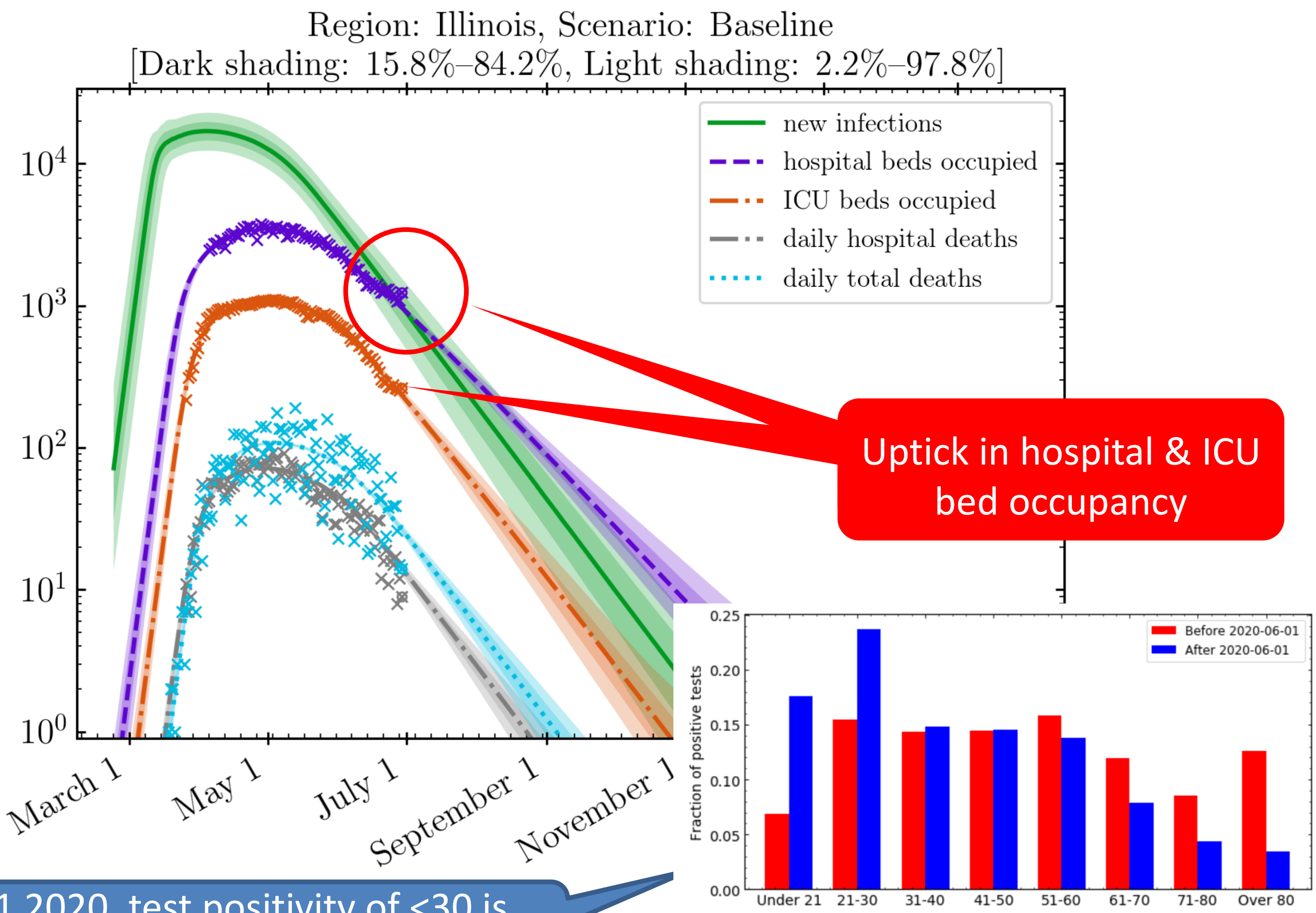
***Figure* 1**. *Calculations of the progression of COVID-19 in Illinois, as computed from an extended SEIR model calibrated to daily death, ICU occupancy and hospital bed occupancy. The crosses represent data provided by the Illinois Department of Public Health. The solid line represents the best fit to the data, with the color bars representing simulations with lower likelihood functions. In these simulations, seasonal forcing with an amplitude of 0.2 has been assumed, comparable to what is known for other coronaviruses [19].*

How did the prediction pan out?

Good!

But we did not know when the State would be reducing mitigation and increasing epidemic transition

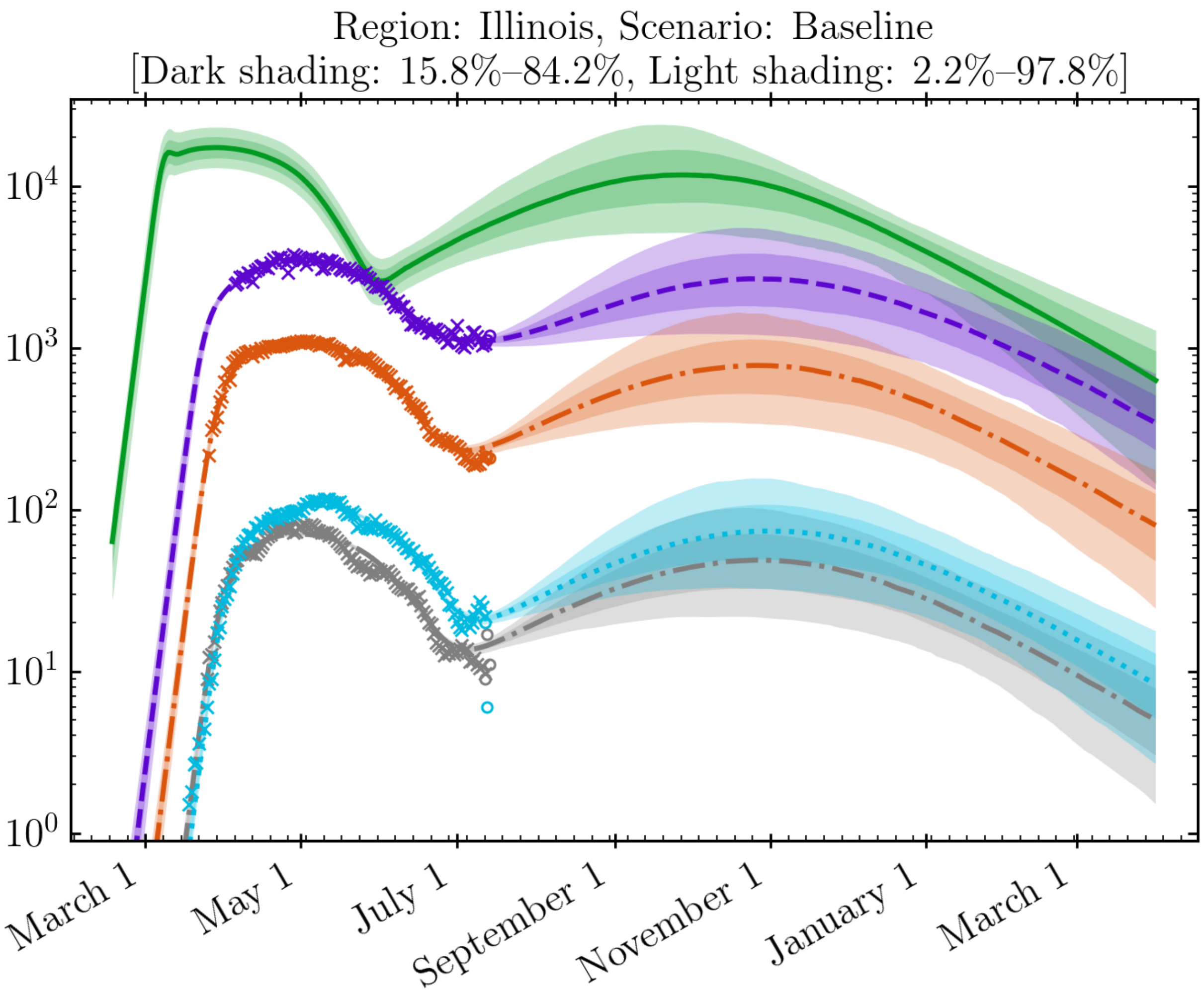
Predictions for Illinois July 1 2020



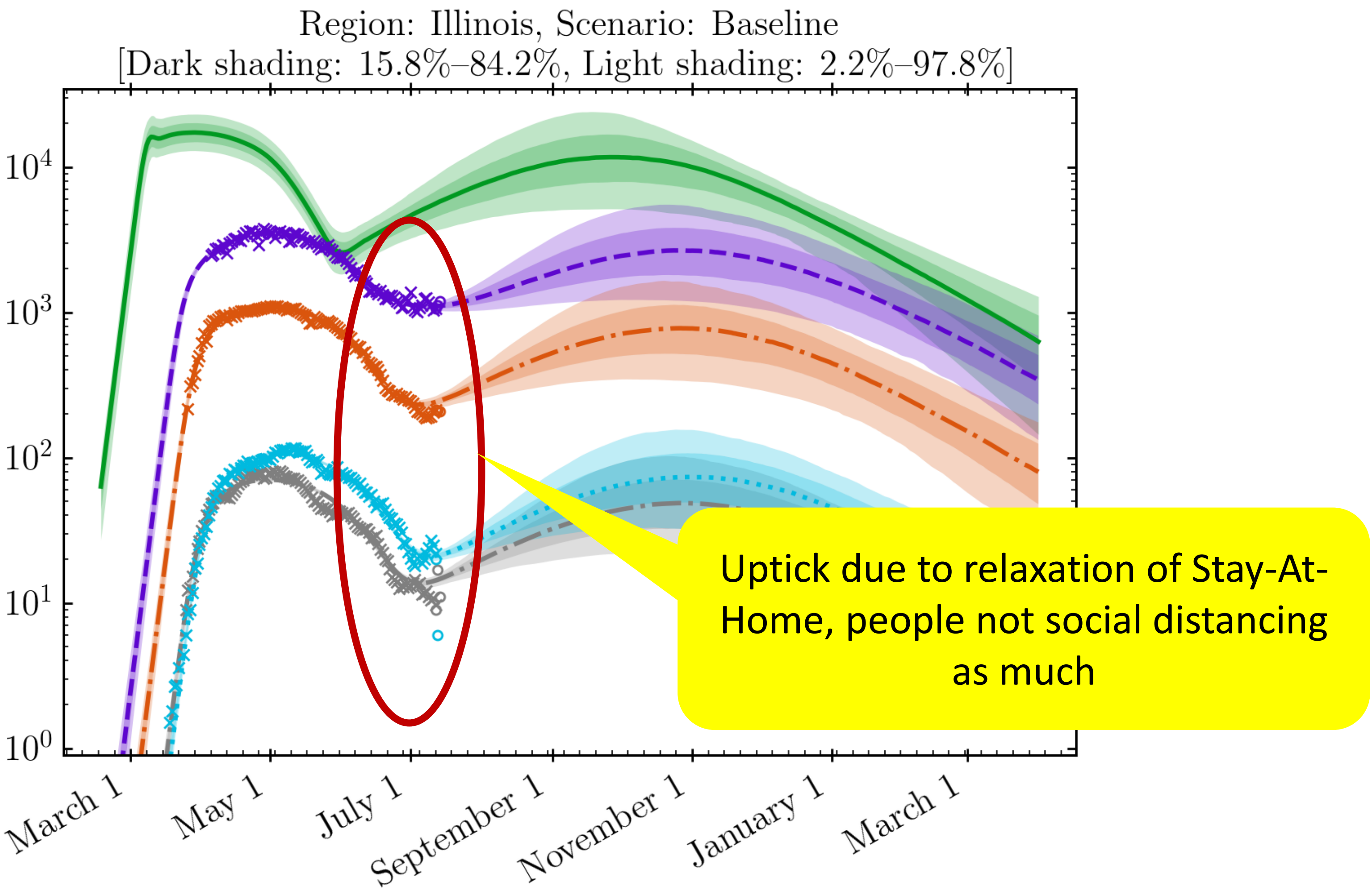
Uptick in hospital & ICU bed occupancy

After June 1 2020, test positivity of <30 is rising (here showing Southern Illinois)

Predictions for Illinois July 15 2020

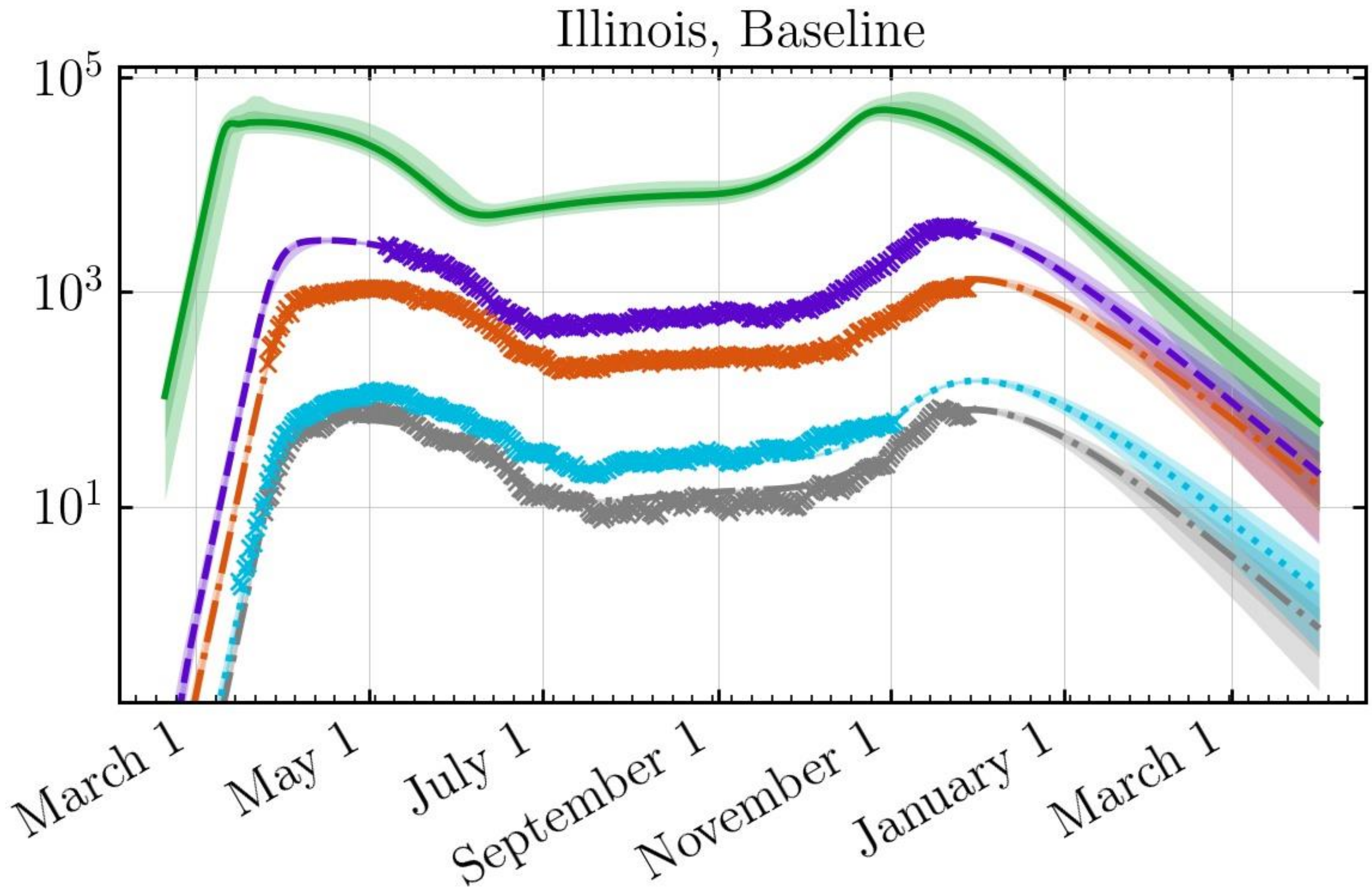


Predictions for Illinois July 15 2020



Uptick due to relaxation of Stay-At-Home, people not social distancing as much

Predictions for Illinois Dec 2 2020



Hospitals at Risk

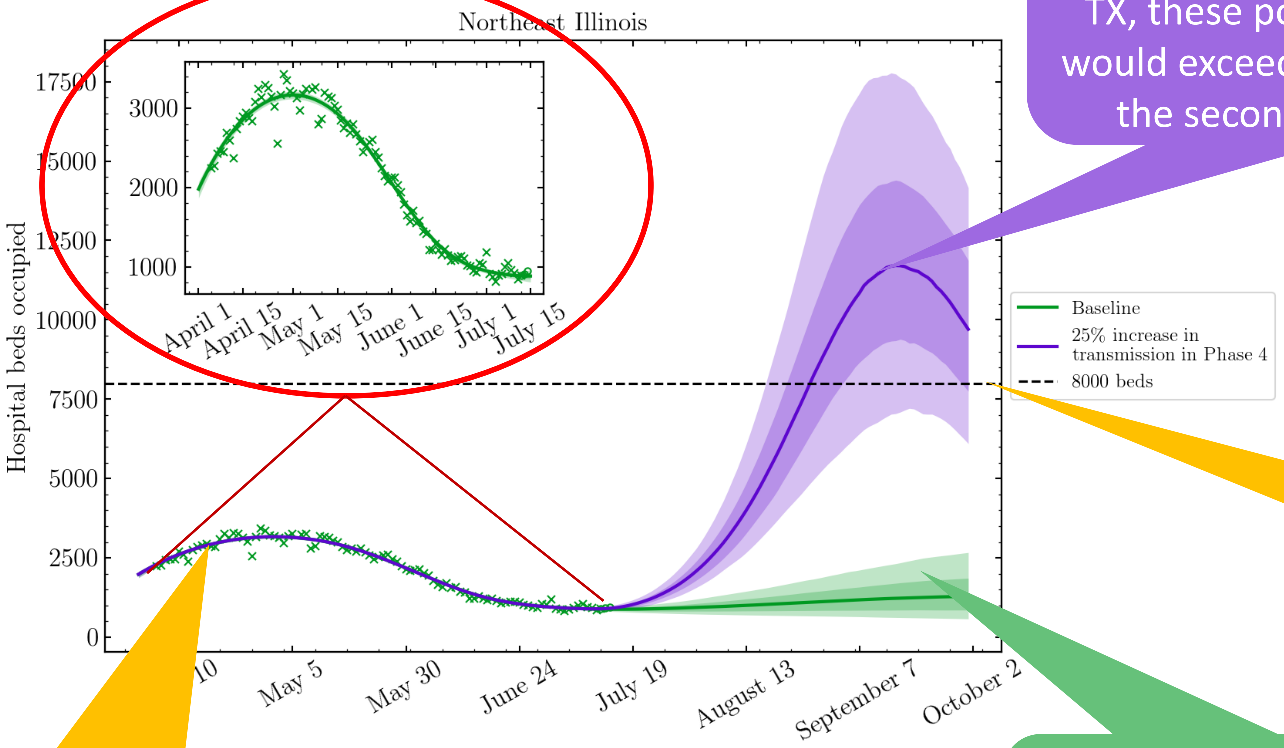
- We project forward scenarios from our model that is calibrated to fit the historical data on ICU, hospitals, and deaths very accurately.

- We compute the probability density for the occupancy in hospital and ICU forward in time

- We compare with the warning signal proposed by IDPH: 75% of available occupancy for COVID patients

- No region has much chance to breach this value for ICU or hospital until mid-October. The highest probability of breaching at the end of our simulations is in the region 9 (both hospital and ICU) but this situation improved since last week

How we calculate the likelihood of COVID-19 exceeding hospital capacity



If Illinois were to see a growth in COVID-19 similar to that of AZ, FL, TX, these possible future scenarios would exceed the hospital capacity in the second half of August 2020

Hospital capacity available for COVID-19 patients

Current baseline situation for NE region: if new phase 4 policies contain outbreaks

Our model matches historical data on hospital occupancy

Learn more about our modeling

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Modeling COVID-19 dynamics in Illinois under non-pharmaceutical interventions

George N. Wong[1,†], Zachary J. Weiner[1,†], Alexei V. Tkachenko[2],
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(Dated: June 16, 2020)

We present modeling of the COVID-19 epidemic in Illinois, USA, capturing the implementation of a Stay-at-Home order and scenarios for its eventual release. We use a non-Markovian age-of-infection model that is capable of handling long and variable time delays without changing its model topology. Bayesian estimation of model parameters is carried out using Markov Chain Monte Carlo (MCMC) methods. This framework allows us to treat all available input information, including both the previously published parameters of the epidemic and available local data, in a uniform manner. To accurately model deaths as well as demand on the healthcare system, we calibrate our predictions to total and in-hospital deaths as well as hospital and ICU bed occupancy by COVID-19 patients. We apply this model not only to the state as a whole but also its sub-regions in order to account for the wide disparities in population size and density. Without prior information on non-pharmaceutical interventions (NPIs), the model independently reproduces a mitigation trend closely matching mobility data reported by Google and Unacast. Forward predictions of the model provide robust estimates of the peak position and severity and also enable forecasting the regional-dependent results of releasing Stay-at-Home orders. The resulting highly constrained narrative of the epidemic is able to provide estimates of its unseen progression and inform scenarios for sustainable monitoring and control of the epidemic.

