Sandia National Laboratories

SAND2020-11240PE

COVID-19 Pandemic Modeling

Phase 2 Project Final Report

September 17, 2020

National Virtual Biotechnology Laboratory

Partners: Los Alamos, Oak Ridge, and Argonne National Laboratories

U.S. DEPARTMENT OF ENERGY NNSA

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COVID-19 Modeling and Analysis Activities

Recovery Modeling
Testing and contact tracing needs for different levels of reopening

Mobility
Cell phone mobility data to inform contact tracing planning

Vaccine Distribution
Supply chain needs and assessment of distribution strategies

Medical Resource Demands
State and county risk indicators of medical resource shortfalls

Medical Resource Routing
Optimal distribution of limited resources and feasibility of national sharing strategies

Economic Impacts
GDP impact of the COVID-19 event and associated reopening scenarios

Comorbidity Analysis
How do comorbidities affect infection severity?

Epidemiological Forecasting
Data-driven, short-term forecasts of new cases by state and region

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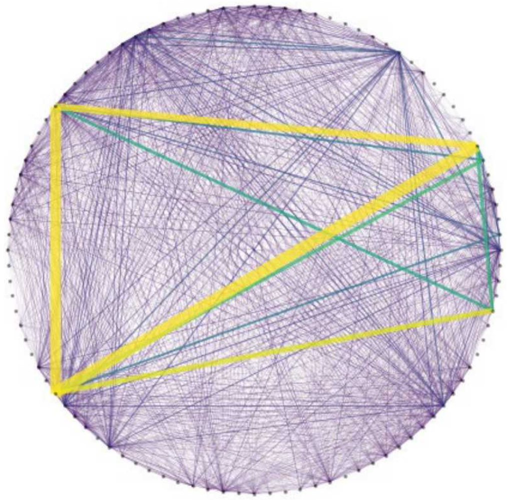
Recovery Modeling and Analysis

As social distancing is relaxed, develop optimized testing and contact tracing strategies to enable effective outbreak management given resource constraints

Hybrid Modeling Approach

1. Network-based model to explicitly represent contacts between people
2. Compartmental SEIR model to quantitatively represent population level dynamics
3. High-resolution cellphone movement pattern data to locate contact-rich locations



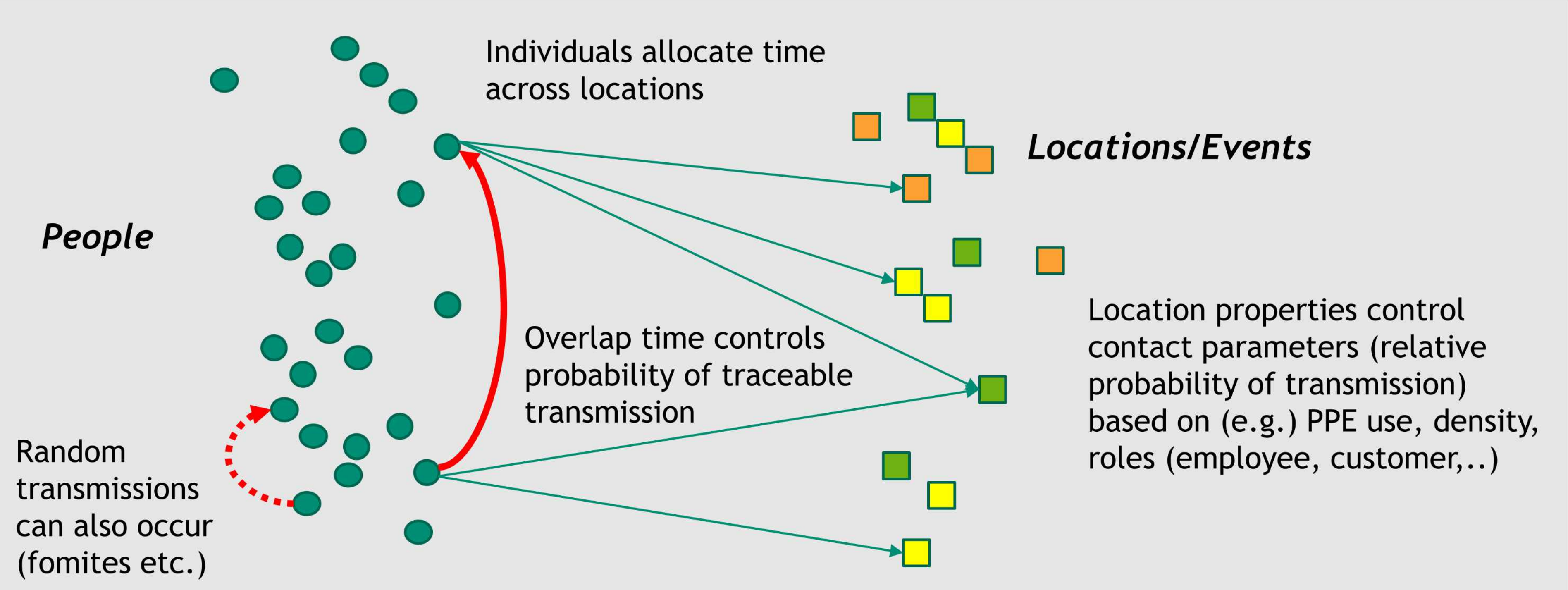
Uses

- Determine optimal use of constrained testing and contact tracing resources
- Evaluate disease-control trade-offs of tracing strategies and testing delays
- Evaluate effectiveness of targeted strategies to address locations with high levels of contact
- Design robust strategies for targeted vaccine delivery

Model Component 1: Network based simulation

Contacts among individuals are constructed from descriptions of locations and events