On January 24, 2020, the second known COVID-19 case to be diagnosed in the USA was reported in Chicago, Illinois. Community transmission of the disease was confirmed on March 8, 2020. During the subsequent ten days, the epidemic grew with a case doubling time of approximately 2.3 days, while testing capacity was essentially fixed. On March 21, 2020, a Stay-at-Home order was issued for the entire state of Illinois and subsequently extended on March 31, 2020 and again on April 23, 2020. The order was lifted on May 30, 2020 [1]. Responsible relaxation of the mitigation of COVID-19 must be informed by realistic and well-calibrated epidemiological modeling of the outcomes of any scenarios under consideration—not just of the resulting (increased) death toll but also of the stress placed upon the healthcare system. The purpose of this report is to present such an analysis.

A variety of modeling approaches are used by hospitals, public health officials, and state governments. These range between phenomenological models that use a curve-fitting procedure to match data, such as the daily death rate, and mechanistic methods that model the trajectory of the epidemic as individuals transition through several disease and healthcare-bound stages [2–5]. Only mechanistic models are able to make justifiable predictions while accounting for changes in the epidemic environment, such as the imposition or relaxation of community mitigation efforts. Of these, compartmental models like the Susceptible-Infectious-Recovered (SIR) models, and Susceptible-Exposed-Infectious-Recovered (SEIR) extensions, are widely used. Compartmental models describe how fractions of a homogeneous, well-mixed population progress through different states the disease, driven by interactions between infectious and susceptible individuals. In the simplest models, the dynamics is deterministic and the rates are constant in time, but many variants and extensions exist and are widely used.

In order to be practically useful, models must be calibrated to observed data [4, 6–8]. We calibrate the important dynamics of the model to several simultaneous streams of empirical data including total and in-hospital deaths, as well as hospital and ICU bed occupancy by COVID-19 patients. To avoid biases resulting from non-uniform and non-constant testing rates, which may be difficult to parameterize, we do not consider positive case data. The resulting model is a description of the epidemic as it progresses through the hospital system in Illinois; as it is clear that a non-negligible number of COVID-19 deaths occur outside the hospital environment (e.g., in homes and nursing homes especially), we augment our model with an effective description of the net incidence of deaths due to COVID-19.

There are many limitations to the types of models that we and others use to describe COVID-19, and these have been explored extensively in the literature, especially with regard to spatial structure [9], superspreader events and individuals [10–13], and the structure of contact networks [14–16]. A geographical region as large as the state of Illinois is not well-described as homogeneous, due to

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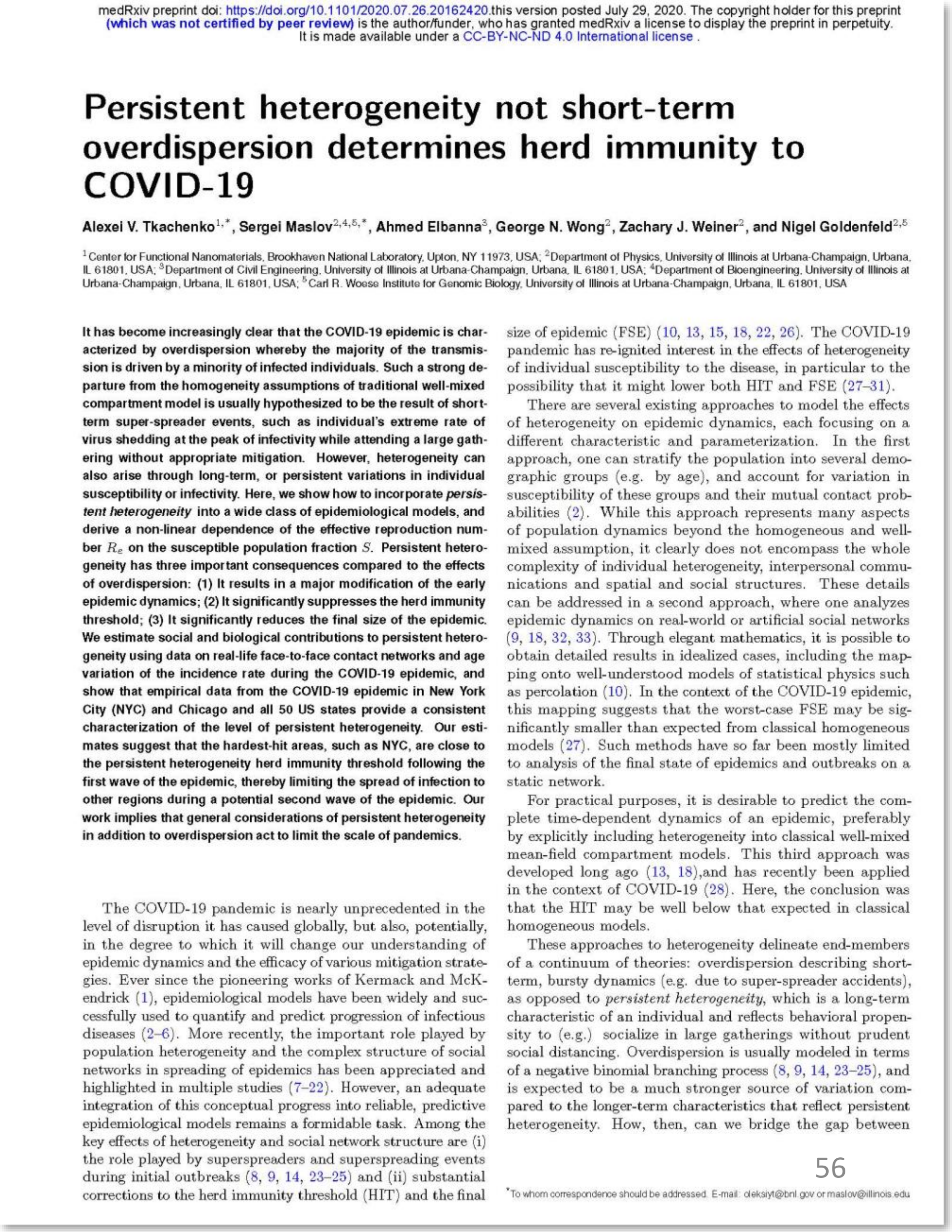

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Persistent heterogeneity not short-term overdispersion determines herd immunity to COVID-19

Alexei V. Tkachenko[1,*], Sergei Maslov[2,4,5,*], Ahmed Elbanna[3], George N. Wong[2], Zachary J. Weiner[2], and Nigel Goldenfeld[2,5]

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It has become increasingly clear that the COVID-19 epidemic is characterized by overdispersion whereby the majority of the transmission is driven by a minority of infected individuals. Such a strong departure from the homogeneity assumptions of traditional well-mixed compartment model is usually hypothesized to be the result of short-term super-spreader events, such as individual's extreme rate of virus shedding at the peak of infectivity while attending a large gathering without appropriate mitigation. However, heterogeneity can also arise through long-term, or persistent variations in individual susceptibility or infectivity. Here, we show how to incorporate *persistent heterogeneity* into a wide class of epidemiological models, and derive a non-linear dependence of the effective reproduction number R_e on the susceptible population fraction S. Persistent heterogeneity has three important consequences compared to the effects of overdispersion: (1) It results in a major modification of the early epidemic dynamics; (2) It significantly suppresses the herd immunity threshold; (3) It significantly reduces the final size of the epidemic. We estimate social and biological contributions to persistent heterogeneity using data on real-life face-to-face contact networks and age variation of the incidence rate during the COVID-19 epidemic, and show that empirical data from the COVID-19 epidemic in New York City (NYC) and Chicago and all 50 US states provide a consistent characterization of the level of persistent heterogeneity. Our estimates suggest that the hardest-hit areas, such as NYC, are close to the persistent heterogeneity herd immunity threshold following the first wave of the epidemic, thereby limiting the spread of infection to other regions during a potential second wave of the epidemic. Our work implies that general considerations of persistent heterogeneity in addition to overdispersion act to limit the scale of pandemics.

The COVID-19 pandemic is nearly unprecedented in the level of disruption it has caused globally, but also, potentially, in the degree to which it will change our understanding of epidemic dynamics and the efficacy of various mitigation strategies. Ever since the pioneering works of Kermack and McKendrick (1), epidemiological models have been widely and successfully used to quantify and predict progression of infectious diseases (2–6). More recently, the important role played by population heterogeneity and the complex structure of social networks in spreading of epidemics has been appreciated and highlighted in multiple studies (7–22). However, an adequate integration of this conceptual progress into reliable, predictive epidemiological models remains a formidable task. Among the key effects of heterogeneity and social network structure are (i) the role played by superspreaders and superspreading events during initial outbreaks (8, 9, 14, 23–25) and (ii) substantial corrections to the herd immunity threshold (HIT) and the final size of epidemic (FSE) (10, 13, 15, 18, 22, 26). The COVID-19 pandemic has re-ignited interest in the effects of heterogeneity of individual susceptibility to the disease, in particular to the possibility that it might lower both HIT and FSE (27–31).

There are several existing approaches to model the effects of heterogeneity on epidemic dynamics, each focusing on a different characteristic and parameterization. In the first approach, one can stratify the population into several demographic groups (e.g. by age), and account for variation in susceptibility of these groups and their mutual contact probabilities (2). While this approach represents many aspects of population dynamics beyond the homogeneous and well-mixed assumption, it clearly does not encompass the whole complexity of individual heterogeneity, interpersonal communications and spatial and social structures. These details can be addressed in a second approach, where one analyzes epidemic dynamics on real-world or artificial social networks (9, 18, 32, 33). Through elegant mathematics, it is possible to obtain detailed results in idealized cases, including the mapping onto well-understood models of statistical physics such as percolation (10). In the context of the COVID-19 epidemic, this mapping suggests that the worst-case FSE may be significantly smaller than expected from classical homogeneous models (27). Such methods have so far been mostly limited to analysis of the final state of epidemics and outbreaks on a static network.

For practical purposes, it is desirable to predict the complete time-dependent dynamics of an epidemic, preferably by explicitly including heterogeneity into classical well-mixed mean-field compartment models. This third approach was developed long ago (13, 18),and has recently been applied in the context of COVID-19 (28). Here, the conclusion was that the HIT may be well below that expected in classical homogeneous models.

These approaches to heterogeneity delineate end-members of a continuum of theories: overdispersion describing short-term, bursty dynamics (e.g. due to super-spreader accidents), as opposed to *persistent heterogeneity*, which is a long-term characteristic of an individual and reflects behavioral propensity to (e.g.) socialize in large gatherings without prudent social distancing. Overdispersion is usually modeled in terms of a negative binomial branching process (8, 9, 14, 23–25), and is expected to be a much stronger source of variation compared to the longer-term characteristics that reflect persistent heterogeneity. How, then, can we bridge the gap between

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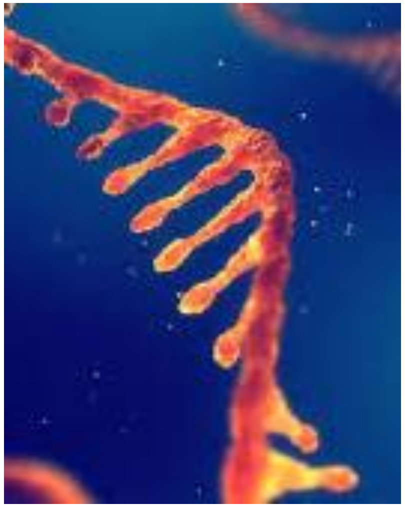
COVID-19
SHIELD
Target TEST Tell

Target

Algorithms for prioritized testing guided by exposure risk and overall effectiveness of the SHIELD mitigation strategy

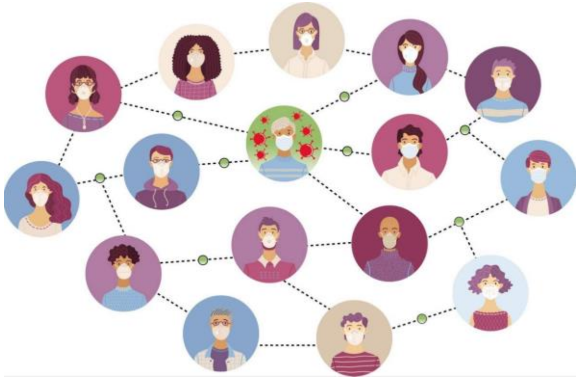
Test



COVID TEST

Saliva-based test for COVID-19 that is cheap, non-intrusive, fast turn-around, accurate and scalable

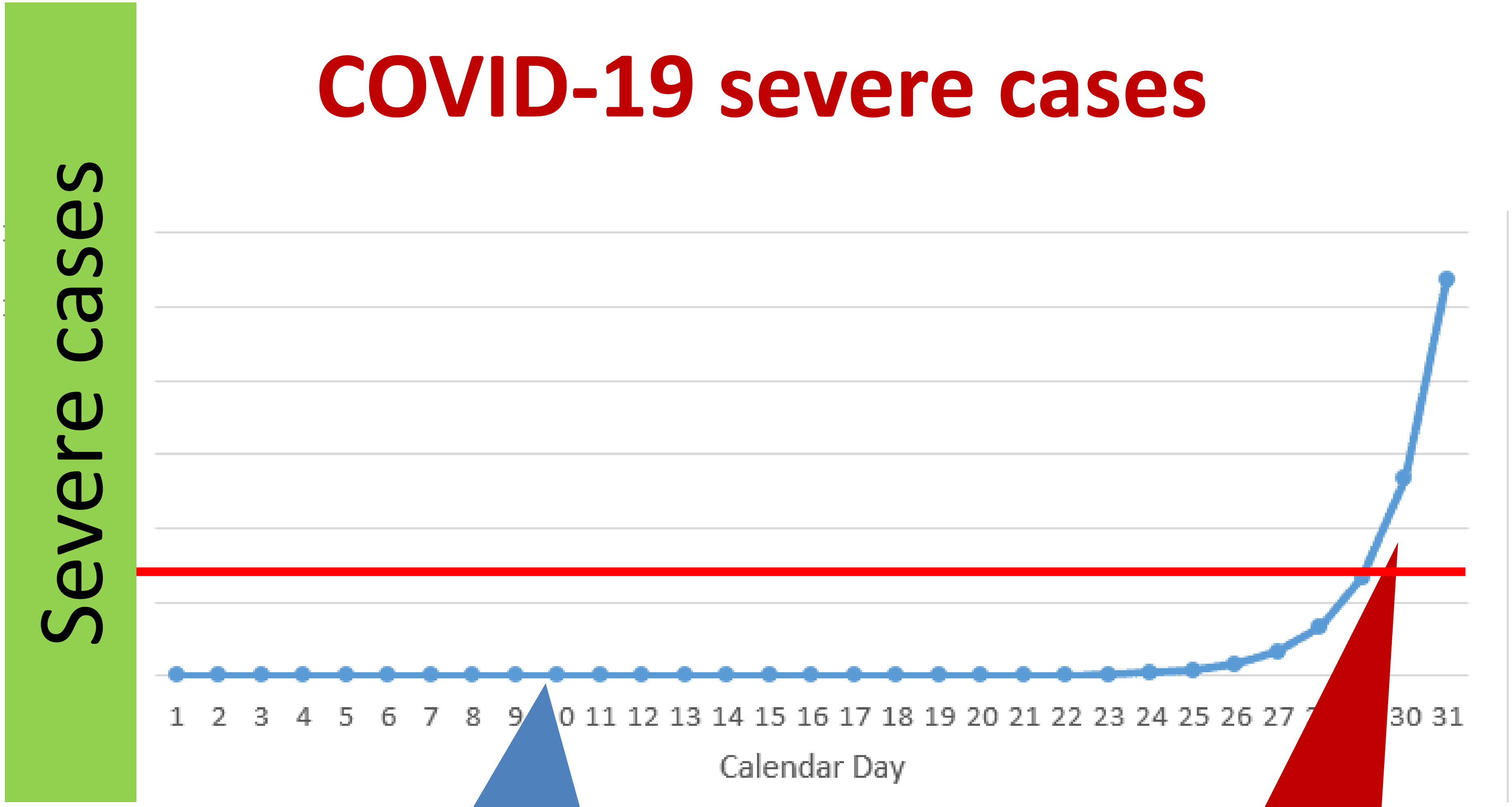
Tell



Exposure notifications in partnership with Champaign-Urbana Public Health District and via Safer in Illinois app; Individualized healthcare support in partnership with OSF

Goal of SHIELD

COVID-19 severe cases

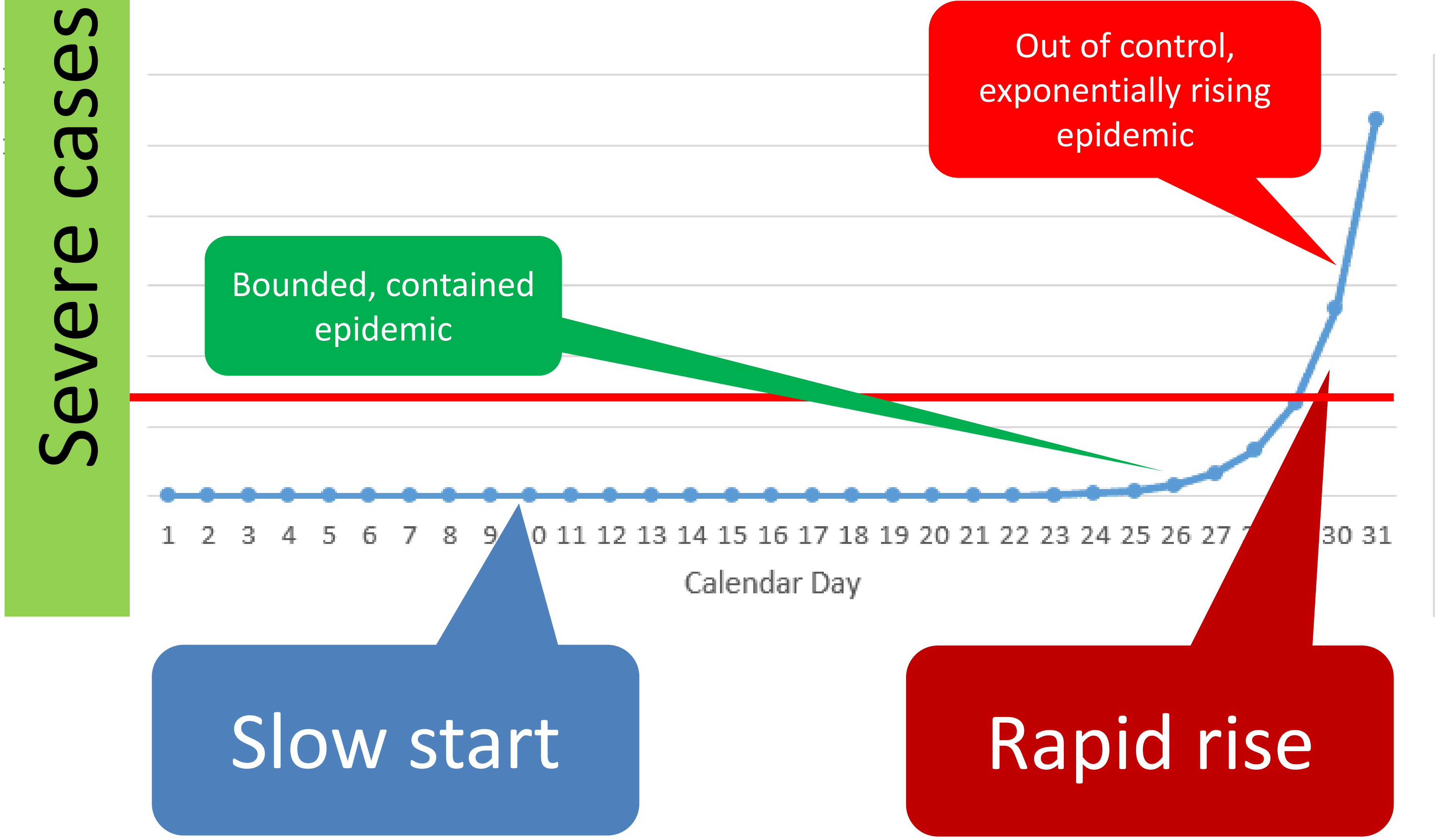


Slow start

Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

COVID-19 severe cases



Out of control, exponentially rising epidemic

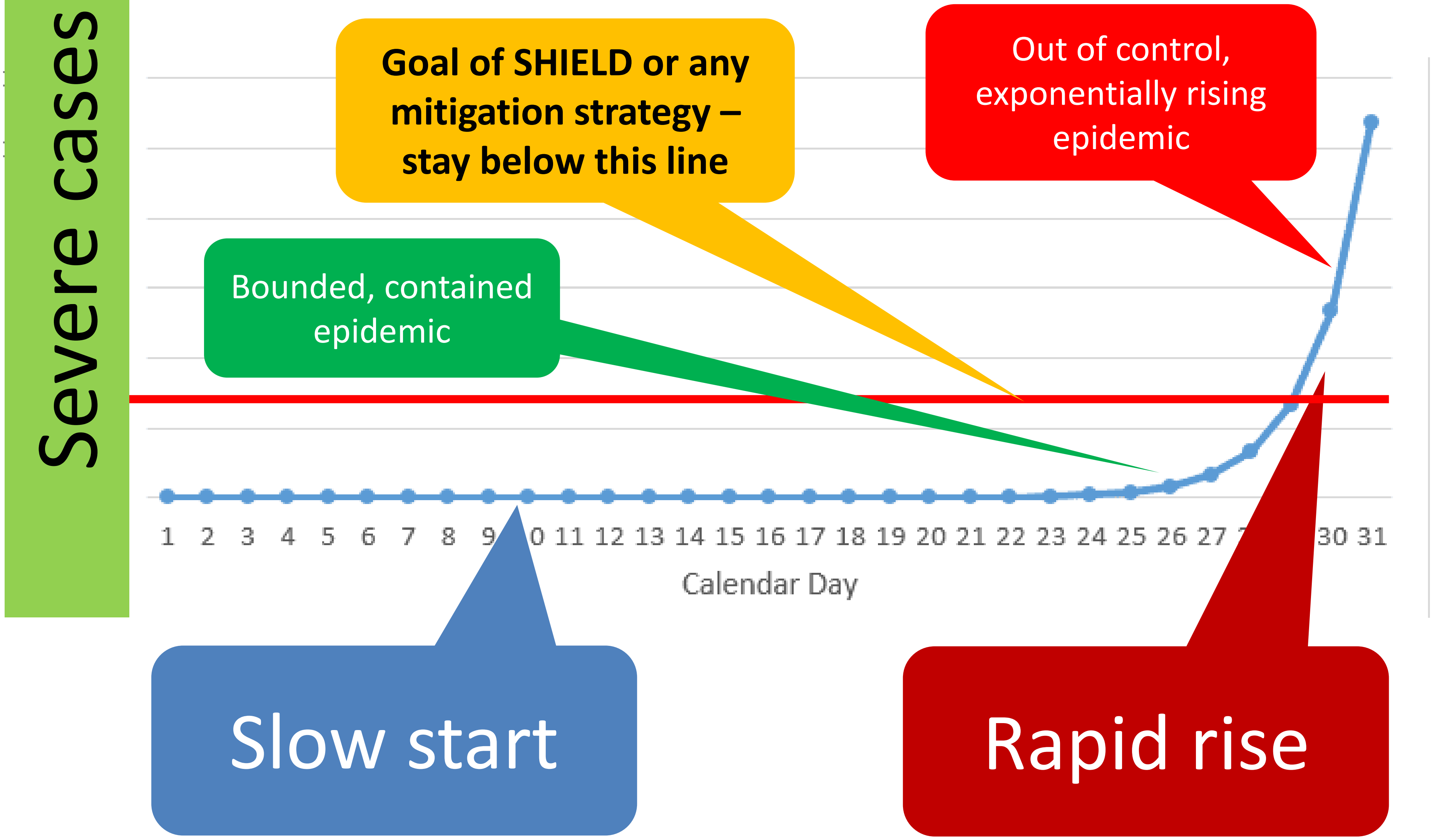
Bounded, contained epidemic

Slow start

Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

COVID-19 severe cases



Goal of SHIELD or any mitigation strategy – stay below this line

Out of control, exponentially rising epidemic

Bounded, contained epidemic

Slow start

Rapid rise

https://populationeducation.org/exponential-growth-and-doubling-time/

The only way to contain an epidemic is to make $R < 1$

We reduce transmission by social distancing, small class size, universal masks, testing and isolation, contact tracing or exposure notification and quarantining

Will these mitigation steps make R < 1?

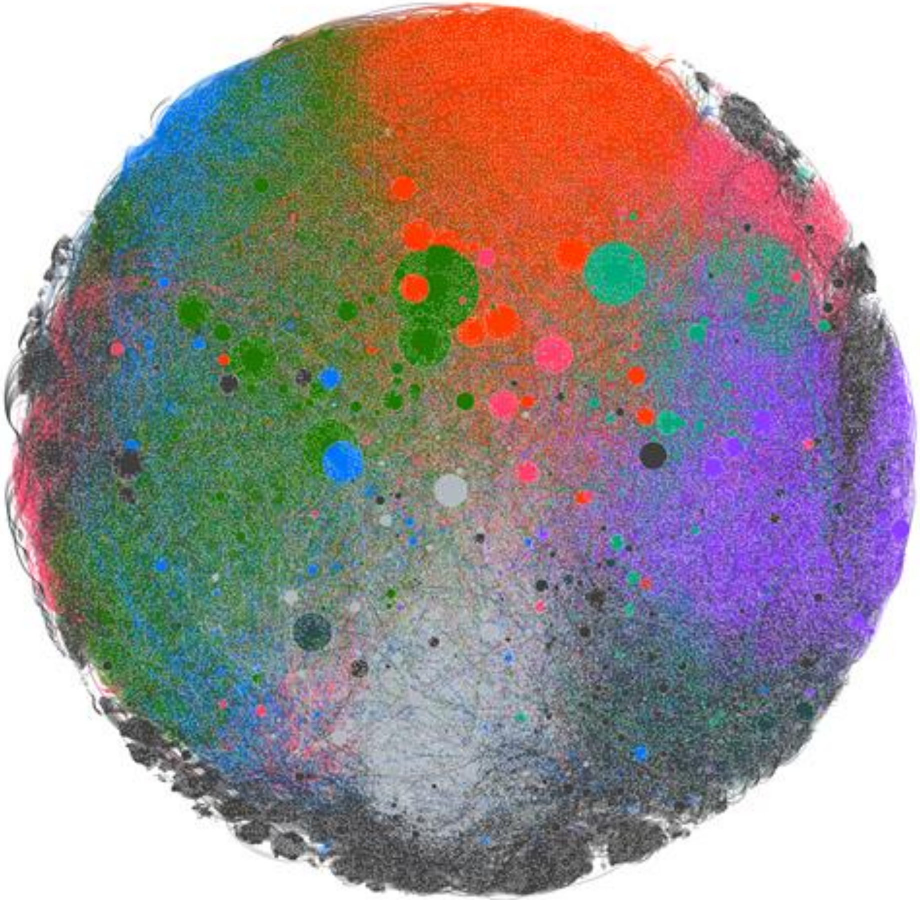
SHIELD Target Team

- Questions
  - Who to test?
  - When?
  - How often?
  - What other mitigation strategies can be effective?
  - Can we re-open in a hybrid way safely?
- Answers
  - Everyone
  - On arrival on campus, and frequently throughout semester
  - Twice a week
  - Modeling suggests that the synergistic combination of frequent testing, contact tracing, isolation, universal masks, restricting class size, use of app-based exposure notification can bring epidemic to manageable and relatively safe levels.

High level description of model

- Students and faculty come together at specific times and places for classes
  - Agents (45,000 = students + workers)
  - Zones (classrooms, bars, restaurants, dorms, coffee shops, library, other gathering places)
- Data input: we constructed the network of students and classroom zones from anonymized data of all students at UIUC in Fall 2019

UIUC is a giant network



- Nodes are classes
- Edges are students
- Small-world network with ~2.5 “degrees of separation”
  - Students cluster by major, common classes
- COVID-19 spreads rapidly in network
- Social bubbles are connected by social activities outside of class scheduled time

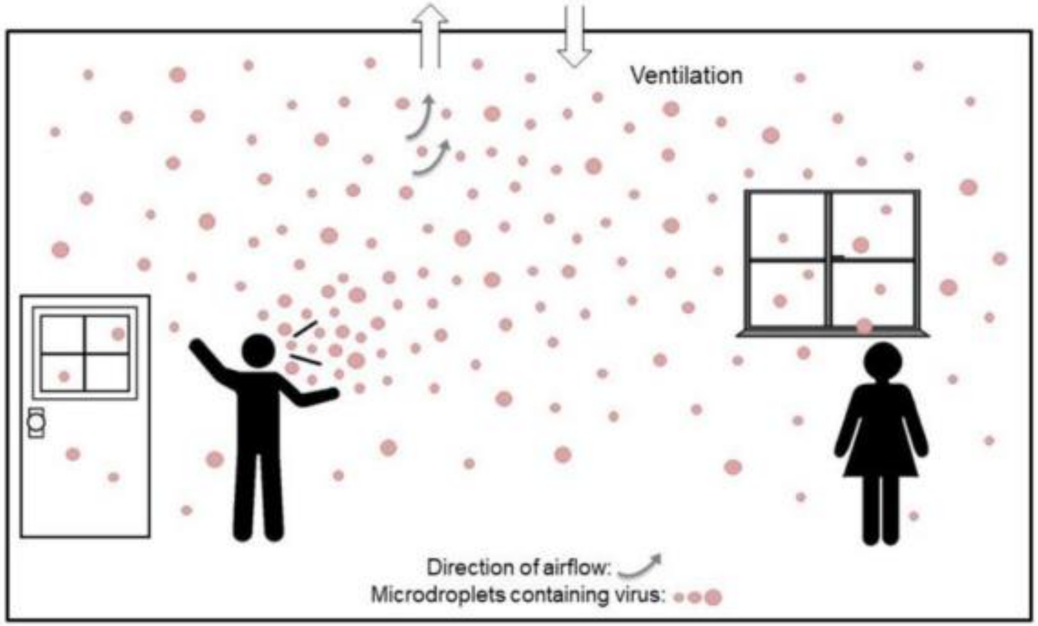
Why is COVID-19 so dangerous?

- Spread by aerosols
- You do not just need to be within 6 feet
- COVID-19 can be spread by people with no symptoms
- 10% of the cases contribute 80% of the transmission

The Coronavirus Can Be Airborne Indoors, W.H.O. Says

The agency also explained more directly that people without symptoms may spread the virus. The acknowledgments should have come sooner, some experts said.

NYT July 9, 2020



Morawska et al. https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa939/5867798

How to model COVID-19 in UIUC

- Follow each student as they go to class, home, restaurants, coffee shops, bars/parties (7000 students in parties, 3 nights a week)
- Model the physics of aerosol spread and virus infection in different locations
- Model mitigation steps: online classes, masks on campus, testing, contact tracing, exposure notifications
- Conservative, worst case assumptions

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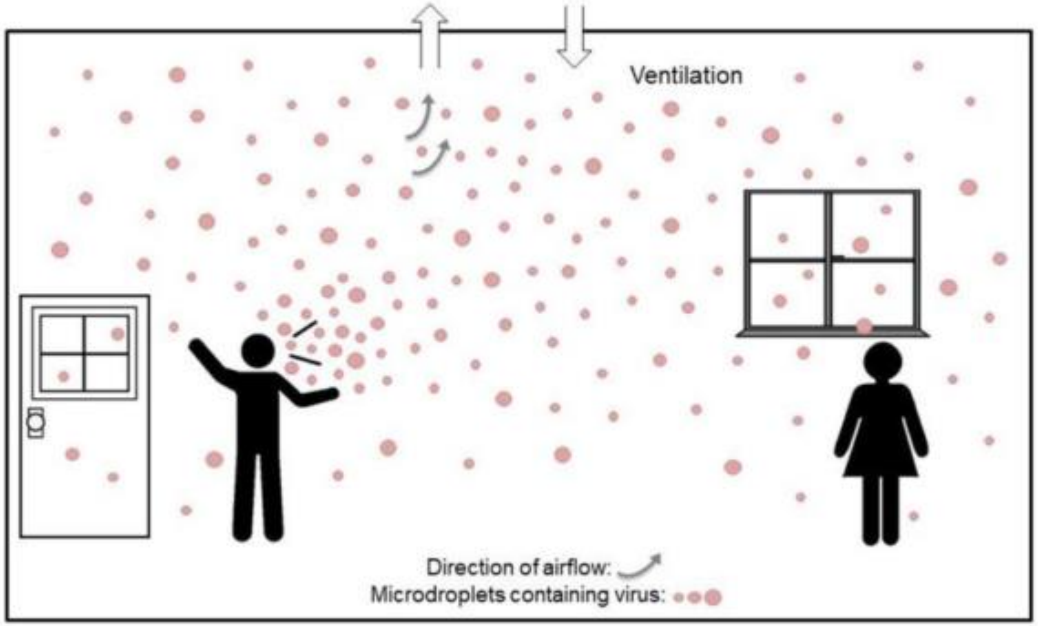


Morawska et al. https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa939/5867798

What happens next …

… when 45,000 students return

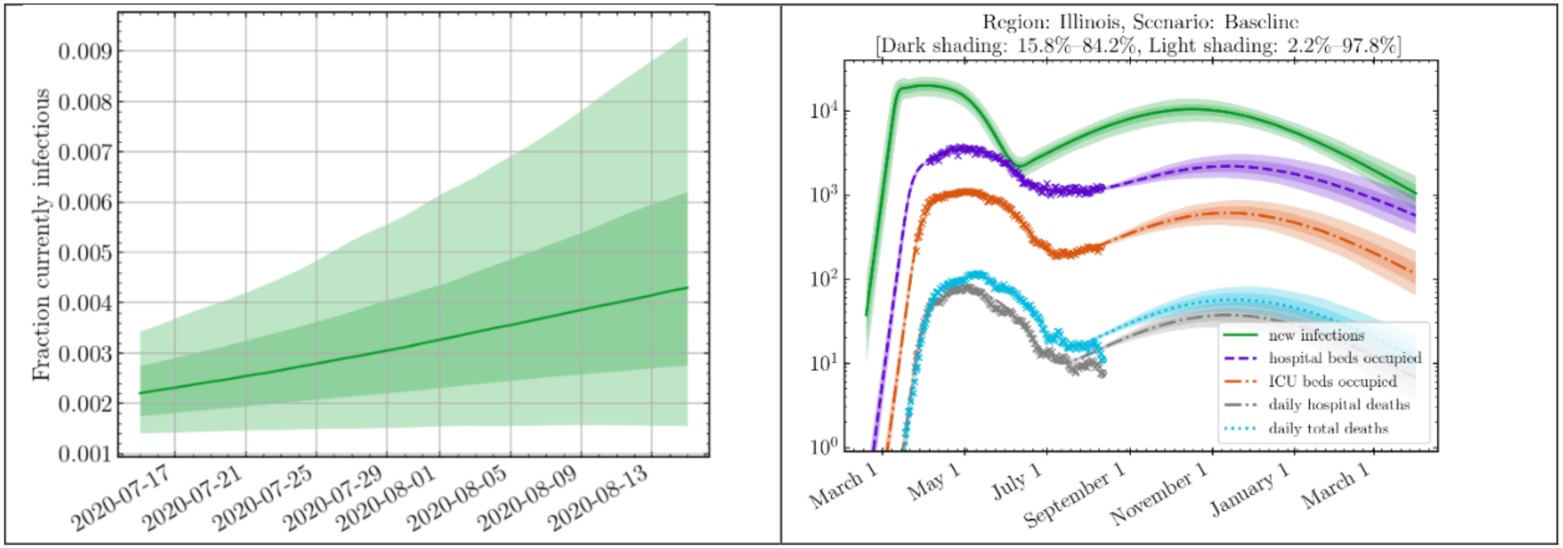


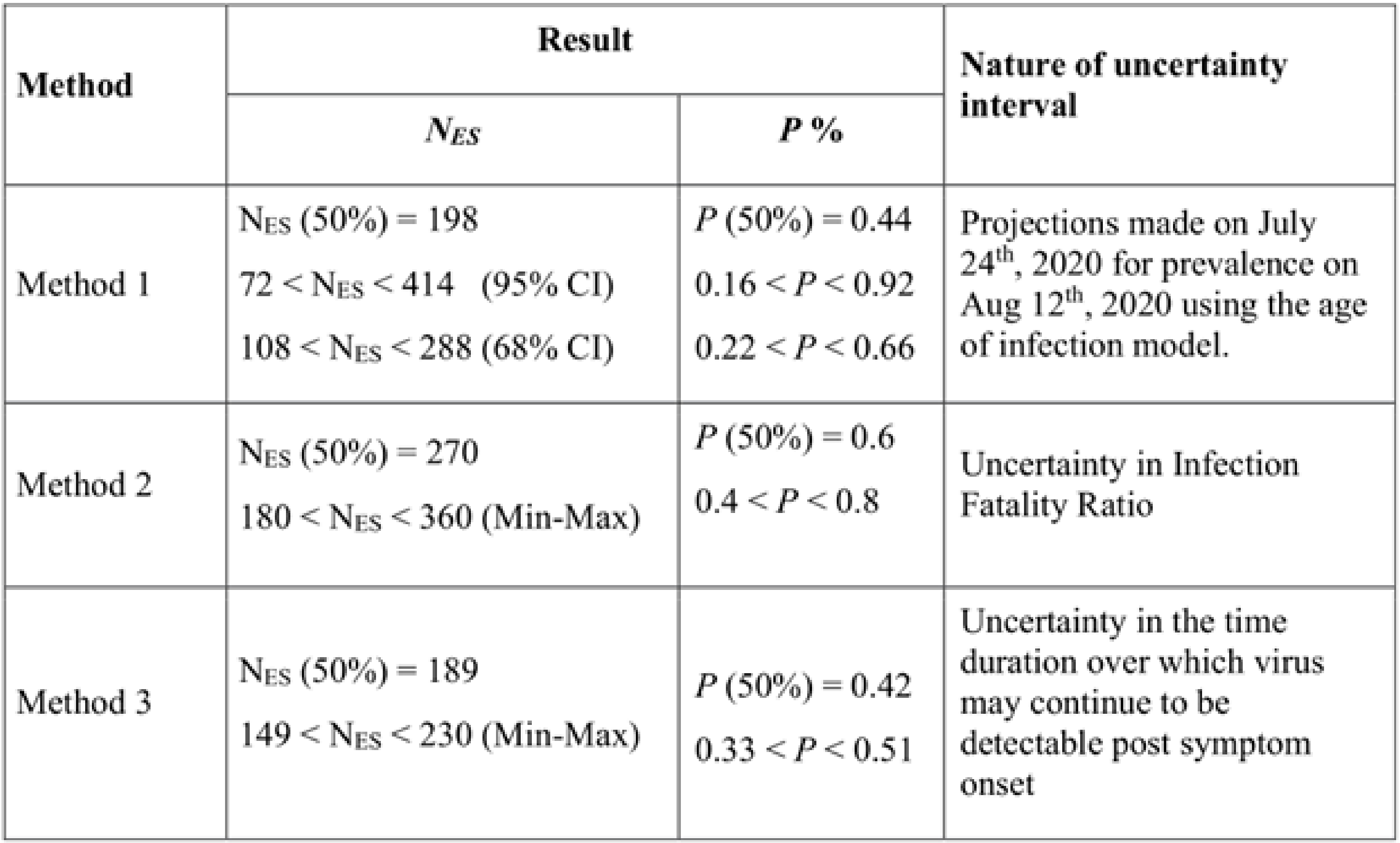
Figure 1. Simulation of the COVID-19 epidemic in Illinois. Left panel: projected fraction of currently infectious individuals within the State. Right panel: projected epidemic curves for hospital occupancy, ICU occupancy, hospital deaths, all deaths and new infections (computed 8/12/2020). Crosses indicate data from IDPH.