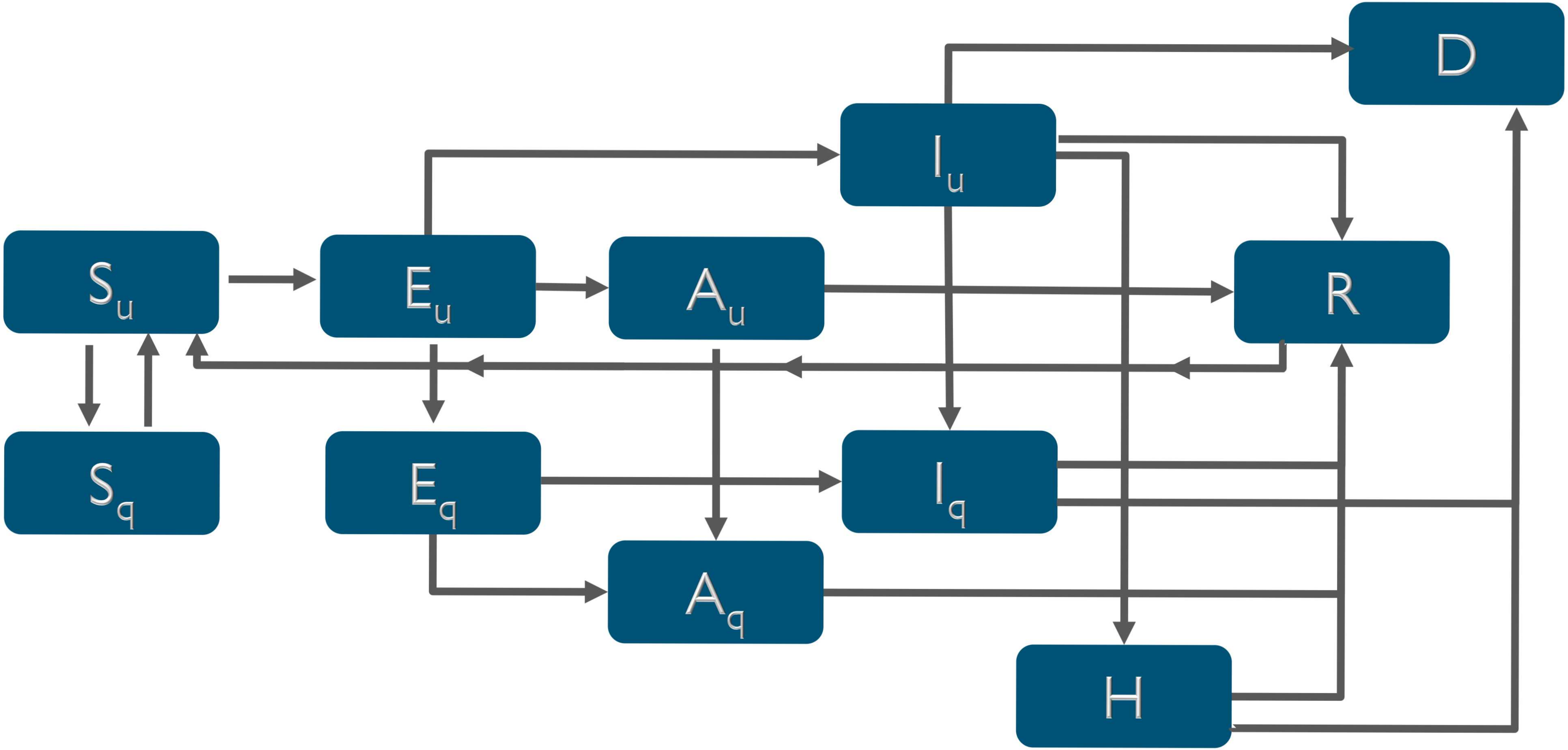
- Natural way to build heterogeneity into contact patterns
- Can be used to study differential risk associated with different recovery plans



This formalism provides

- A natural way to create heterogeneity on contact networks to examine implications for tracing/testing
- A way to explore the effect of different mitigation/closure scenarios on outbreak potential – **a powerful tool for connecting policies to "beta" parameters in SEIR models**

Model Component 2: Compartmental Model

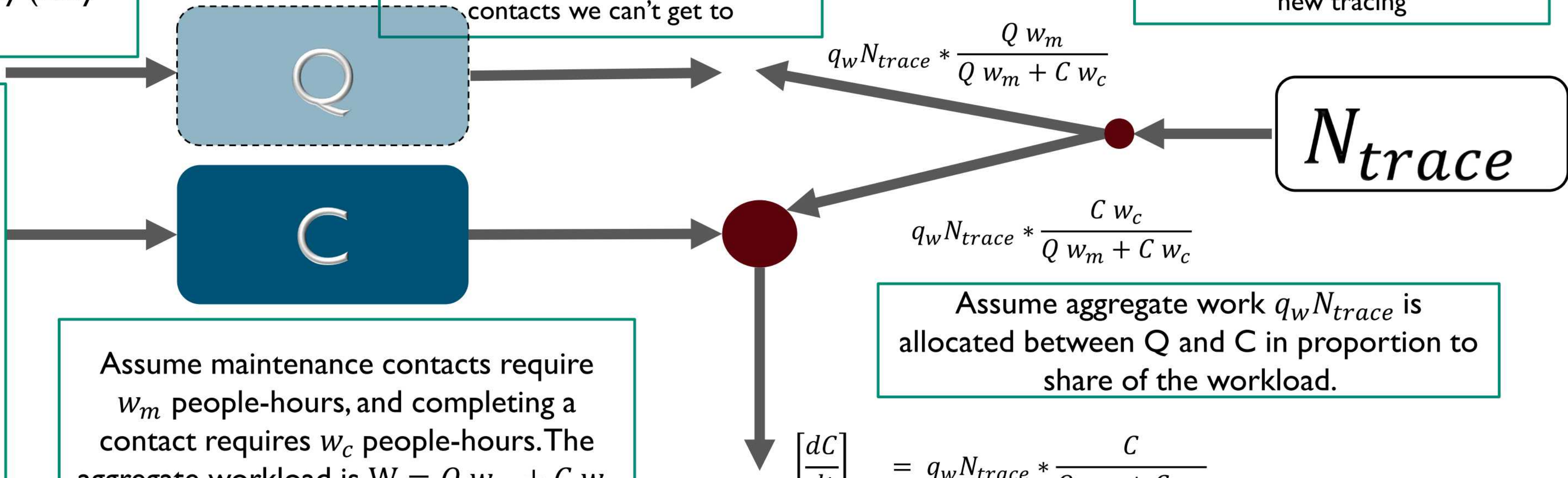


Compartmental Model: Rethinking Contact Tracing Mechanisms

The total quarantined (non-hospitalized) population needs to be contacted periodically (daily say).