The model predicts a prevalence of about 0.44 ± 0.2% by August 15, assuming individuals are infectious for a Gamma-distributed period with mean 5 days and standard deviation 2 days (see, e.g. [2], although such viral dynamics data are very difficult to measure precisely and were recently revised).

Thus, we estimate the number of positive cases detected = 45,000 * 0.0044 ± 0.002 = 198 ± 90

Initial "bump" of around 2-300 imported cases as students return

Entry screening



Method	**Result**		**Nature of uncertainty interval**
	N_{ES}	P %	
Method 1	N_{ES} (50%) = 198 $72 < N_{ES} < 414$ (95% CI) $108 < N_{ES} < 288$ (68% CI)	P (50%) = 0.44 $0.16 < P < 0.92$ $0.22 < P < 0.66$	Projections made on July 24th, 2020 for prevalence on Aug 12th, 2020 using the age of infection model.
Method 2	N_{ES} (50%) = 270 $180 < N_{ES} < 360$ (Min-Max)	P (50%) = 0.6 $0.4 < P < 0.8$	Uncertainty in Infection Fatality Ratio
Method 3	N_{ES} (50%) = 189 $149 < N_{ES} < 230$ (Min-Max)	P (50%) = 0.42 $0.33 < P < 0.51$	Uncertainty in the time duration over which virus may continue to be detectable post symptom onset

- Aug 15-Aug 23: 288 cases detected in entry screening
- Aug 15-Aug 24 (first day of class): 367 cases

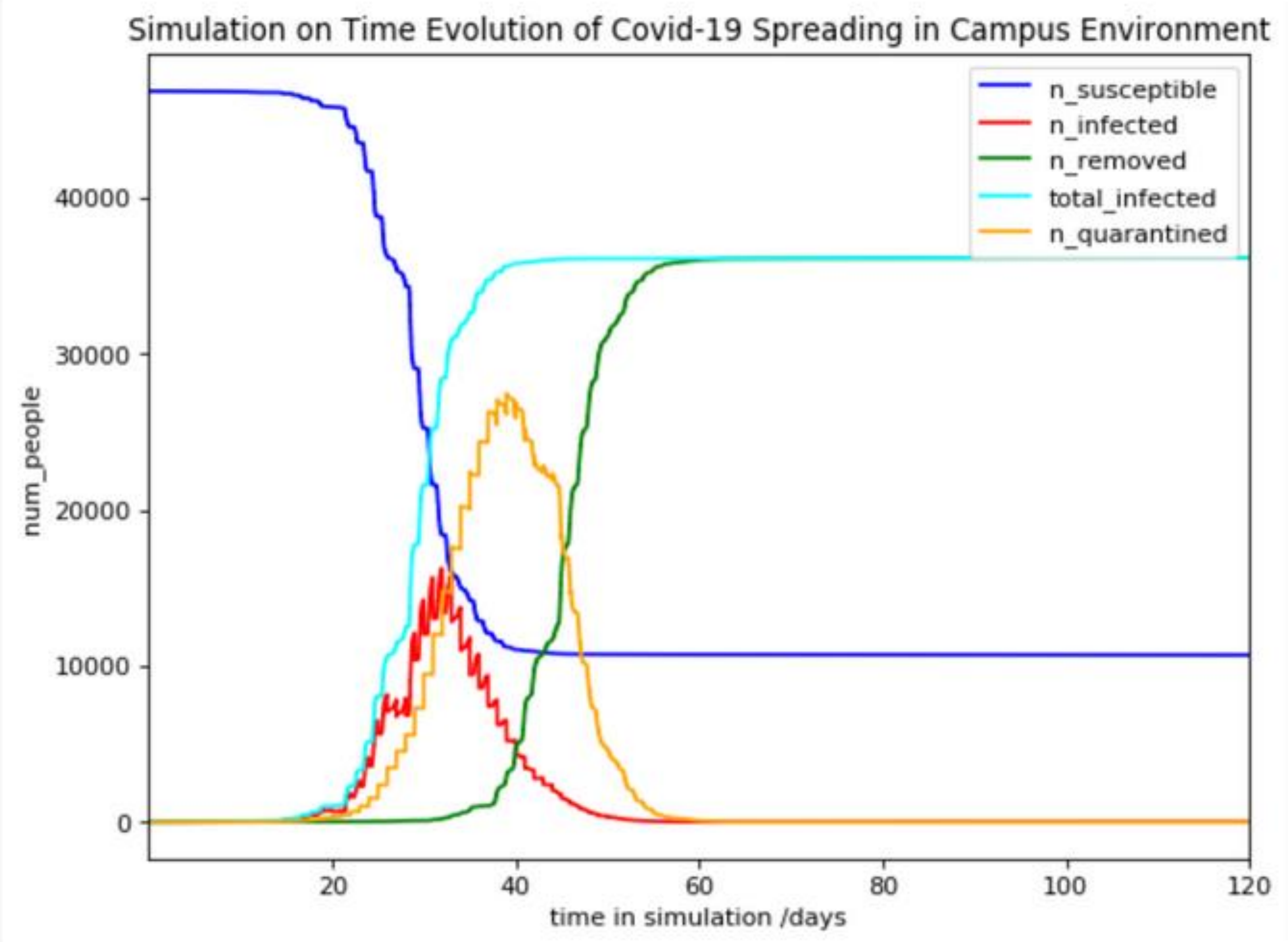
How does modeling help?

Indicate trends not precise numbers
to design mitigation strategies

Testing Frequency

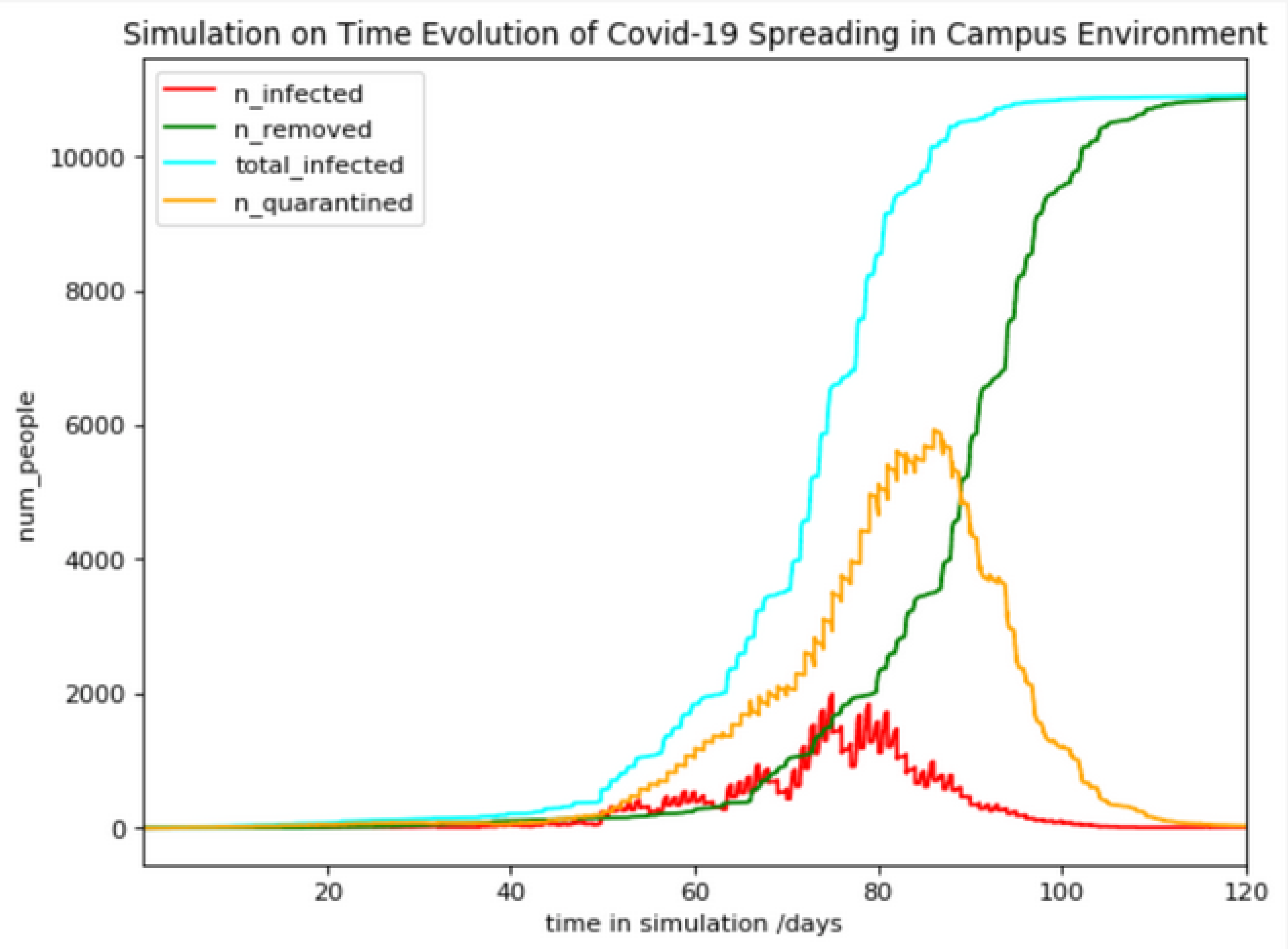
7-day testing frequency + quarantine

Testing and isolation: 7-days cycle (every one gets tested once every 7 days): In this case, testing helps a bit but ultimately almost 35000 agents get infected and the peak quarantine population is almost 26000.



3-day testing frequency + quarantine

Testing and Isolation: 3-days cycle: The peak quarantine population reduces to 6000. Total infected drops to almost 11,000

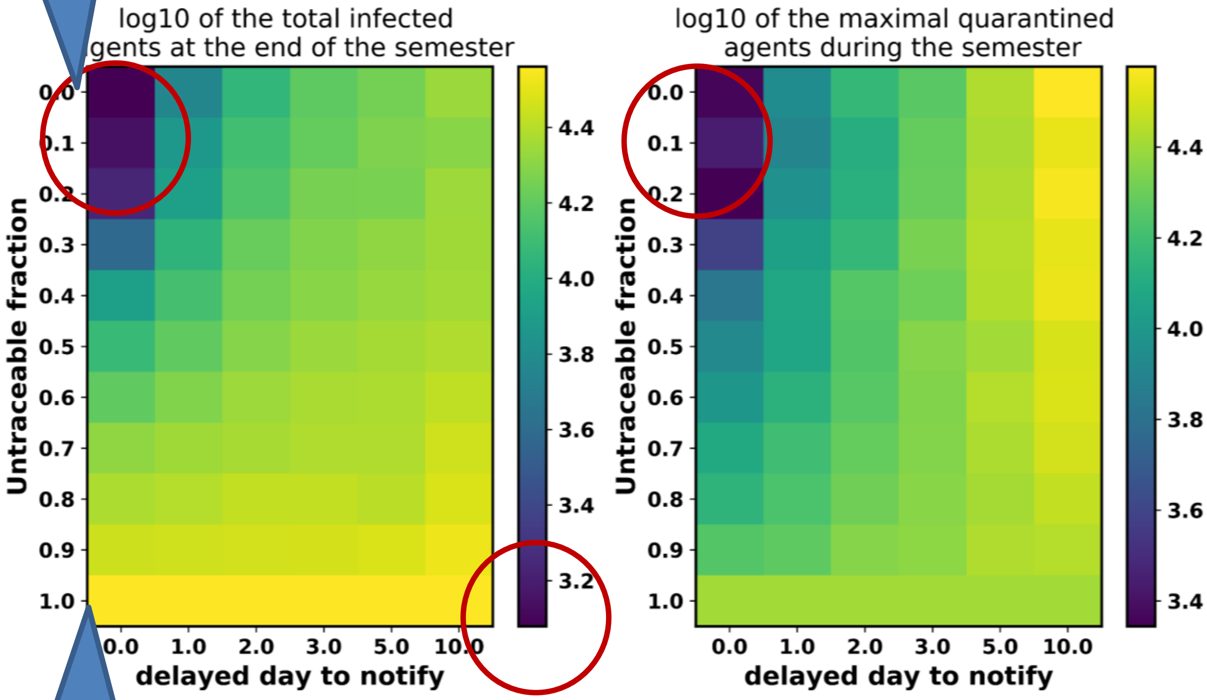


Multi-layer approach to reducing transmission

A race against time

Contact tracing phase diagram

Everyone is traced



No one is traced

Lower is better

Delay in notification of one day increases quarantine population by > 10-fold

Unreachable fraction needs to be small for contact tracing to work

Digital exposure notification

Advantage: Fast!

Effective?

False positives?

Challenges for digital apps

- Both manual contact tracing and naïve digital exposure notification expected to have high false positive rate, because the prevalence is low
  - This can cause exposure notifications to be ignored by users
- Digital apps also need to be highly adopted to increase the chance that they can detect when an infected person is close to a susceptible person
- Is there a critical threshold for adoption?
- Can we beat the false positive problem?

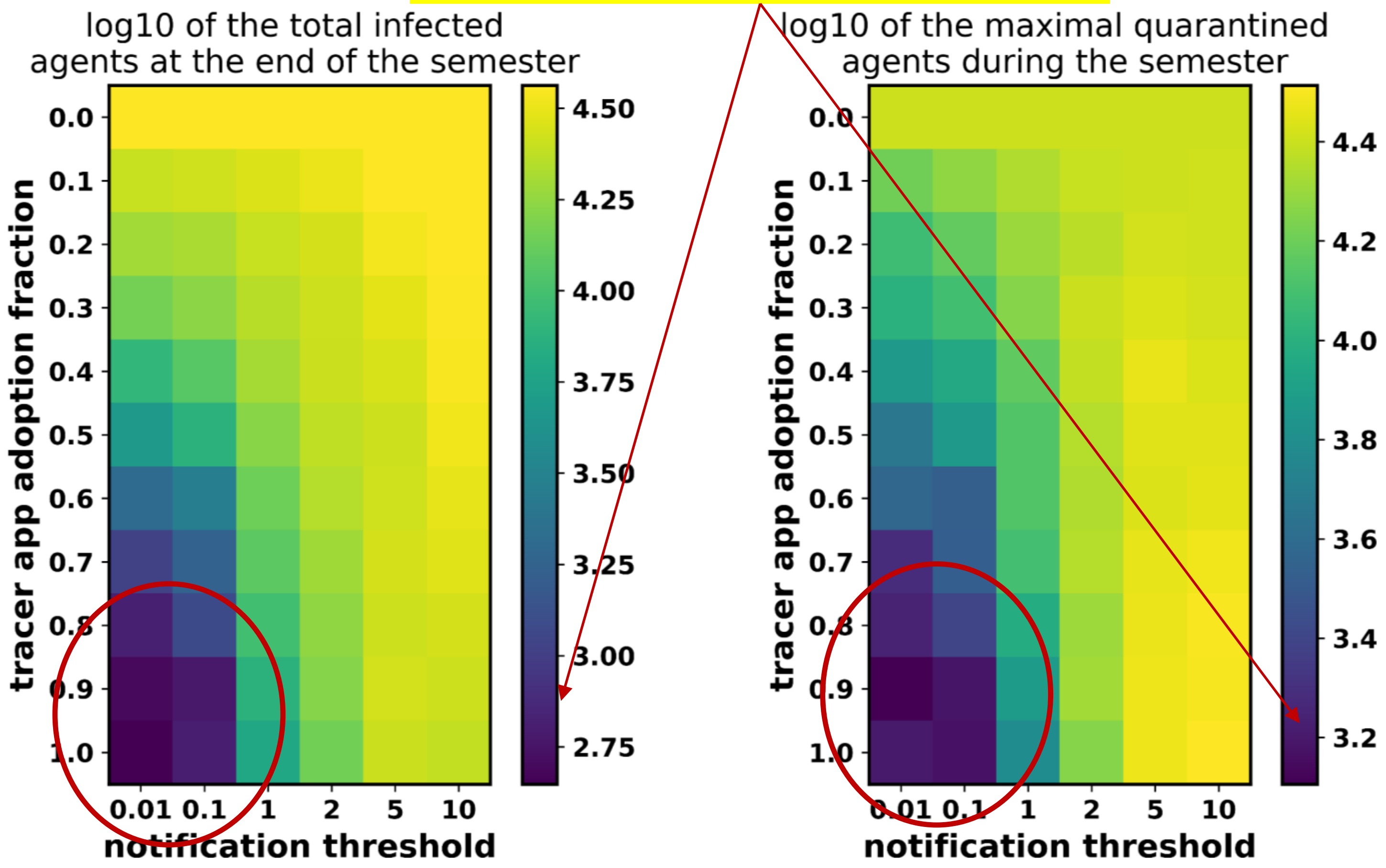
Adoption of app needs to be > 60%

Low

App adoption fraction

High

Lower color score is better

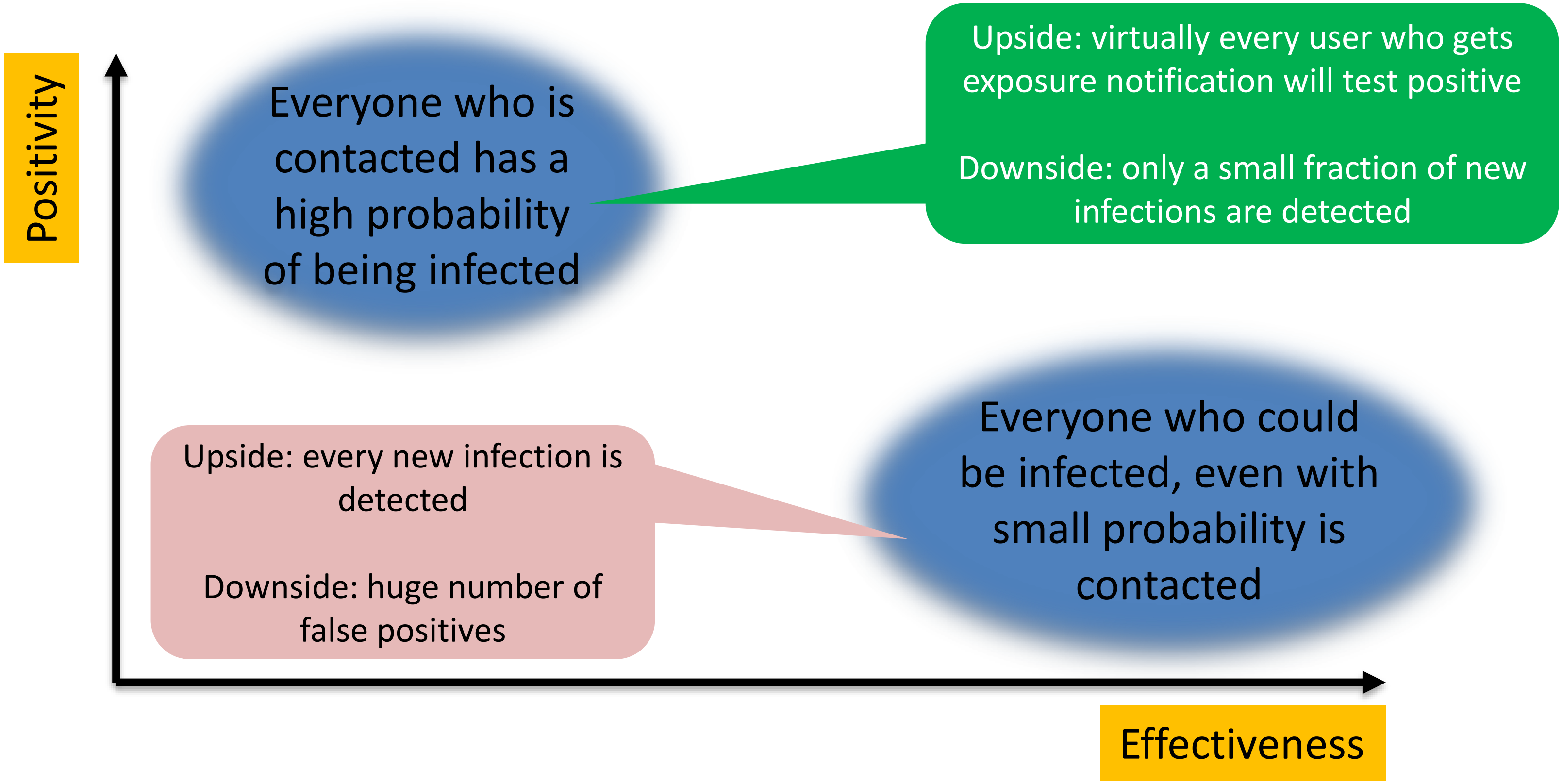


App sensitivity

App sensitivity

German “CoronaWarn” App

Positivity vs Effectiveness



Positivity

Everyone who is contacted has a high probability of being infected

Upside: virtually every user who gets exposure notification will test positive

Downside: only a small fraction of new infections are detected

Upside: every new infection is detected

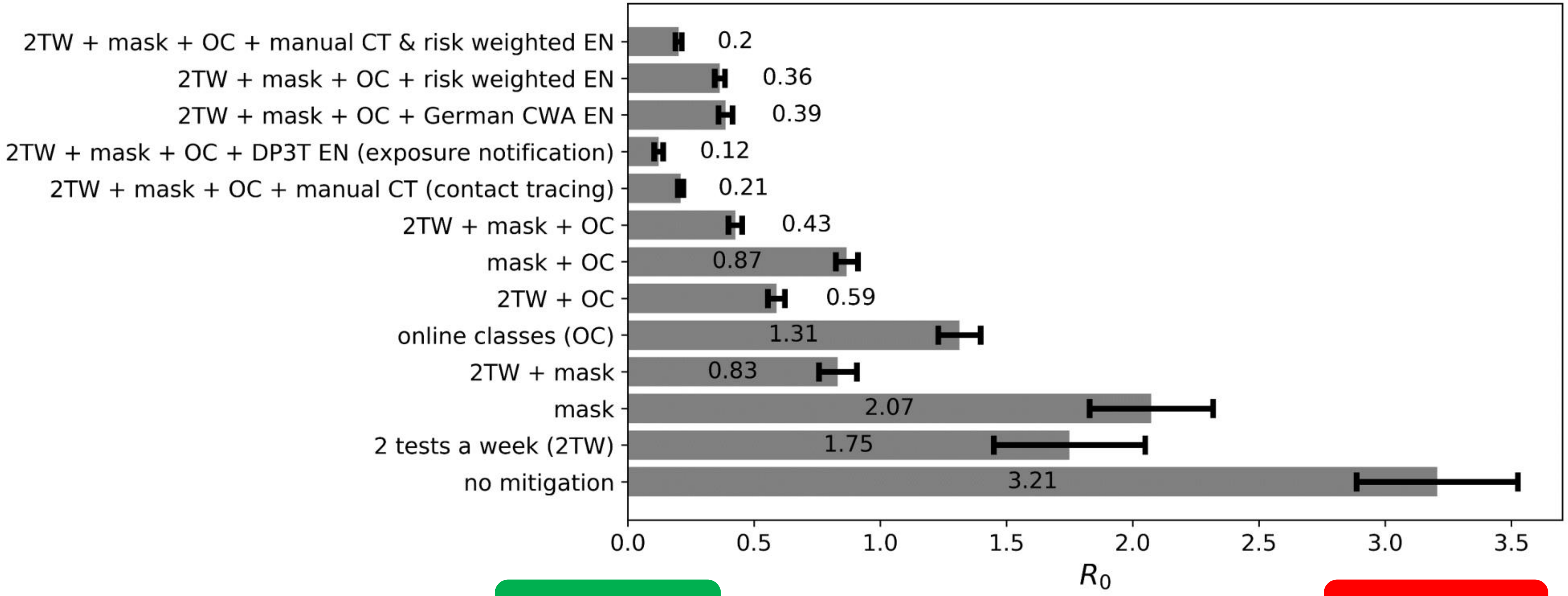
Downside: huge number of false positives

Everyone who could be infected, even with small probability is contacted

Effectiveness

- Positivity: probability that if you get notification & get tested, it will be positive
- Apps need high positivity or else users will disregard the exposure notification
  - Achieve by tuning protocol to transmission characteristics
- Effectiveness: fraction of new cases actually identified before testing
  - Achieved by lowering positivity

SHIELD works by multi-layer approach



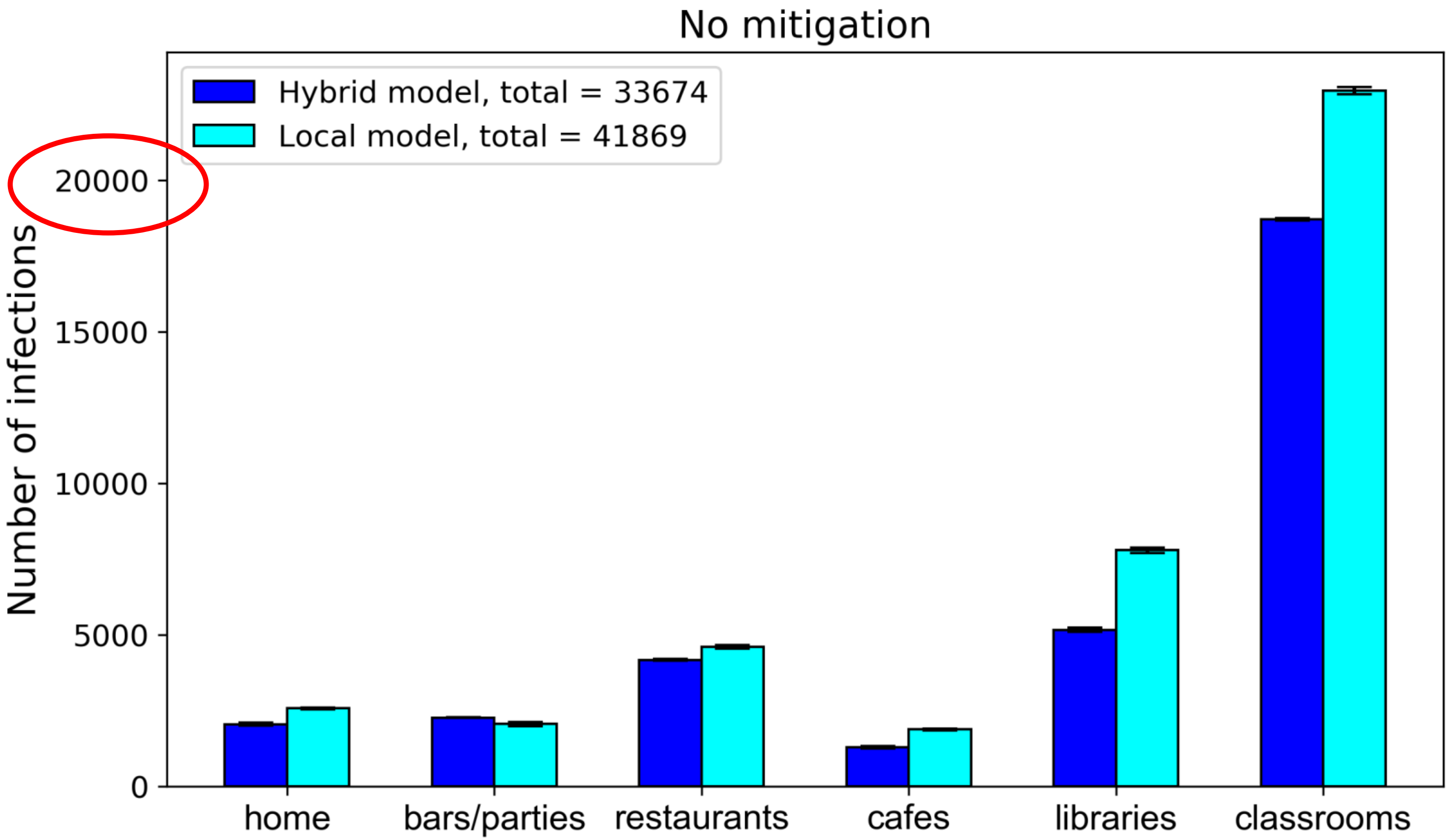
Good

Bad

How many people you infect with different layers of SHIELD

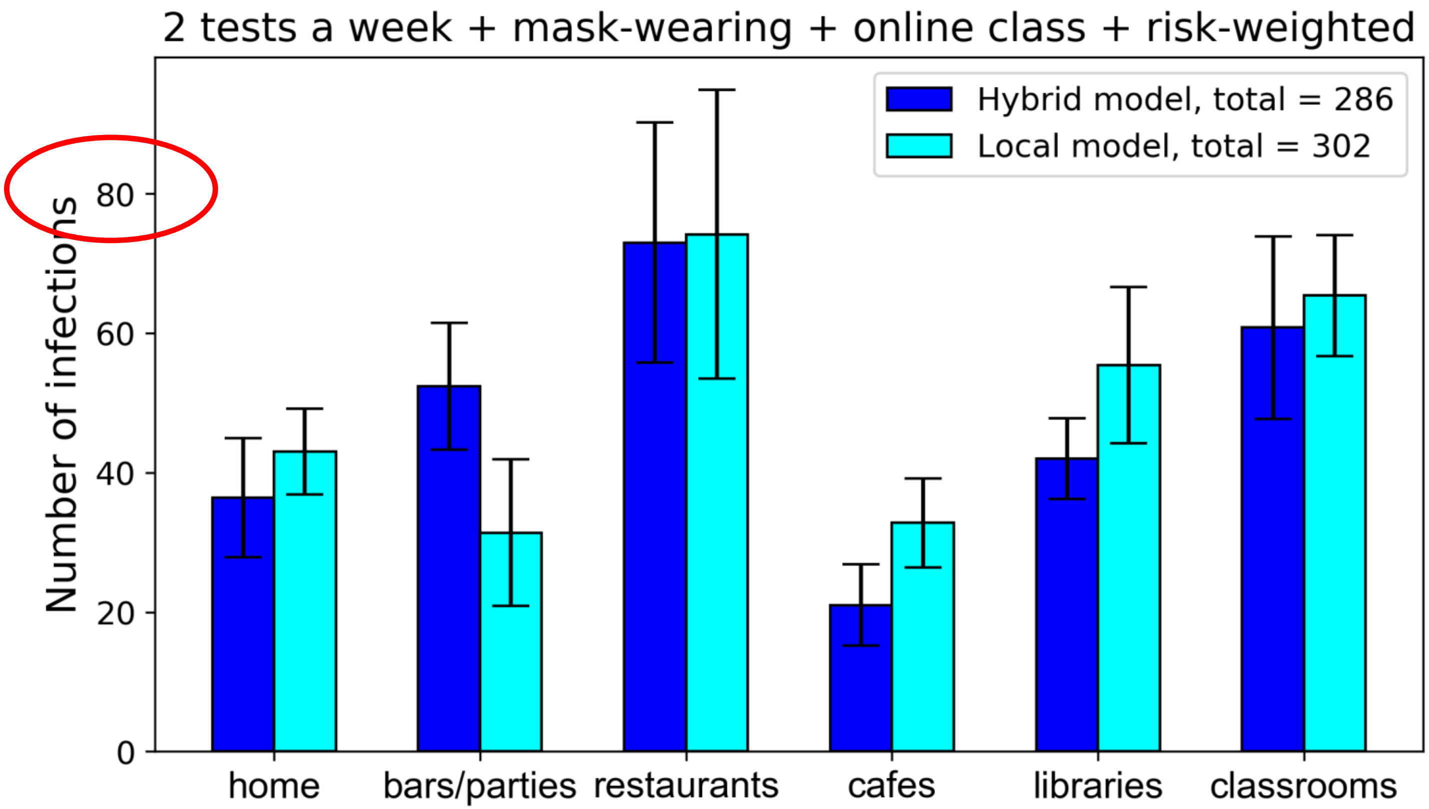
Where does transmission occur?

Where do infections happen?



Hybrid model more faithful description of aerosol transmission

Where do infections happen?



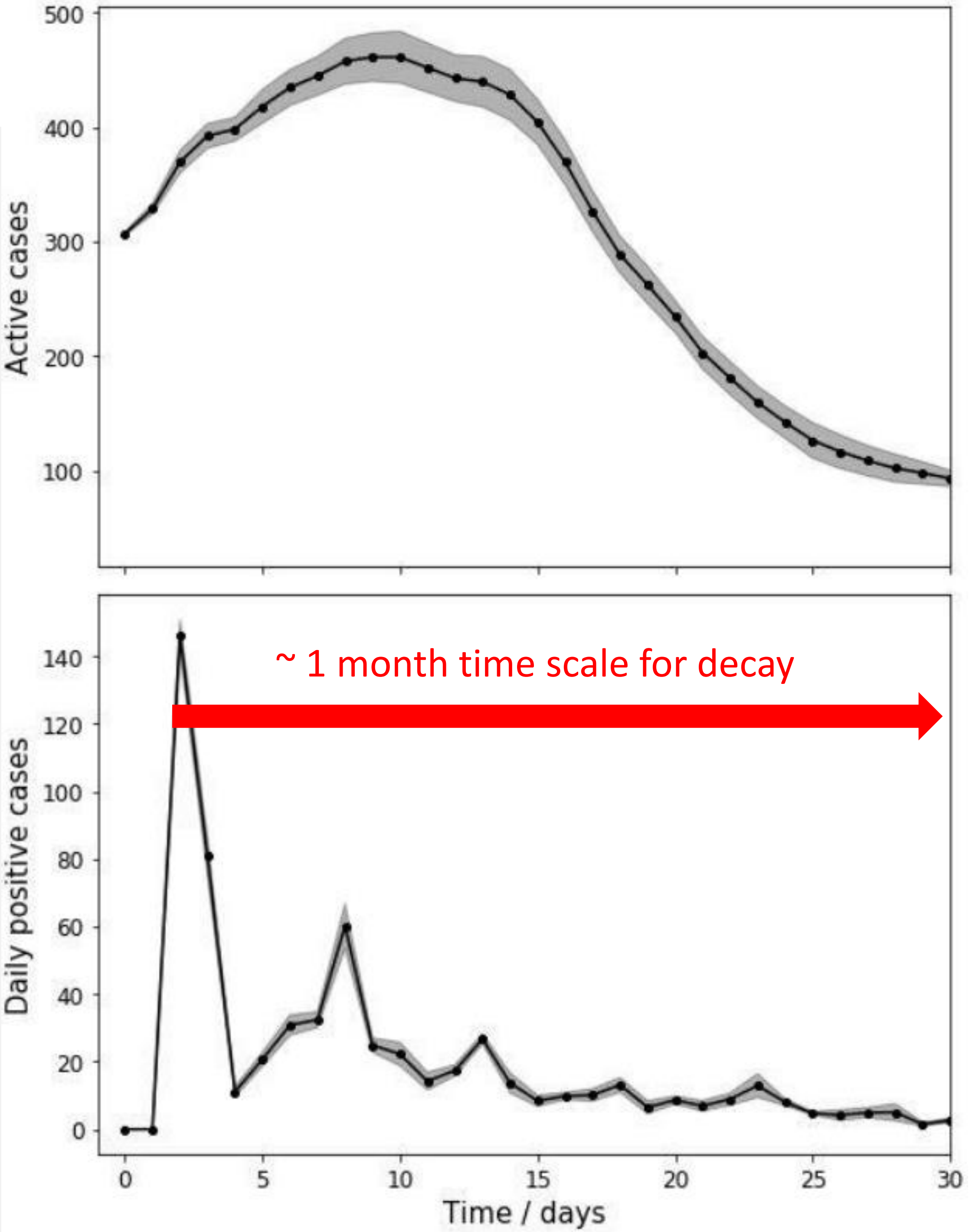
Hybrid model more faithful description of aerosol transmission

Long time scales

- Example calculation (from Aug 26) with 24 hour test turnaround

- **Time scale of decay of spike is > 4 weeks**

- Applicability
  - Non-compliance and test processing time have similar outcomes
  - Illustrative of 12 hour test turnaround and partial compliance by extremely socially active students



~ 1 month time scale for decay

Long time scales

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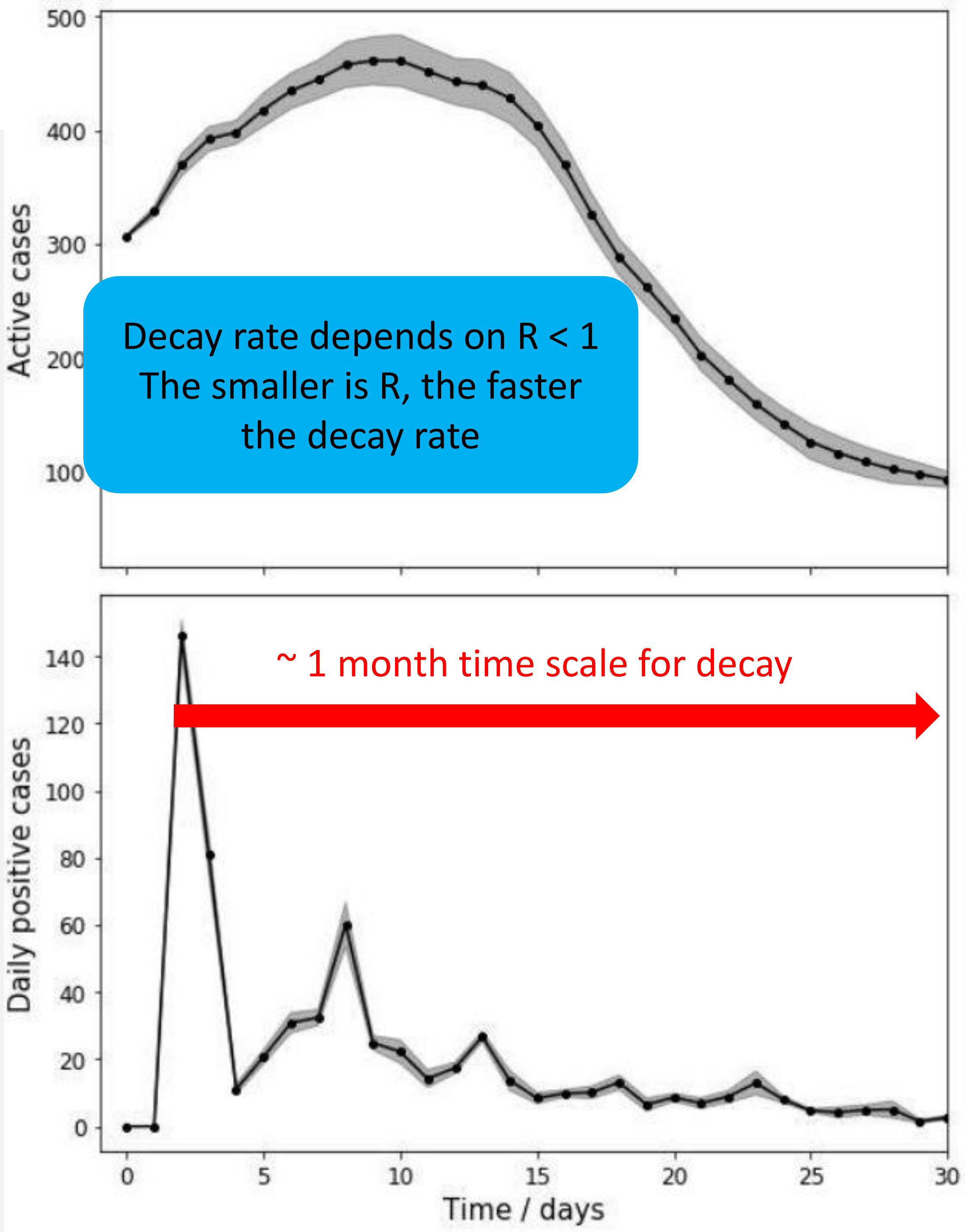


Decay rate depends on R < 1
The smaller is R, the faster the decay rate

~ 1 month time scale for decay

SHIELD Testing Results

What have we learned from doing nearly 1,000,000 tests since July?