The stock Q is notional; we won't model the dynamics associated with working off call lists and expiring contacts we can't get to

Assume N_{trace} personnel are the limiting resource. They can each devote q_w people-hours per day to both maintenance contacts and new tracing



$$q_w N_{trace} * \frac{Q\, w_m}{Q\, w_m + C\, w_c}$$

$$q_w N_{trace} * \frac{C\, w_c}{Q\, w_m + C\, w_c}$$

$$\left[\frac{dC}{dt}\right]_{in}$$

The rate in to the contact tracing queue, is dependent on the rate of new identified infected cases which is modeled by C_{new}. This makes assumptions about the likelihood of recalling a contact and the true uniqueness of each contact

Assume maintenance contacts require w_m people-hours, and completing a contact requires w_c people-hours. The aggregate workload is $W = Q\, w_m + C\, w_c$

Assume aggregate work $q_w N_{trace}$ is allocated between Q and C in proportion to share of the workload.

$$\left[\frac{dC}{dt}\right]_{out} = q_w N_{trace} * \frac{C}{Q\, w_m + C\, w_c}$$

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

Case discharge rates follow from the work required for each case

Publishing this advancement in contact tracing planning in November issue of SIAM News

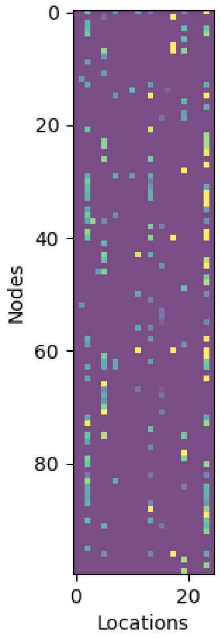
We want to smooth out the min functions
to analytically describe the boundary constraint relative to contact tracing limitations

Model Component 3: Data-derived individual Contact Locations

Interaction matrix stores the time person spends at each location. Network edge weights based on the overlap between node trajectories.

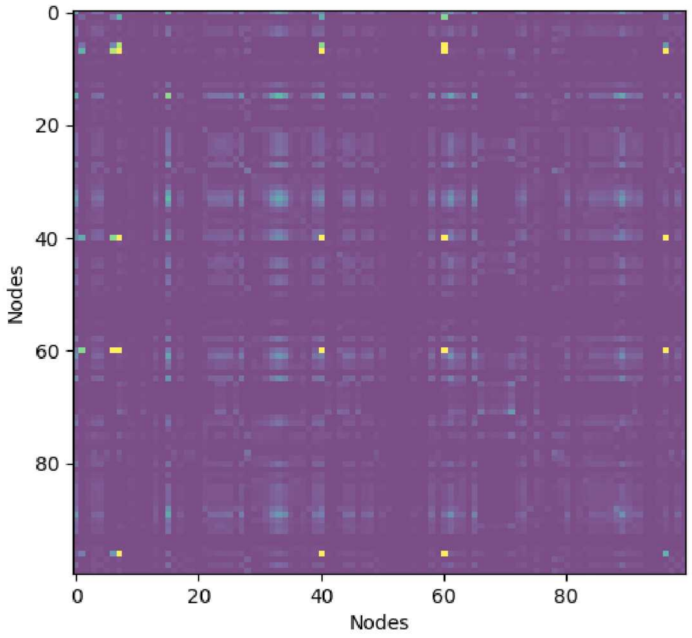
Interaction matrix (IM)

X axis = locations
Y axis = nodes
Values = person-hours per day

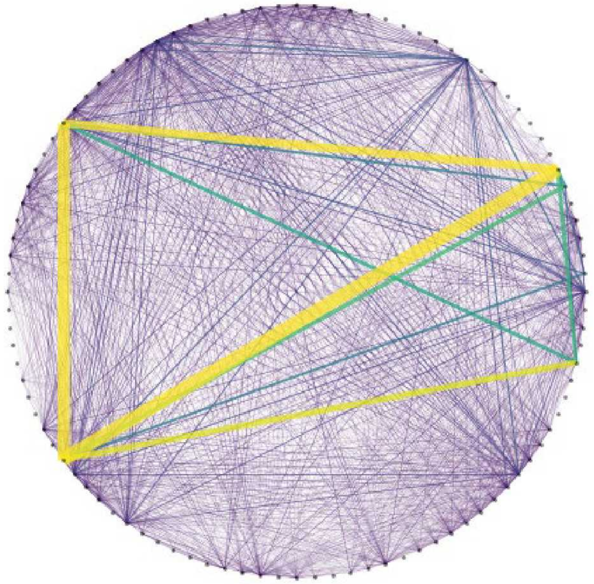


Edge weights

Sum of the product of each node, location combination (IM.dot(IM.T)). The weights are then normalized by the max weight.

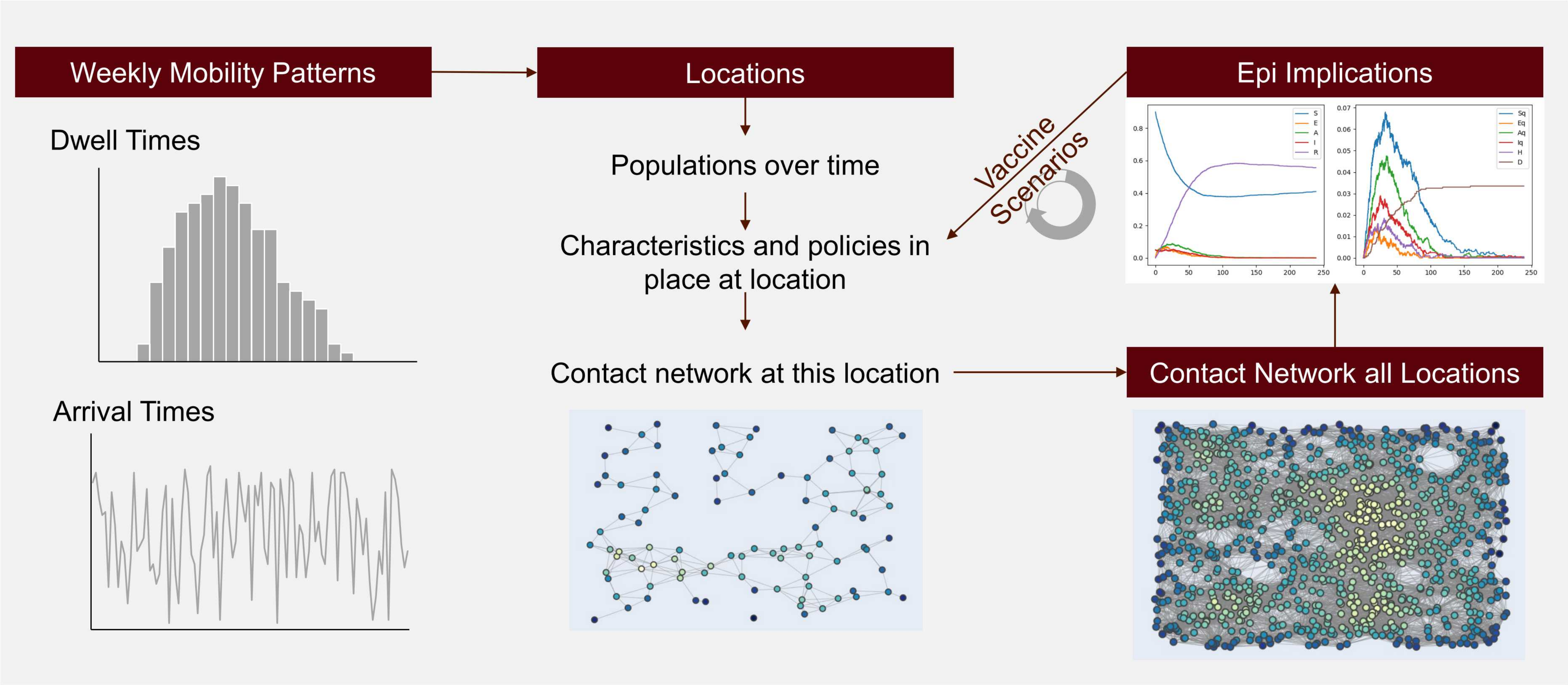


Contact network



A set of structural metrics (centrality, weighted degree,..) were derived for ranking potential location importance.
Epi significance will be assessed by suppressing contacts and targeting testing at locations suggested by these rankings.