Positivity

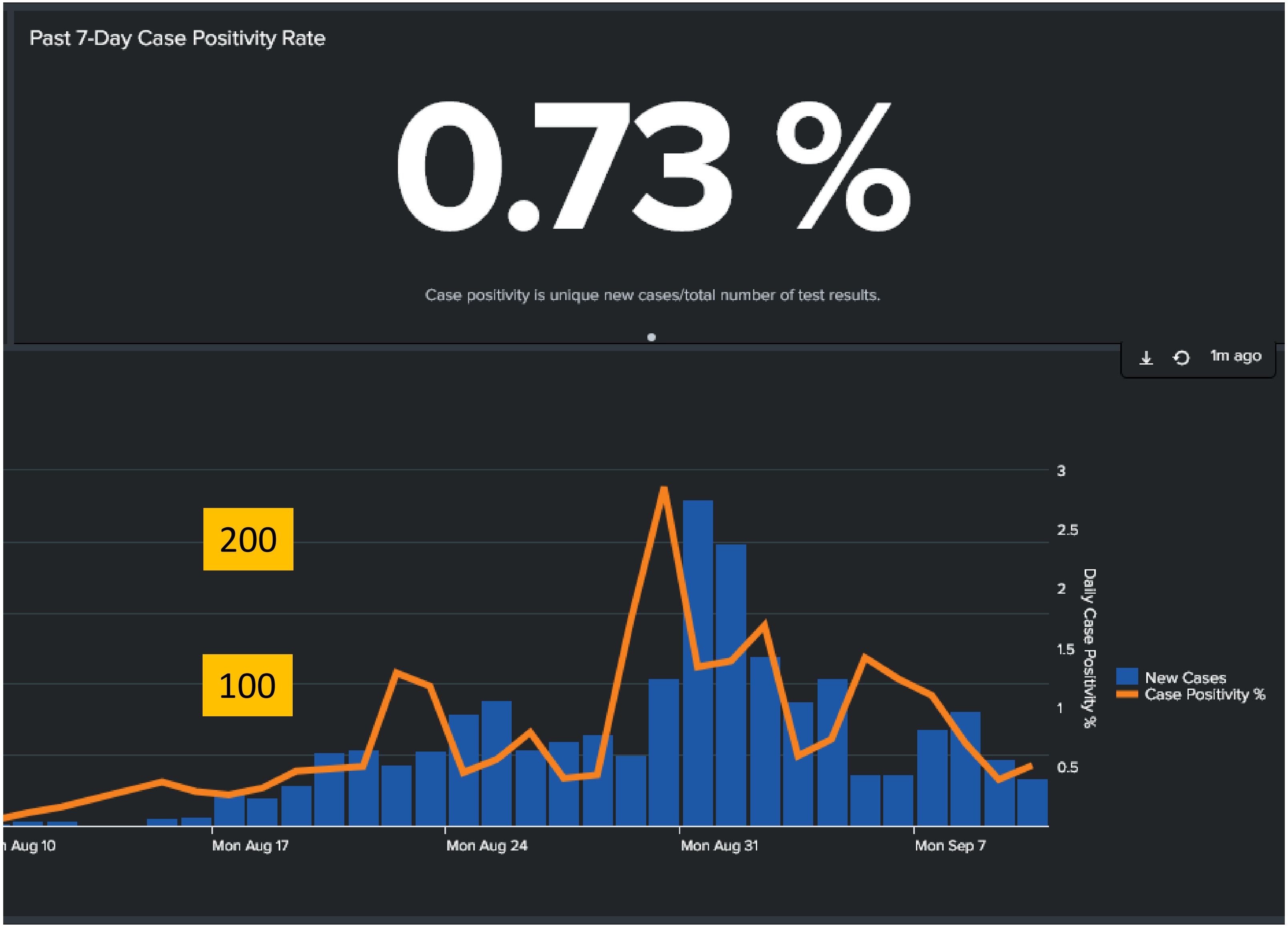
- Case positivity = new cases/tests

- What does it tell you?
  - Invert case positivity ➔ Tests/new cases
  - It answers the question: how many tests do you need to do in order to find a new infected person?

- Positivity ~ 1% ➔ you need to do 100 tests to find a new infected person **GOOD**

- Positivity ~ 25% ➔ you need to do 4 tests to find a new infected person **BAD**

SHIELD testing results



Past 7-Day Case Positivity Rate

0.73 %

Case positivity is unique new cases/total number of test results.

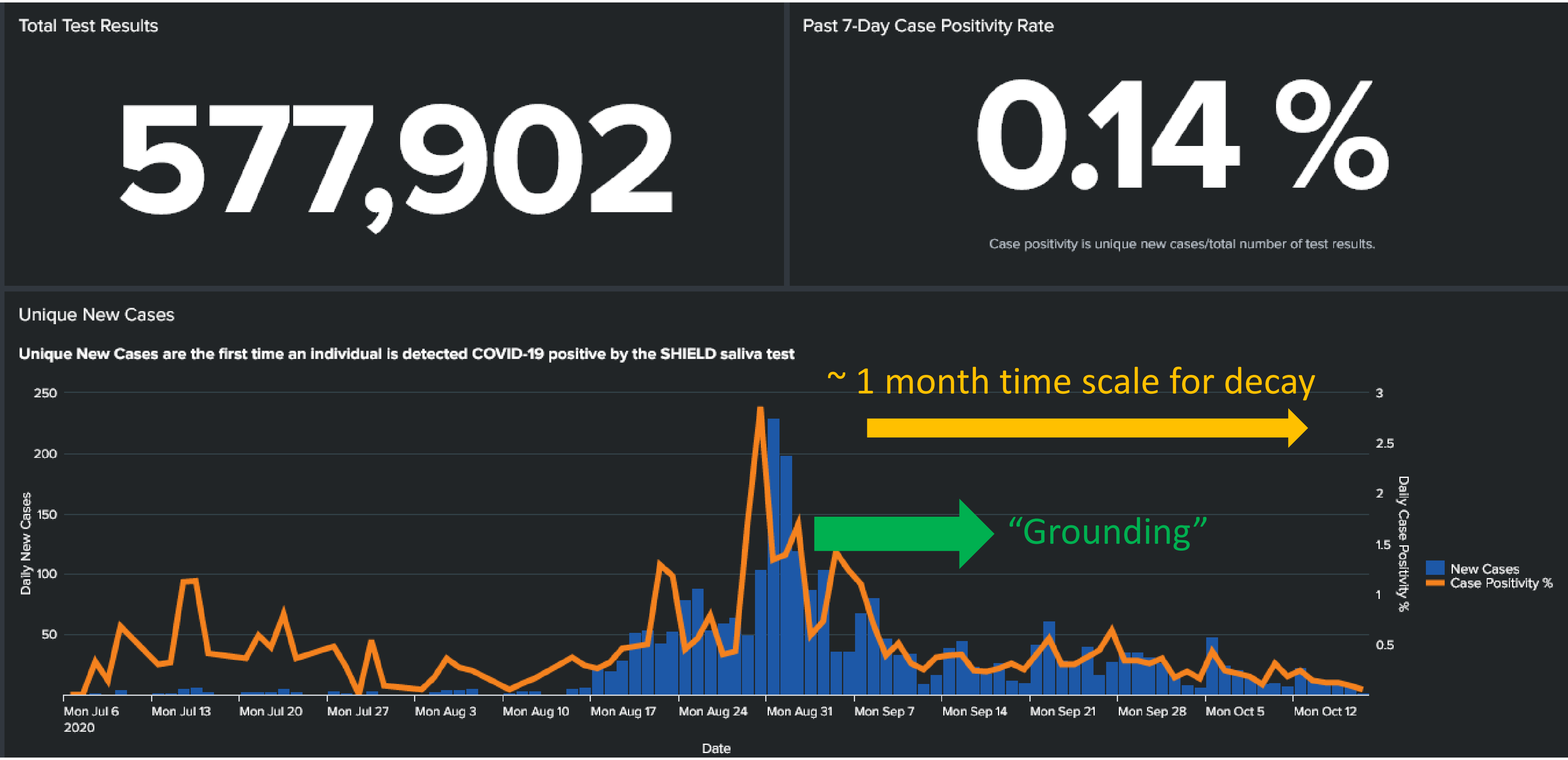
Case positivity is unique new cases/total number of test results

SHIELD testing results

This was the situation on September 10 2020

Case positivity is unique new cases/total number of test results

SHIELD testing results (Oct 19 2020)



Total Test Results

577,902

Past 7-Day Case Positivity Rate

0.14 %

Case positivity is unique new cases/total number of test results.

Unique New Cases

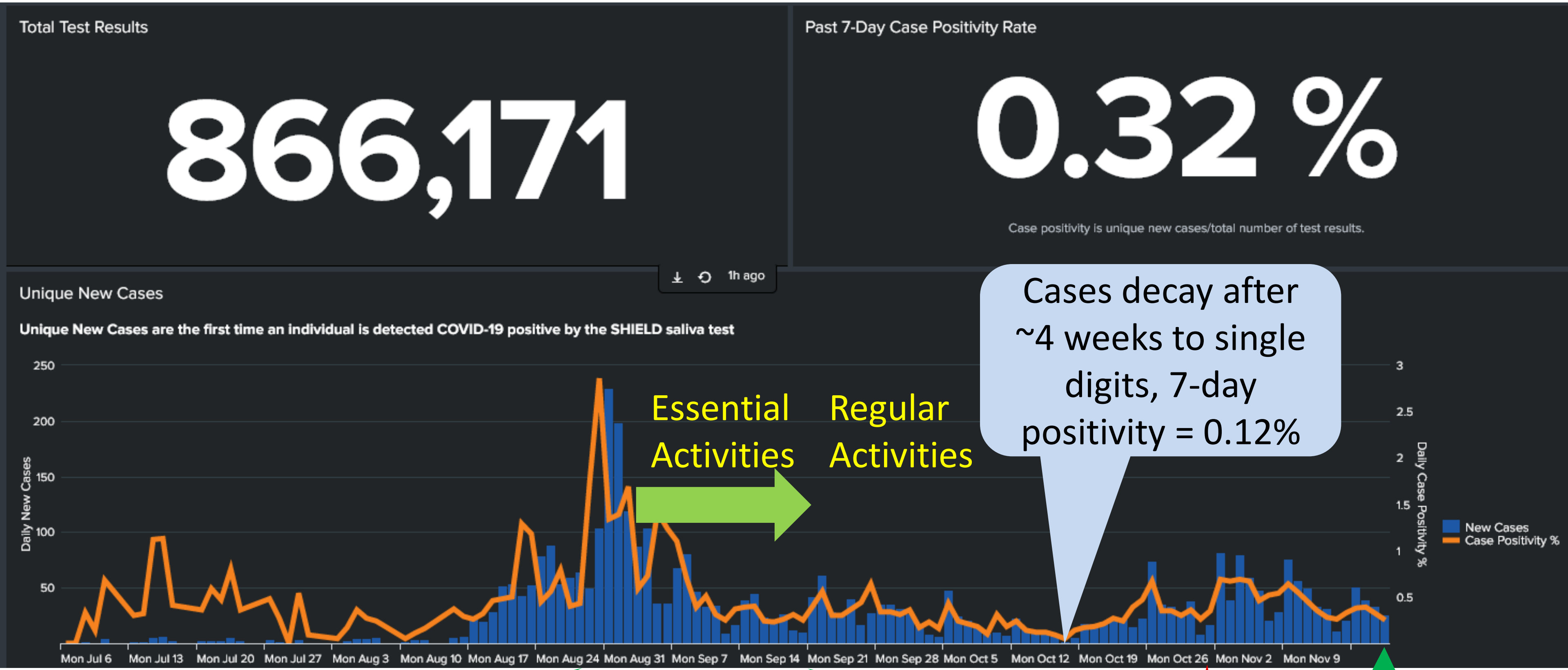
Unique New Cases are the first time an individual is detected COVID-19 positive by the SHIELD saliva test

Case positivity is unique new cases/total number of test results

Question: how many tests do you need to do in order to find a new infected person?
Answer: 1/(positivity) ~ 700 tests!

Positivity comparison: Champaign County 0.8% Region 6 7.6% State 5.3%

Last day of in-person instruction



Total Test Results

866,171

Past 7-Day Case Positivity Rate

0.32 %

Case positivity is unique new cases/total number of test results.

Unique New Cases

Unique New Cases are the first time an individual is detected COVID-19 positive by the SHIELD saliva test

Essential Activities

Regular Activities

Cases decay after ~4 weeks to single digits, 7-day positivity = 0.12%

Arrival & entry screening

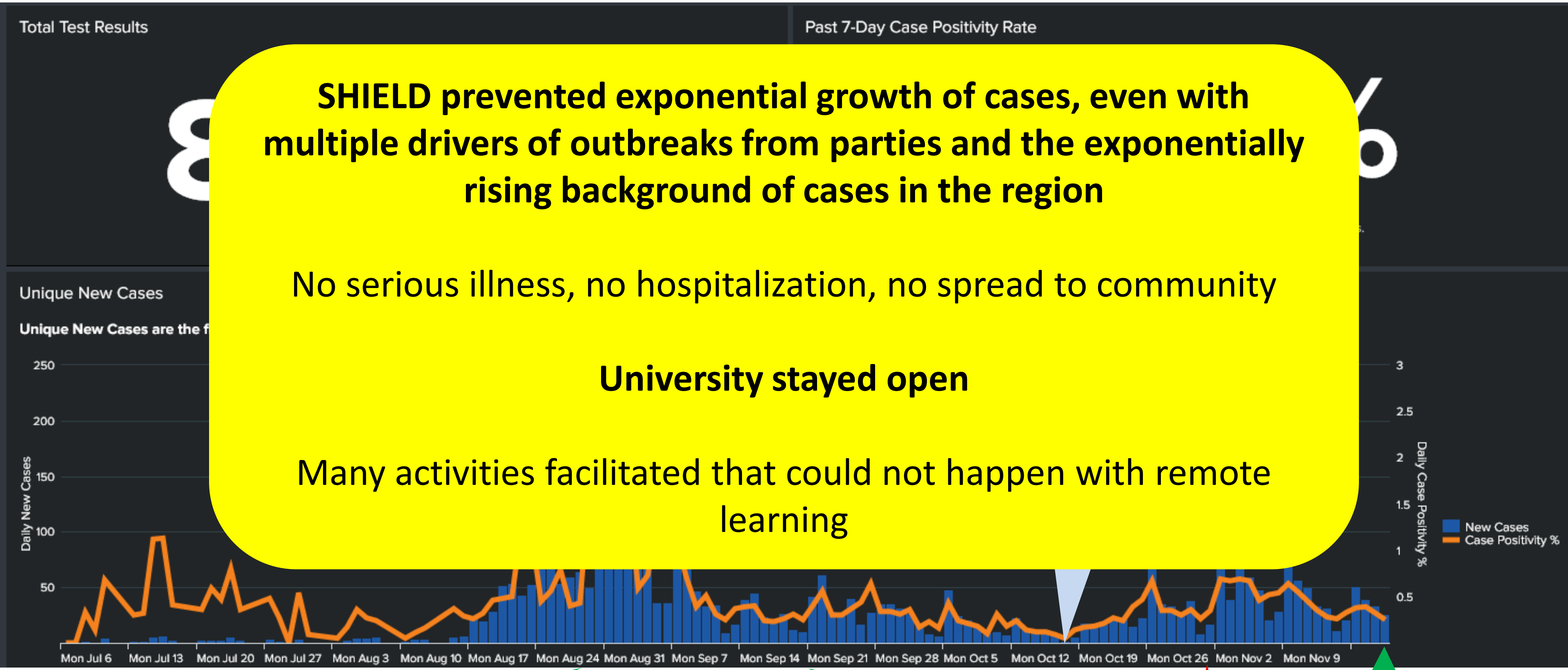
Parties
Non-compliance

Slight rise in cases as regular activities resume

Parties
Cases rising in Region

Last day of in-person class

Last day of in-person instruction



SHIELD prevented exponential growth of cases, even with multiple drivers of outbreaks from parties and the exponentially rising background of cases in the region

No serious illness, no hospitalization, no spread to community

University stayed open

Many activities facilitated that could not happen with remote learning

Arrival & entry screening

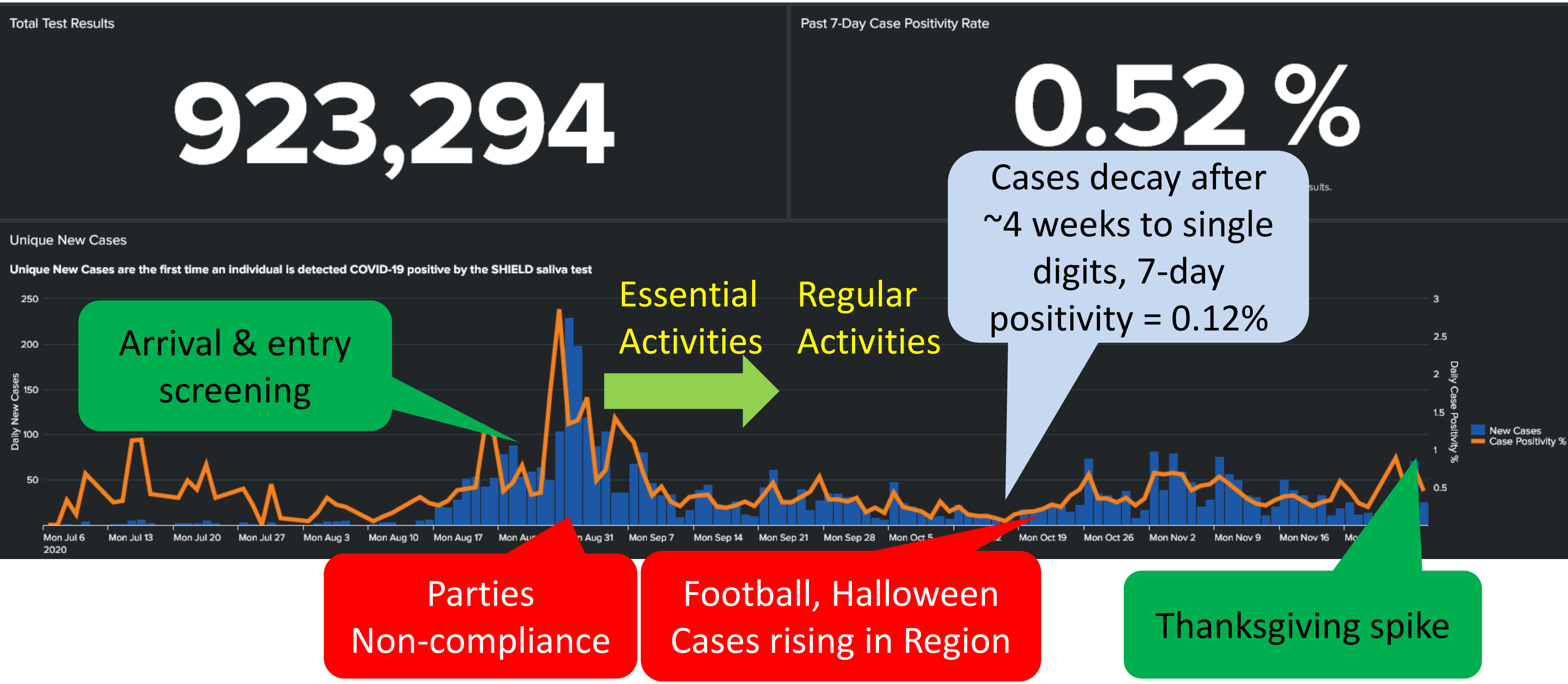
Parties
Non-compliance

Slight rise in cases as regular activities resume

Parties
Cases rising in Region

Last day of in-person class

Dec 2 2020



Total Test Results

923,294

Past 7-Day Case Positivity Rate

0.52 %

sults.

Unique New Cases

Unique New Cases are the first time an individual is detected COVID-19 positive by the SHIELD saliva test

Arrival & entry screening

Essential Activities

Regular Activities

Cases decay after ~4 weeks to single digits, 7-day positivity = 0.12%

Parties
Non-compliance

Football, Halloween
Cases rising in Region

Thanksgiving spike

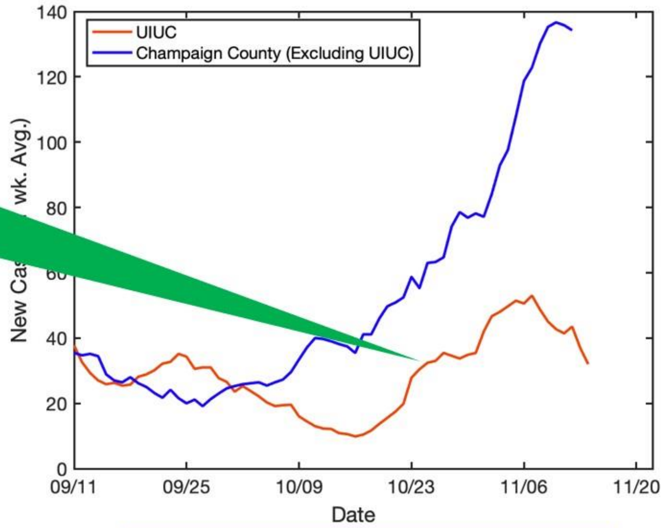
Case positivity is unique new cases/total number of test results

Question: how many tests do you need to do in order to find a new infected person?
Answer: 1/(positivity) ~ 200 tests!

Positivity (UIUC excl.): Champaign County **6.5%** Region 6 **11.9%** State **10.6%**

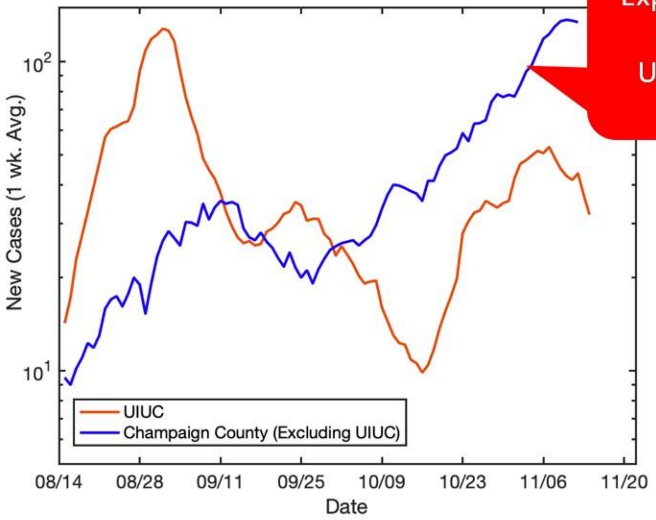
UIUC compared to surroundings

Bounded cases in UIUC despite parties and rising community spread



New cases since 9-11-2020 (linear scale)

Exponential Growth in Champaign-Urbana excluding UIUC



New cases since 8-14-2020 (log scale)

- The purpose of SHIELD was to prevent exponential growth of the epidemic in UIUC
- It did this, even though
  - The epidemic was growing exponentially in the surrounding community
  - Some students not compliant with testing and safe socializing

Spread of COVID-19 in Champaign-Urbana and UIUC

Questions

Most of the cases of COVID-19 on campus are undergraduates.   So …

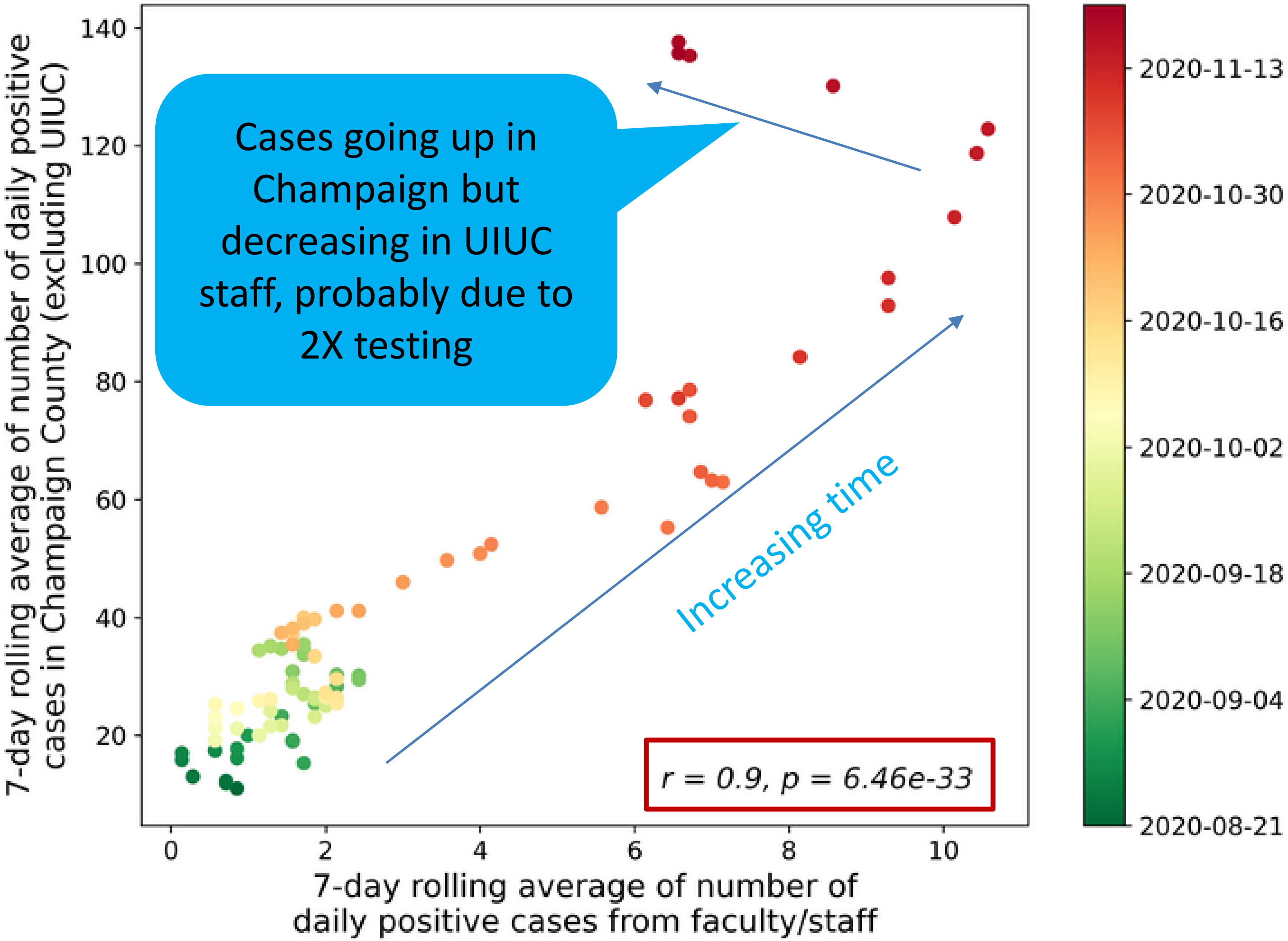
- Is there spread of COVID-19 from the students to the community, as people feared?
- Is there spread of COVID-19 from the students to the staff (including faculty)?

Background prevalence in East Central Illinois and Region 6 is rising. So …

- Is there spread of COVID-19 from the community to UIUC or *vice versa*?

Strong correlation between Champaign County & UIUC staff

(1) Correlation between faculty/staff and residents in Champaign County (excluding UIUC)



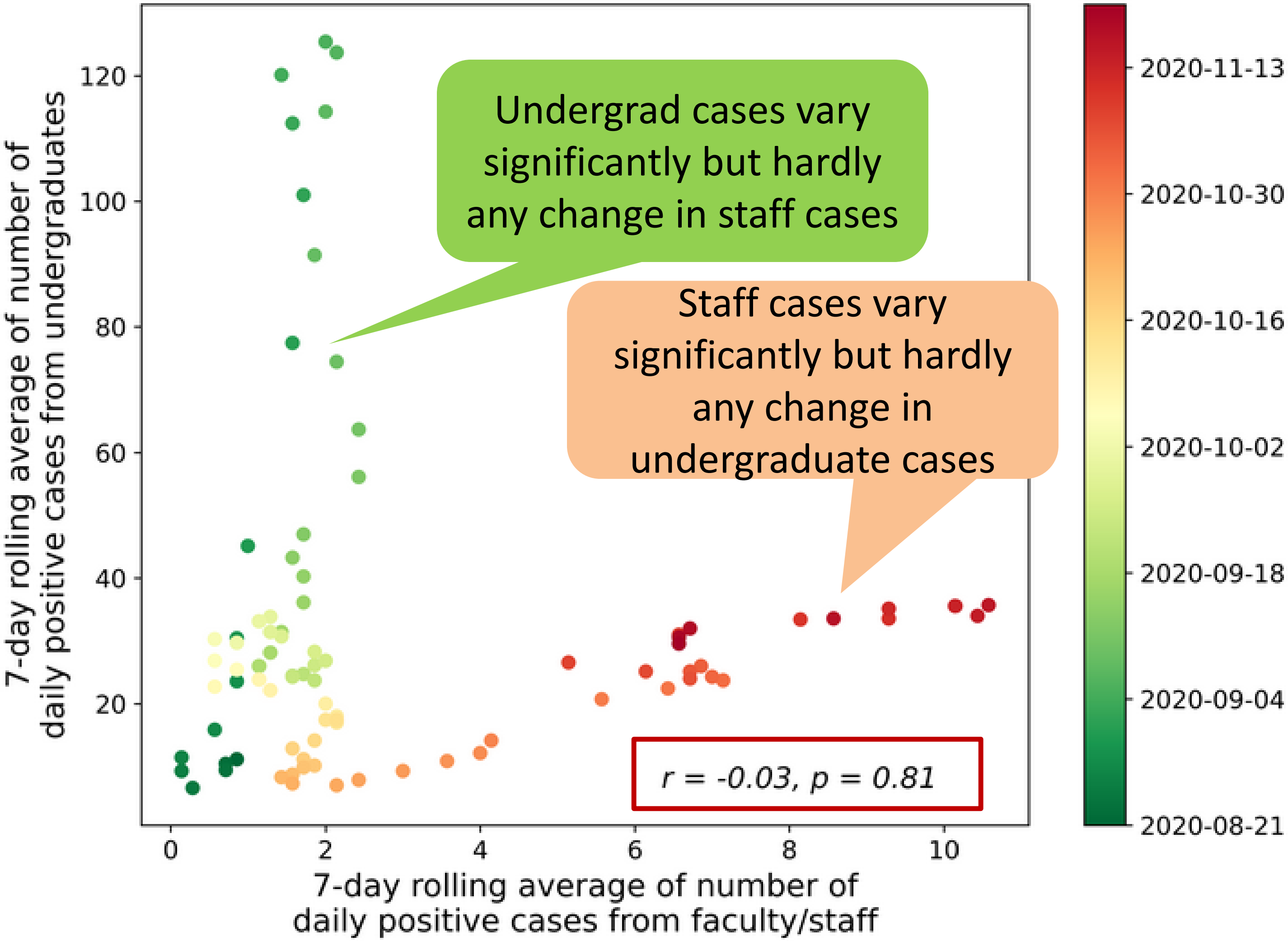
Cases going up in Champaign but decreasing in UIUC staff, probably due to 2X testing

Increasing time

r = 0.9, p = 6.46e-33

Weak correlation between Undergraduates & UIUC staff

(2) Correlation between faculty/staff and undergrads



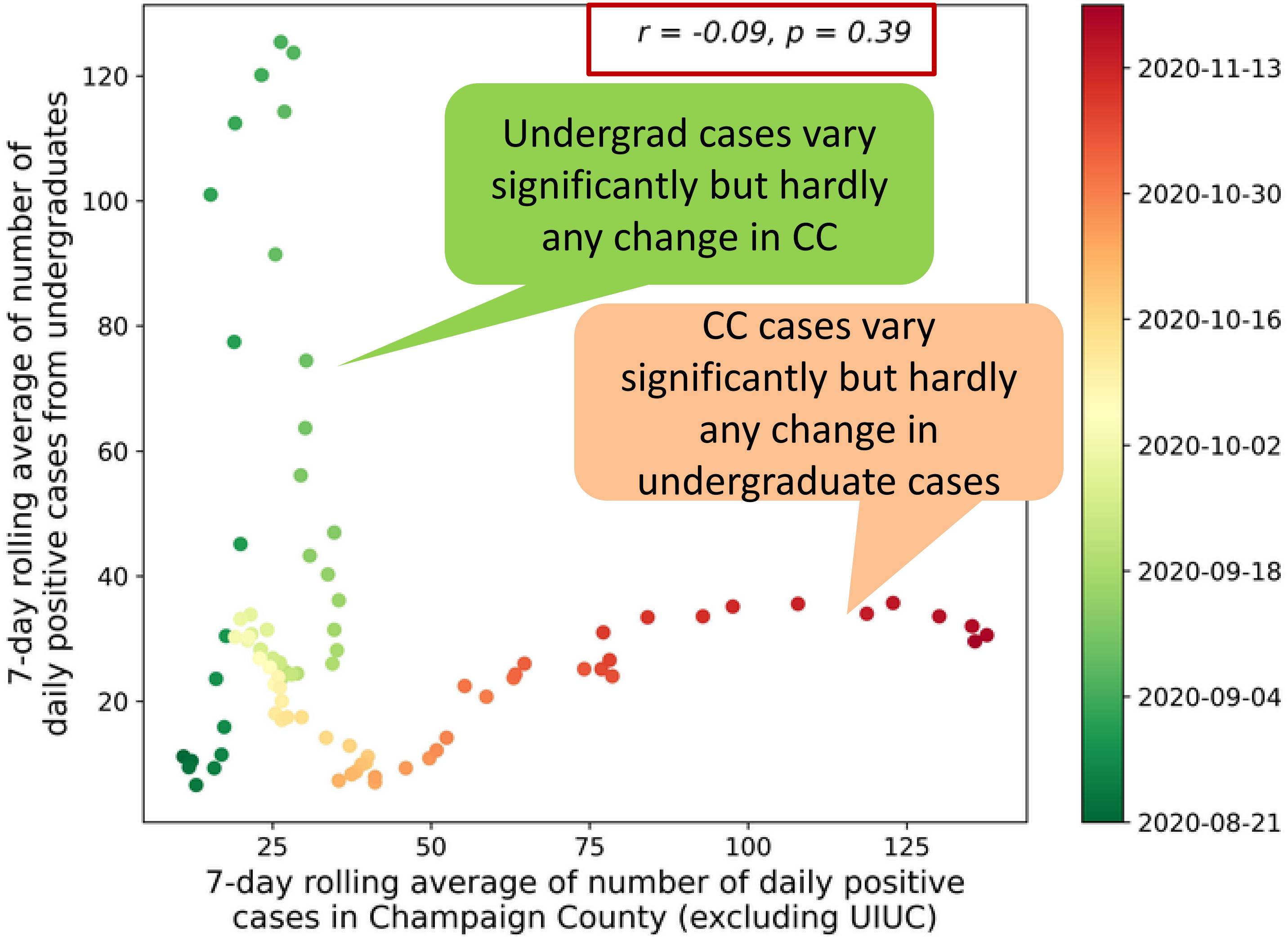
Undergrad cases vary significantly but hardly any change in staff cases

Staff cases vary significantly but hardly any change in undergraduate cases

$r = -0.03$, $p = 0.81$

Weak correlation between Undergraduates & Champaign County

(3) Correlation between undergrads and residents in Champaign County (excluding UIUC)



Undergrad cases vary significantly but hardly any change in CC

CC cases vary significantly but hardly any change in undergraduate cases

Answers

Most of the cases of COVID-19 on campus are undergraduates. So …

- Is there spread of COVID-19 from the students to the community, as people feared? **NO**
- Is there spread of COVID-19 from the students to the staff (including faculty)? **NO**

Background prevalence in East Central Illinois and Region 6 is rising. So …

- Is there spread of COVID-19 from the community to UIUC or *vice versa*? **YES, from community to UIUC**

SUPER-SPREADERS

One infected person can single-handedly start an epidemic

What are super-spreaders?

- Super-spreaders can be:
  - People
  - Environments
  - Events

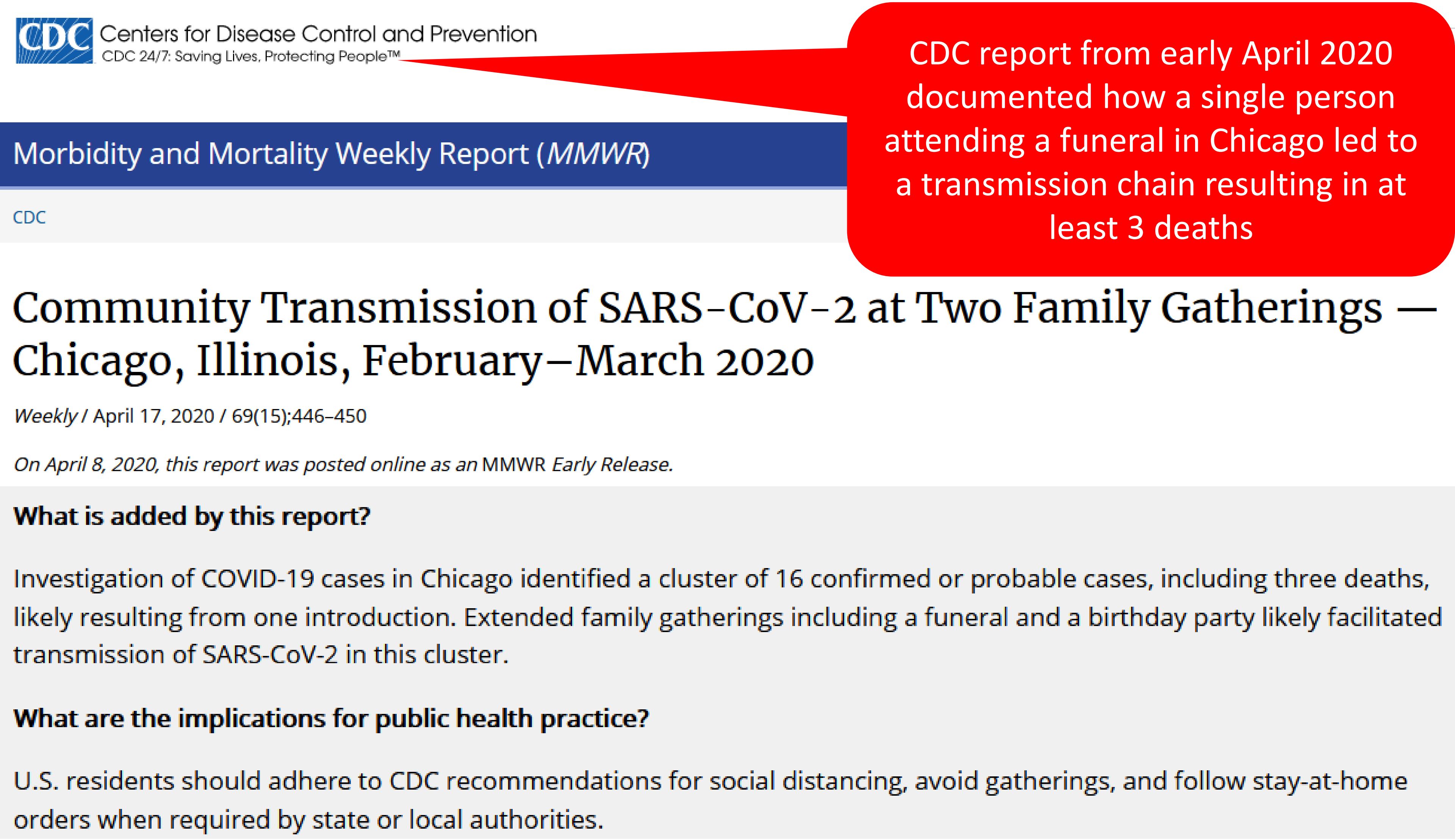
- A super-spreader can be a single person or event that causes multiple chains of infection and deaths

- Examples have very recently been documented in Illinois, Israel, Hong Kong, Korea, Jordan, China,

How COVID-19 is spread

- The R number for COVID-19 assumes that every infected person plays an equal role in transmitting the disease.
  - R > 1 means the epidemic will grow
  - R < 1 means the epidemic will die away
  - We estimate SHIELD will create an R about 0.2-0.3
  - If SHIELD gets broken by illegal violation of isolation and quarantine it will make R about 1.2-1.5
- Recent studies show unequivocally that the vast majority (at least 80%) of transmissions of the virus SARS-CoV-2 which is responsible for COVID-19 come from 10% or less of the infected people.
- The most dangerous mode of spread of the virus is through tiny droplets known as aerosols.
  - One person in a room or even a bus can infect a large number of people even if they are not next to them!
- This is known as **super-spreading**

A famous super-spreader in Chicago



CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Community Transmission of SARS-CoV-2 at Two Family Gatherings — Chicago, Illinois, February–March 2020

Weekly / April 17, 2020 / 69(15);446–450

On April 8, 2020, this report was posted online as an MMWR *Early Release.*

What is added by this report?

Investigation of COVID-19 cases in Chicago identified a cluster of 16 confirmed or probable cases, including three deaths, likely resulting from one introduction. Extended family gatherings including a funeral and a birthday party likely facilitated transmission of SARS-CoV-2 in this cluster.