Using the Adaptive Recovery Model (ARM) for Integrated Analysis



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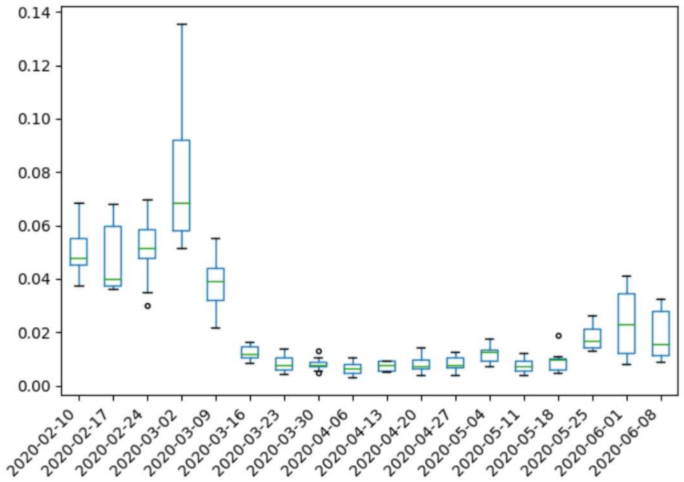
Contact Network Analysis

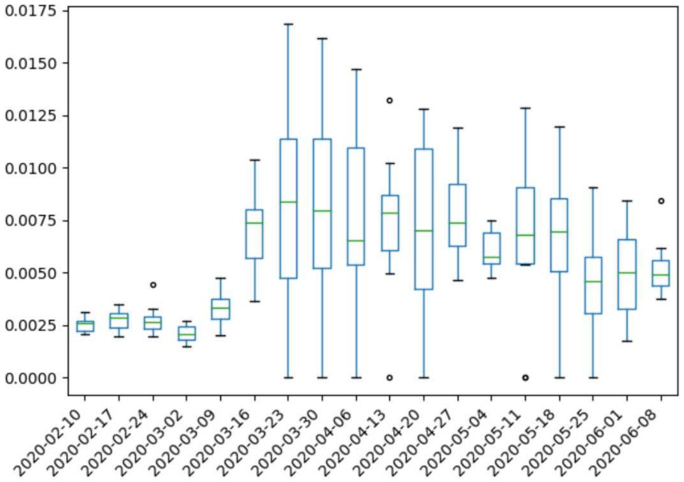
Use mobility data from SafeGraph to create networks that represent person-to-person interactions

Network metrics show how interactions are changing over time:

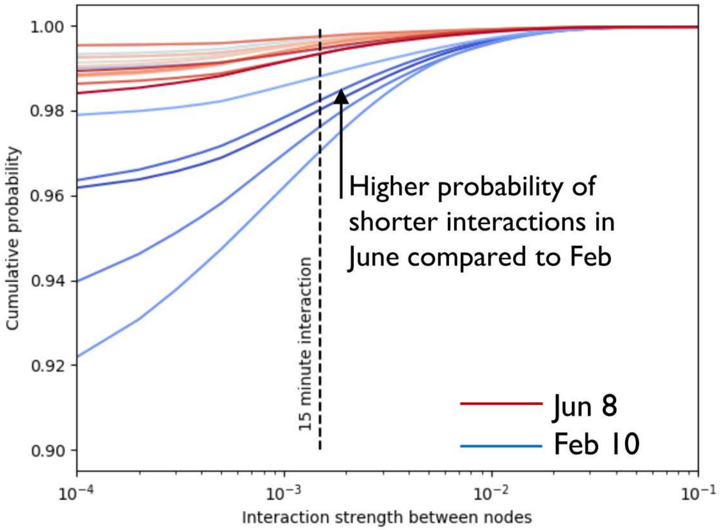
Network **density** for Bernalillo County, Feb-Jun



Clustering coefficient for Bernalillo County, Feb-Jun



Cumulative probability of **interaction strength** in Bernalillo County on two dates

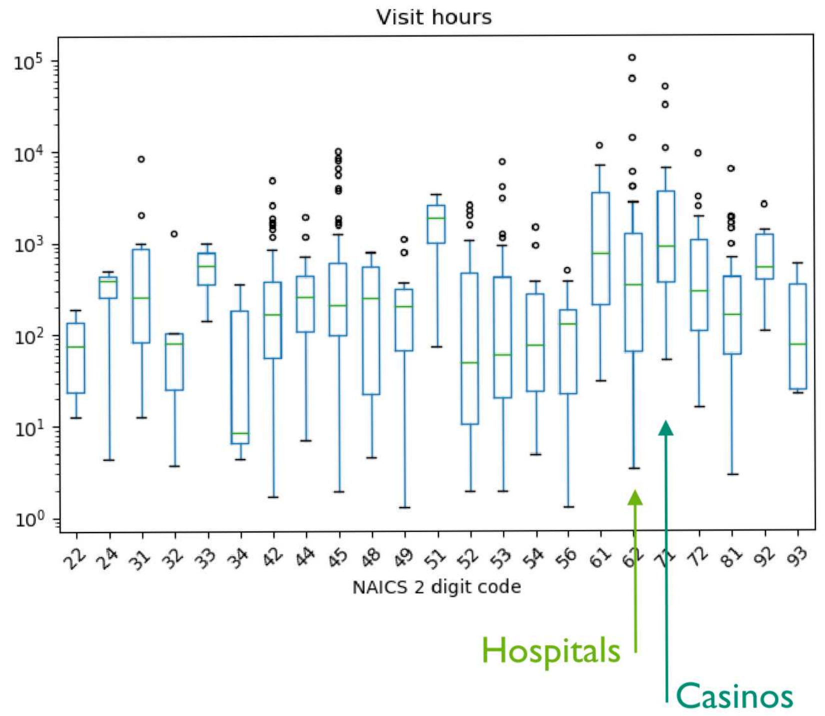


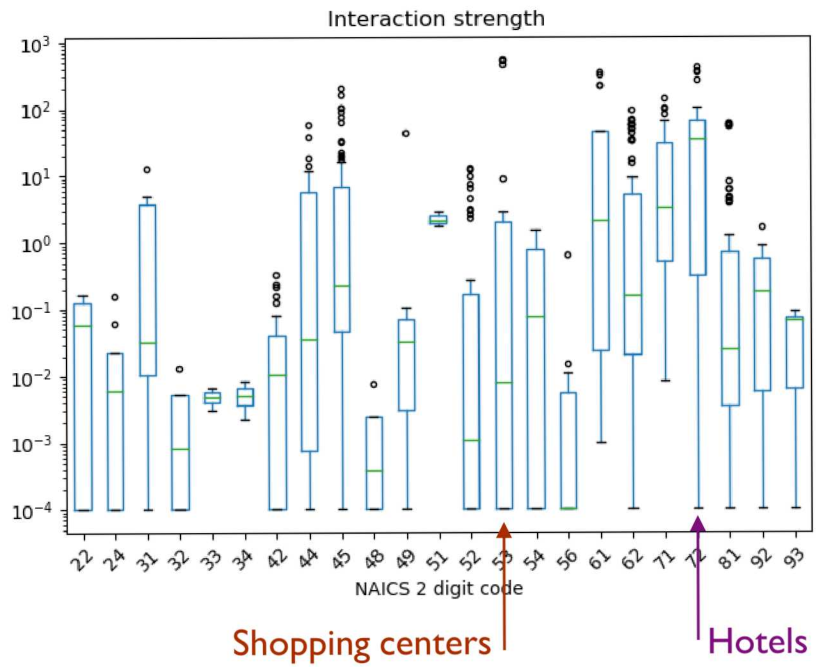
During stay at home orders, people had fewer and shorter interactions (density, left panel) but had higher clustering (right panel).

Inform contact tracing needs: One person over a week (in a Bernalillo-sized county) will generate ~67 close contacts.

Contact Networks and Points of Interest (POIs)

Visit hours and interaction strength at specific NAICS codes can inform targeted closures and mitigation strategies



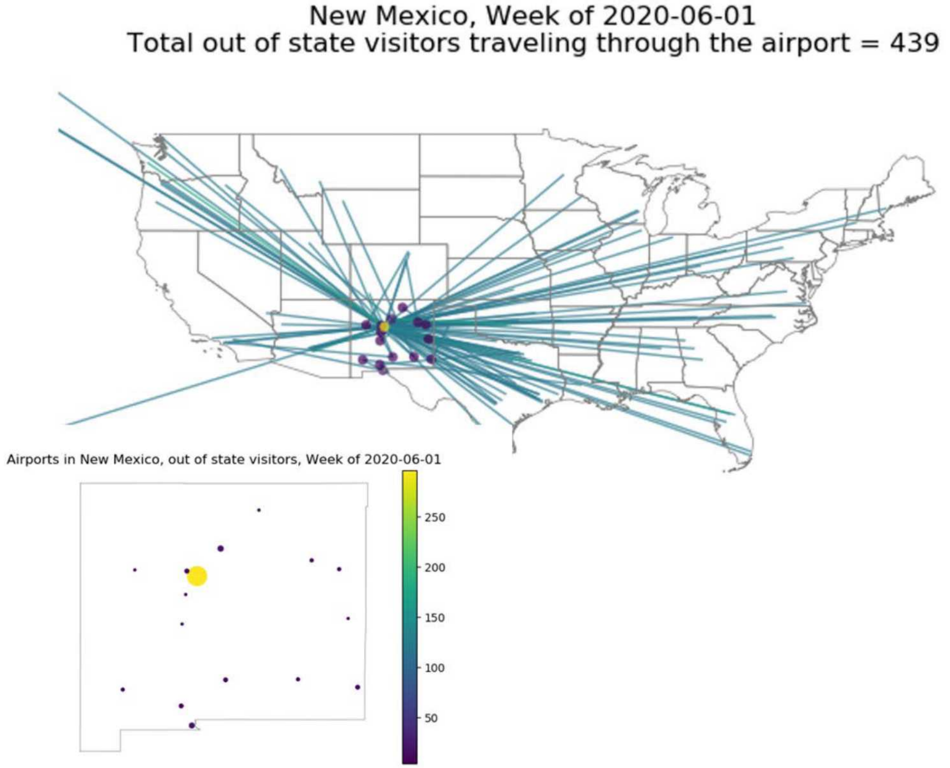


In this county, longest visits occur to hospitals and casinos, but more interactions occur at shopping centers and hotels

Interstate Travel Analysis

Use mobility data to assess questions such as:

- How many people are coming in from out of state (through the airport or other means)?
- Where are they coming from? Are those locations with high rates of infection?
- Are people that travel following quarantine orders? Is their behavior different from that of the local population?



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Efficient and Equitable Distribution of Vaccines

Analysis of current vaccine manufacturing and distribution capabilities and vaccine allocation strategies

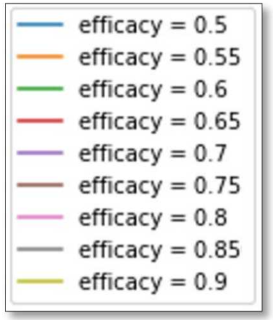
Designed a baseline vaccine distribution strategy and modeled effectiveness of additional strategies to provide insight into the potential for targeted distribution of limited initial vaccine supplies

Goal	Associated strategy	Associated Outcomes
Medical Goal	Vaccinate elderly and those with co-morbid conditions	Mortality and morbidity in key groups
Public Health Goal	Identify and vaccinate those that transmit infection most with aim to reduce transmission	Transmission rates
	Vaccinate in geographic regions with high susceptibility	Transmission rates and mortality and morbidity in key areas
Social Order	Vaccinate essential workers to maintain function of key aspects of society (hospitals, national security, first responders etc)	Mortality and morbidly in key groups
Combination of medical and social order goals	Use recommendation by WHO to vaccinate healthcare workers, adults >65, and adults with comorbidities (12)	Mortality and morbidly in key groups