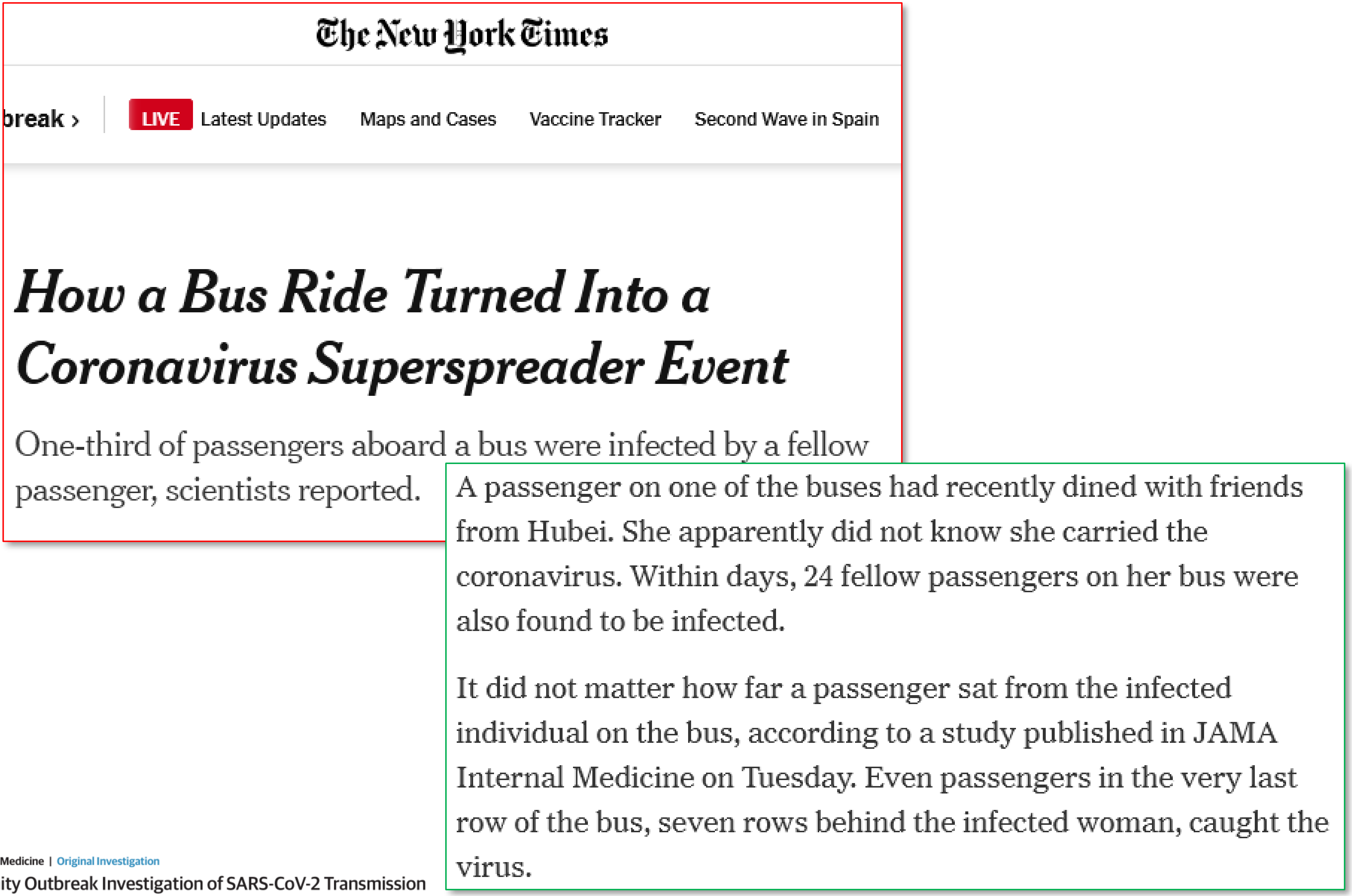
What are the implications for public health practice?

U.S. residents should adhere to CDC recommendations for social distancing, avoid gatherings, and follow stay-at-home orders when required by state or local authorities.

CDC report from early April 2020 documented how a single person attending a funeral in Chicago led to a transmission chain resulting in at least 3 deaths

https://www.businessinsider.com/chicago-super-spreader-shows-the-importance-of-social-distancing-2020-4

A super-spreader on a bus



The New York Times

How a Bus Ride Turned Into a Coronavirus Superspreader Event

One-third of passengers aboard a bus were infected by a fellow passenger, scientists reported.

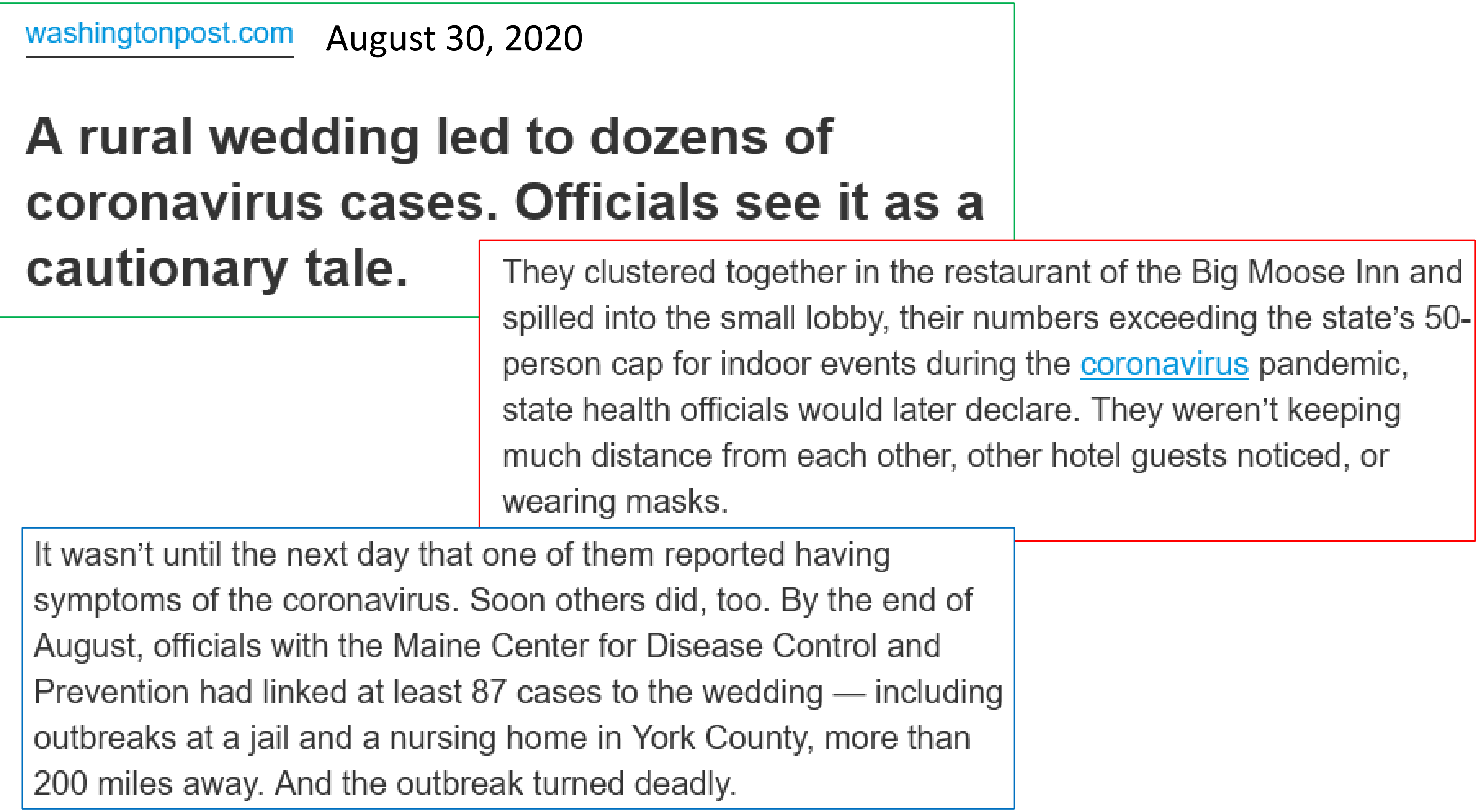
A passenger on one of the buses had recently dined with friends from Hubei. She apparently did not know she carried the coronavirus. Within days, 24 fellow passengers on her bus were also found to be infected.

It did not matter how far a passenger sat from the infected individual on the bus, according to a study published in JAMA Internal Medicine on Tuesday. Even passengers in the very last row of the bus, seven rows behind the infected woman, caught the virus.

JAMA Internal Medicine | Original Investigation

Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China

A deadly super-spreader at a party



washingtonpost.com August 30, 2020

A rural wedding led to dozens of coronavirus cases. Officials see it as a cautionary tale.

They clustered together in the restaurant of the Big Moose Inn and spilled into the small lobby, their numbers exceeding the state's 50-person cap for indoor events during the coronavirus pandemic, state health officials would later declare. They weren't keeping much distance from each other, other hotel guests noticed, or wearing masks.

It wasn't until the next day that one of them reported having symptoms of the coronavirus. Soon others did, too. By the end of August, officials with the Maine Center for Disease Control and Prevention had linked at least 87 cases to the wedding — including outbreaks at a jail and a nursing home in York County, more than 200 miles away. And the outbreak turned deadly.

- **Violation of health code and no social distancing**
- **One person infected 147 others leading to at least three deaths**

A deadly super-spreader at a party

washingtonpost.com August 30, 2020

A rural wedd
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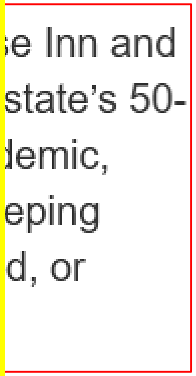
cautionary

This information was correct as of Sept 10 2020



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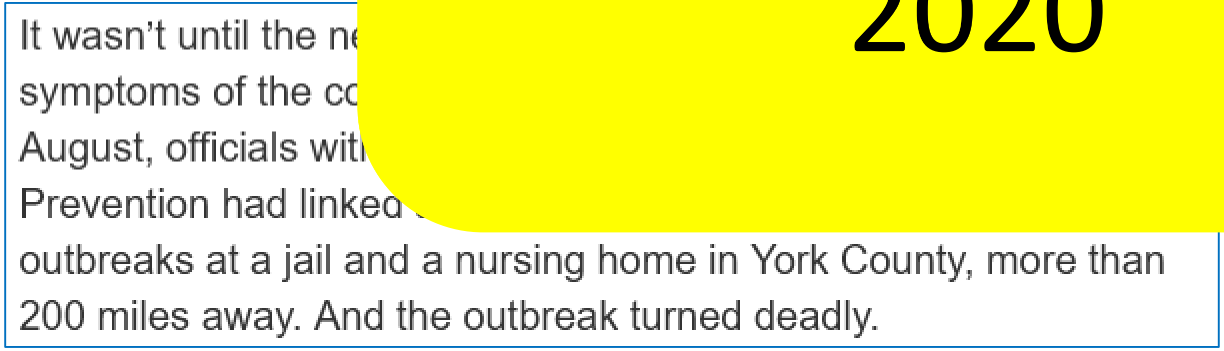

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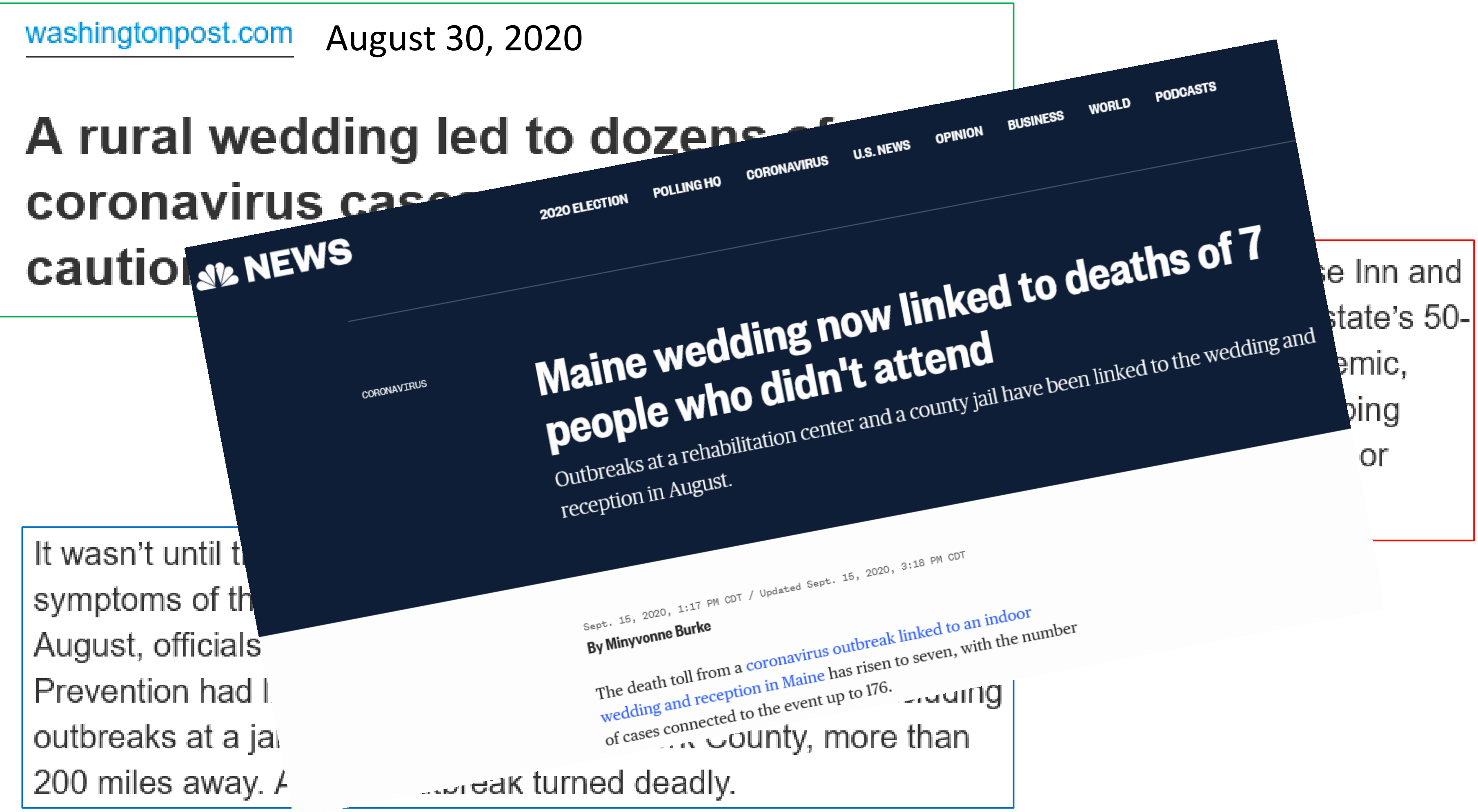
A deadly super-spreader at a party



washingtonpost.com August 30, 2020

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2020 ELECTION POLLING HQ CORONAVIRUS U.S. NEWS OPINION BUSINESS WORLD PODCASTS

NEWS

CORONAVIRUS

Maine wedding now linked to deaths of 7 people who didn't attend

Outbreaks at a rehabilitation center and a county jail have been linked to the wedding and reception in August.

Sept. 15, 2020, 1:17 PM CDT / Updated Sept. 15, 2020, 3:18 PM CDT

By Minyvonne Burke

The death toll from a coronavirus outbreak linked to an indoor wedding and reception in Maine has risen to seven, with the number of cases connected to the event up to 176.

- **Violation of health code and no social distancing**
- **One person infected 147 others leading to at least three deaths**

A deadly sup der at a party

washingtonpost.com August 30, 2020

A rural wedding led to coronavirus case cautio

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NEWS

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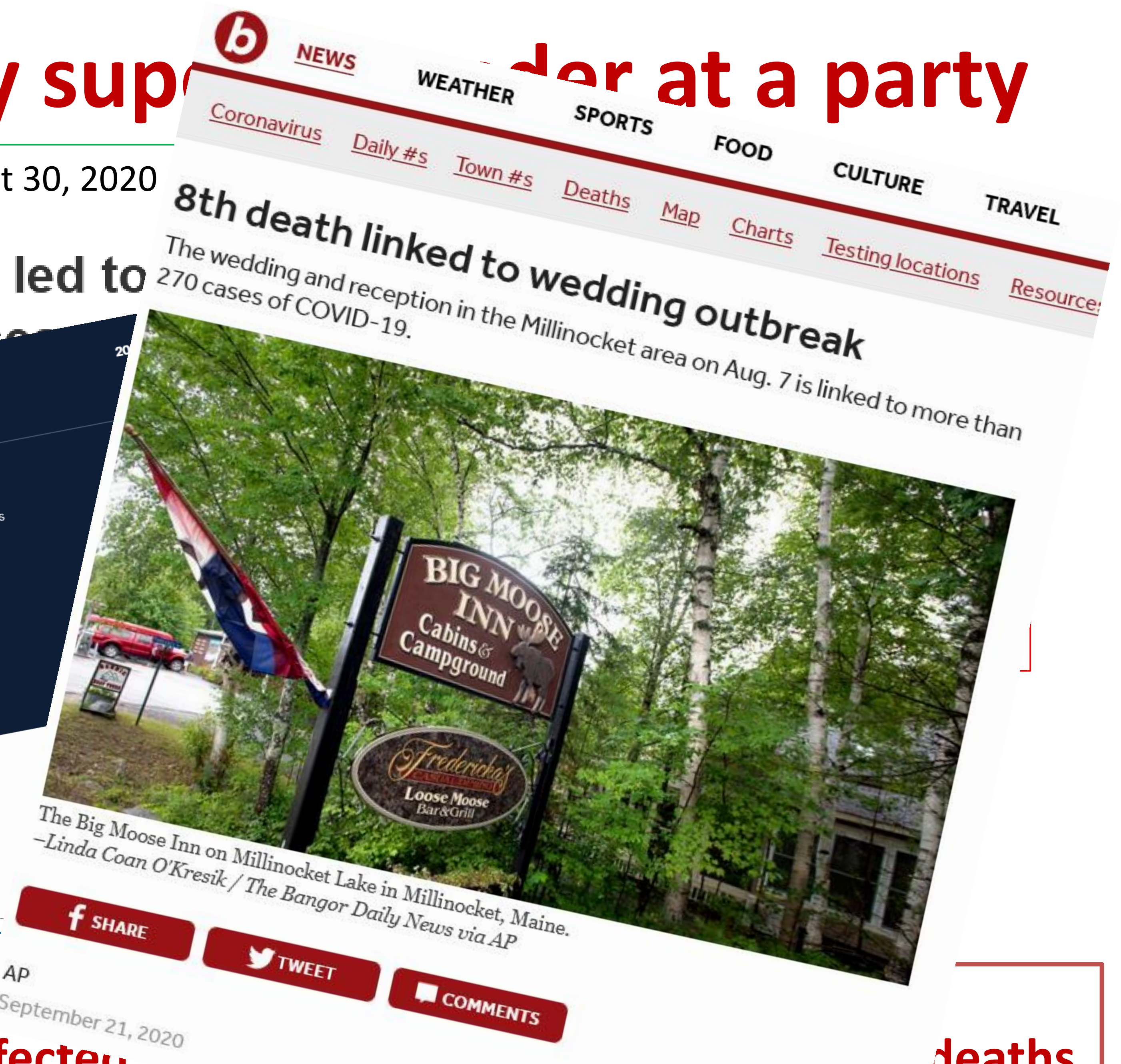
CORONAVIRUS



8th death linked to wedding outbreak

The wedding and reception in the Millinocket area on Aug. 7 is linked to more than 270 cases of COVID-19.

The Big Moose Inn on Millinocket Lake in Millinocket, Maine. *–Linda Coan O'Kresik / The Bangor Daily News via AP*

AP
September 21, 2020

- **Violation of h**
- **One person infecte deaths**

Why super-spreaders matter

- Large gatherings are potential super-spreader events
- Long exposure to people indoors with poor airflow can promote super-spreading
  - Parties
- People talking loudly without masks emit virus at 30-50 times as much as people at rest
- ~50% of infections arise from people who have not yet shown symptoms or may never do so!
- **Illegal violation of CU-PHD statutes and local ordinances can cause super-spreader events**

Summary

- Exponential growth is really hard to stop!
- High frequency, high throughput testing gives a clear picture of the epidemic
- Multiple mitigations will prevent the epidemic from growing
- Transmission can occur through super-spreader events: one person infects hundreds of others