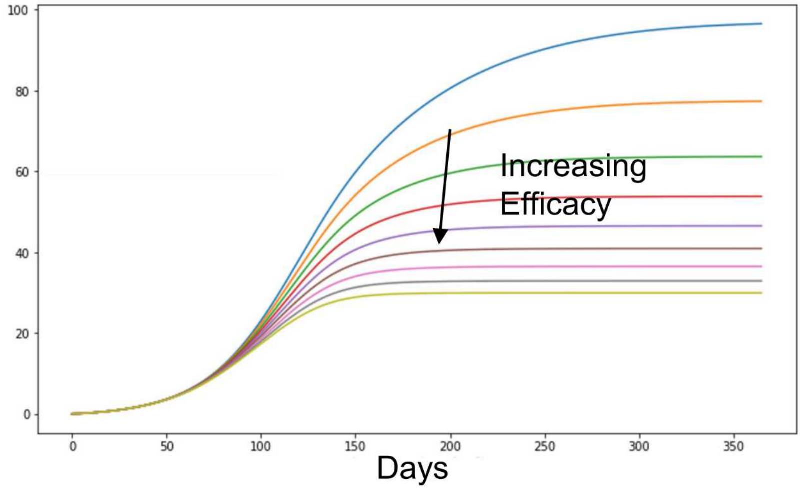
	Manufacturer projections	Baseline scenario vaccine supply	ACIP proposed planning scenario A
Initial national allocation (available doses)	20 Million doses	4.165M doses	2 million doses
Vaccine distribution based on proportional population for a demonstration metropolitan statistical area	45,400 single doses / 22,700 2-dose recommended	9,500 single doses/ 4,800 2-doses recommended	4,600 single doses/ 2,300 2-doses recommended
Number of vaccine candidates	5	3	1
Initial Anticipated delivery	October	End of November	End of October
Follow-on delivery frequency	Weekly	Weekly	Weekly
Estimated supply-growth from initial deliveries	Logarithmic	Linear	Linear

Vaccine Distribution Scenario Analysis Using ARM

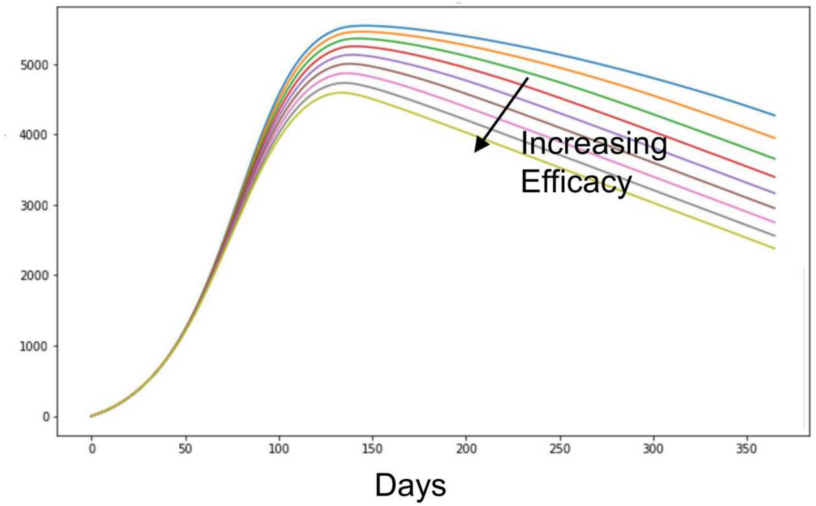
Factor	Value
Scenario	Baseline
Serioprevalence	766
Population	680,000
Initial Doses	4,600
Weekly Doses	2,628
Start	12/1/2020
End	12/1/2021



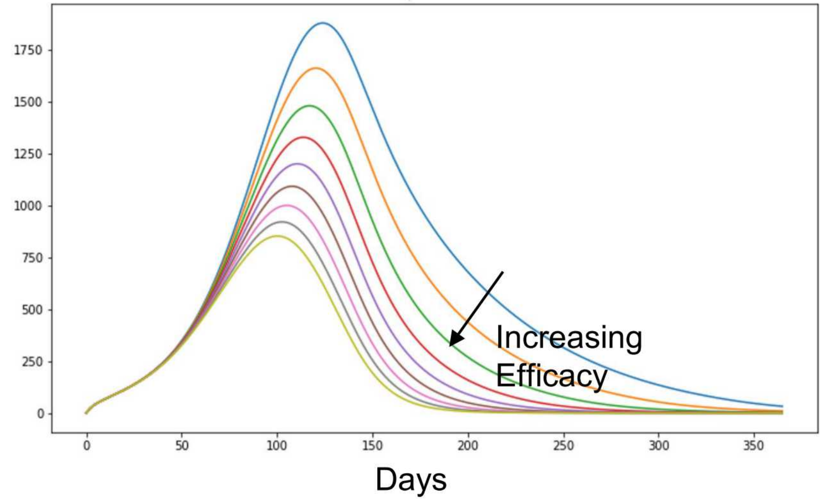
Cumulative Deaths



Contact Tracing Queue



Hospitalizations



ARM is used to model impact of vaccine distribution strategies on cases, hospitalizations, contact tracing needs

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Detailed Surge Modeling of Medical Resource Demands

Goal

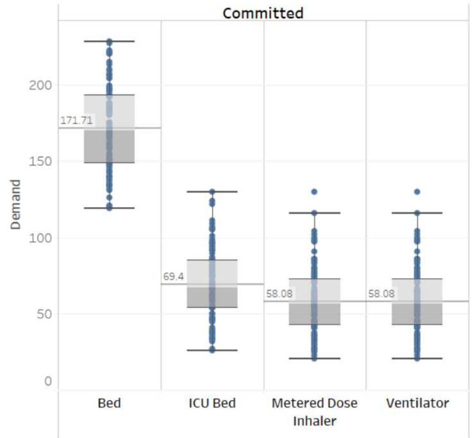
- Calculate resource demands for treating COVID-19 patients based on disease spread projections from epidemiological models
- Anticipate possible times and locations of medical resource shortfalls throughout the pandemic

Approach

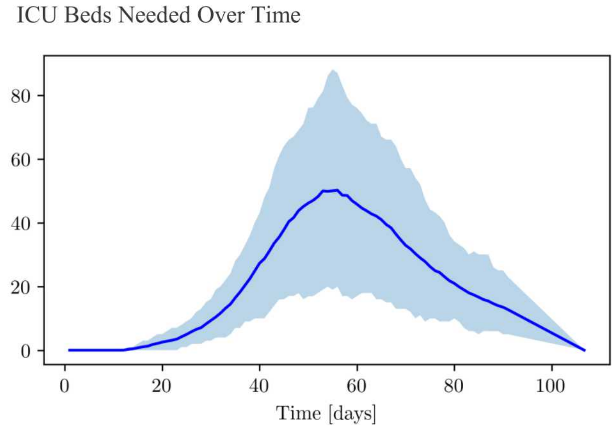
- Use discrete event mathematical model to track patient progress through a hospital treatment system
- Incorporate uncertainty in patient treatment pathways and ranges of resource use per patient to provide risk indicators
- Inputs are patient arrival stream projections from epidemiological models at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

Results

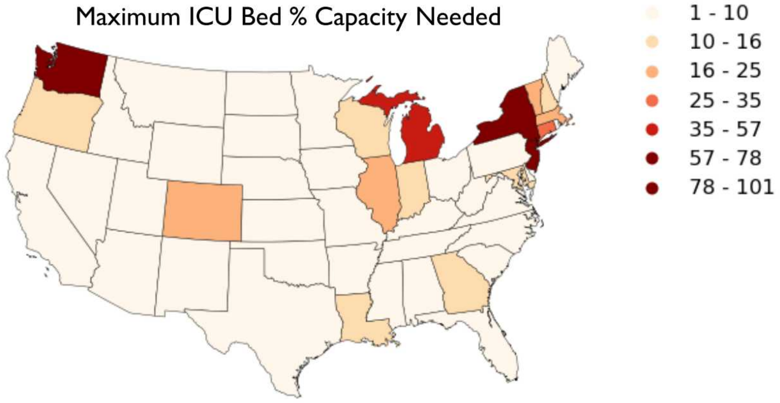
Maximum number of resource needs with a range of uncertainty



Resource needs over time with a range of uncertainty



State or county risk indicators



Approach

Inputs

Local | IHME | EpiGrid

Hospital Arrivals Over Time

The approach is agnostic to which epidemiological model is used; we are prepared to receive data from any epidemiological model

Model

Demographics

Treatment Stage

Fates

Parameters

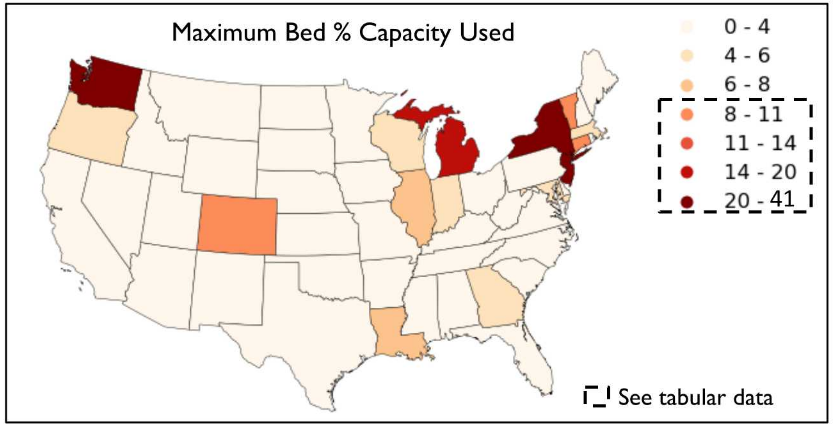
Maximum time on ventilator
Maximum time in ICU if not ventilated
Probability of going to ICU
Probability of needing ventilator
Probability of death if ventilated
Probability of death if not ventilated
etc…

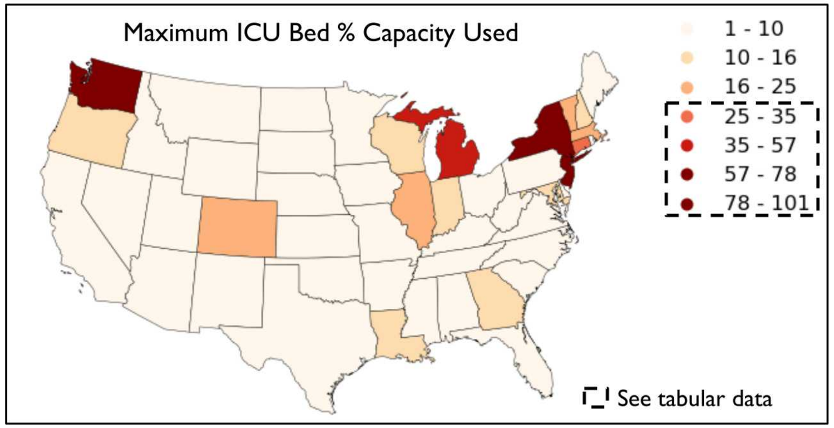
Outputs

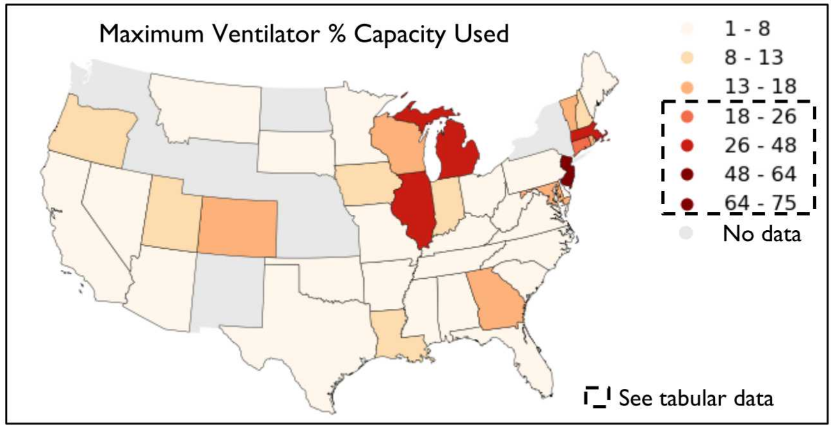
Practitioner Need Over Time	Committed Resource Need Over Time	Consumable Resource Need Over Time
Floor Nurse	Beds	Gown
ICU Nurse	ICU Beds	N95 Mask
Physician	Metered Dose Inhaler	Face Shield
Respiratory Therapist	Ventilator	Gloves
		Sedatives

- Uncertainties in parameters are propagated throughout the model to provide a range of resource projections
- This modeling approach can be applied to any geographic scale for which epidemiological results are available

National Summary: State Resource Sufficiency







States with Resource Utilization >8% Capacity	Maximum Bed % Capacity Used
Washington	41.0
New York	33.4
New Jersey	31.0
Michigan	26.9
Connecticut	14.5
Illinois	13.7
Colorado	12.4
Vermont	11.0
Louisiana	10.4
Indiana	9.3
Wisconsin	8.4
Massachusetts	8.2

States with Resource Utilization > 25% Capacity	Maximum ICU Bed % Capacity Used
New Jersey	100.9
Washington	92.8
New York	92.7
Michigan	77.9
Illinois	34.6
Connecticut	34.5
Vermont	31.6
Colorado	26.7

New Jersey % Capacity for ICU Beds

> 100% from 4/17 – 4/25

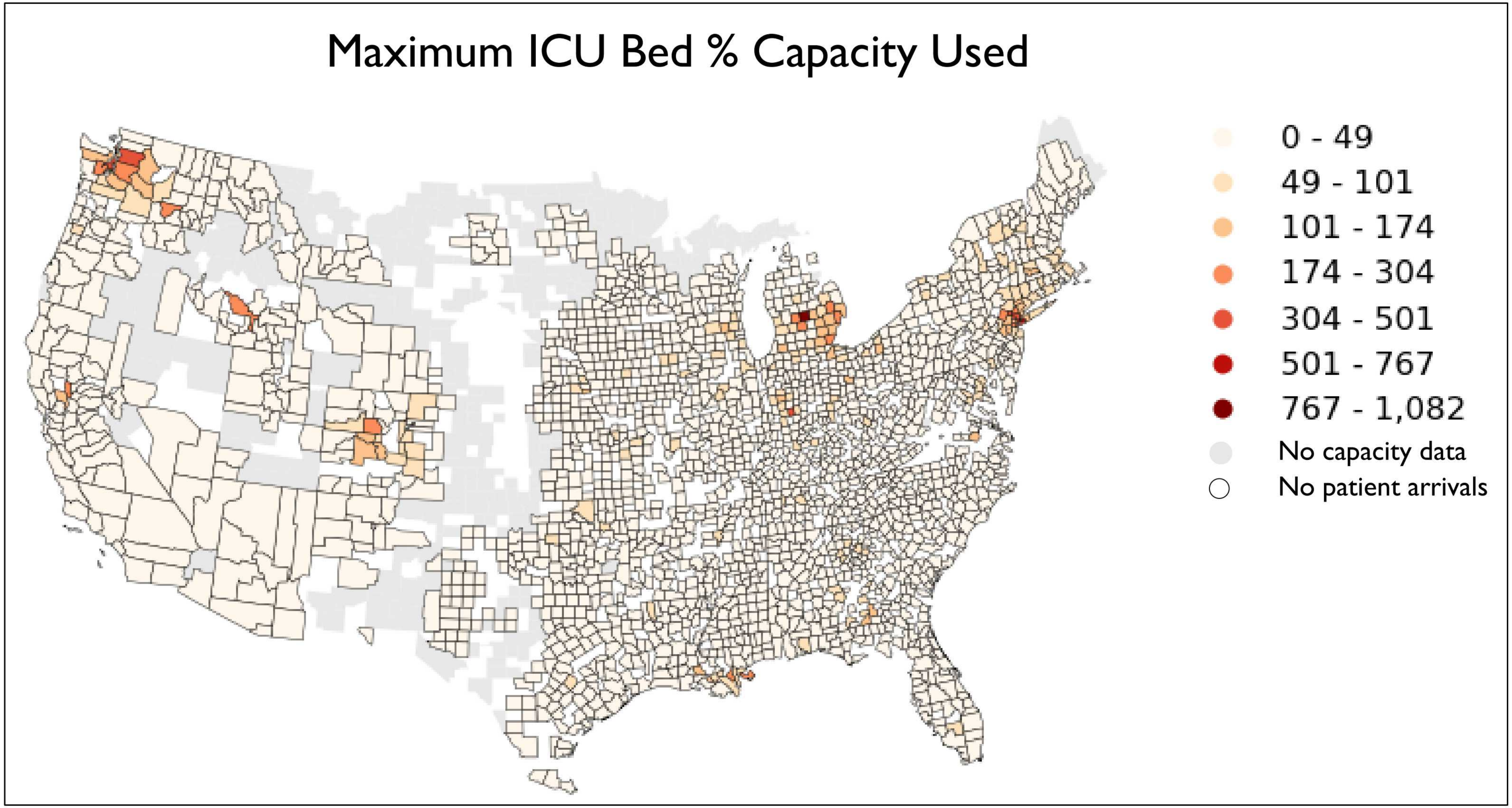
> 95% from 4/11 – 5/9

States with Resource Utilization >18% Capacity	Maximum Ventilator % Capacity Used
New Jersey	75.0
Michigan	64.3
Illinois	48.1
Massachusetts	42.3
Connecticut	24.5
Rhode Island	23.3
Wisconsin	23.2
Vermont	22.4
Georgia	22.1
Maryland	22.0
Colorado	20.6
Indiana	18.4

Resource utilization presented here is the mean value. This can be adjusted based on the level of acceptable risk tolerance.

Using EpiGrid patient streams, 4/26/2020 dataset, β = 0.3
Analysis horizon: 3/3/2020 – 7/20/2020

National Summary: County Resource Sufficiency, ICU Beds



County detail provides specificity for state level, and mirrors the same areas of concern.

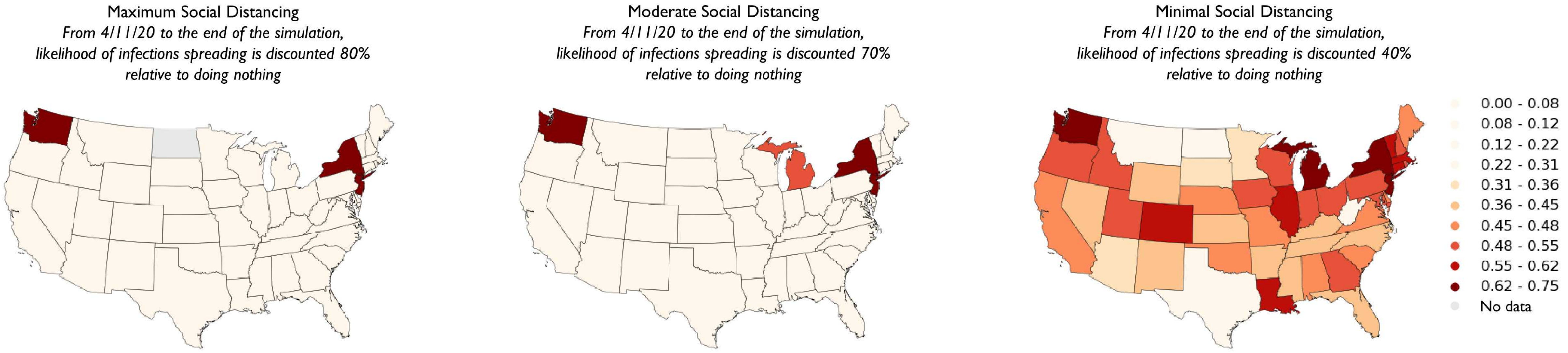
Significant difference in color scale values driven by comparison of county demand to county capacity (vs. state capacity).

Resource utilization presented here is the mean value. This can be adjusted based on the level of acceptable risk tolerance.

Using EpiGrid patient streams, 4/26/2020 dataset, $\beta = 0.3$
Analysis horizon: 3/3/2020 – 7/20/2020

National Summary: Exceedance of Capacity, Social Distancing

Probability of Exceeding ICU Bed Capacity



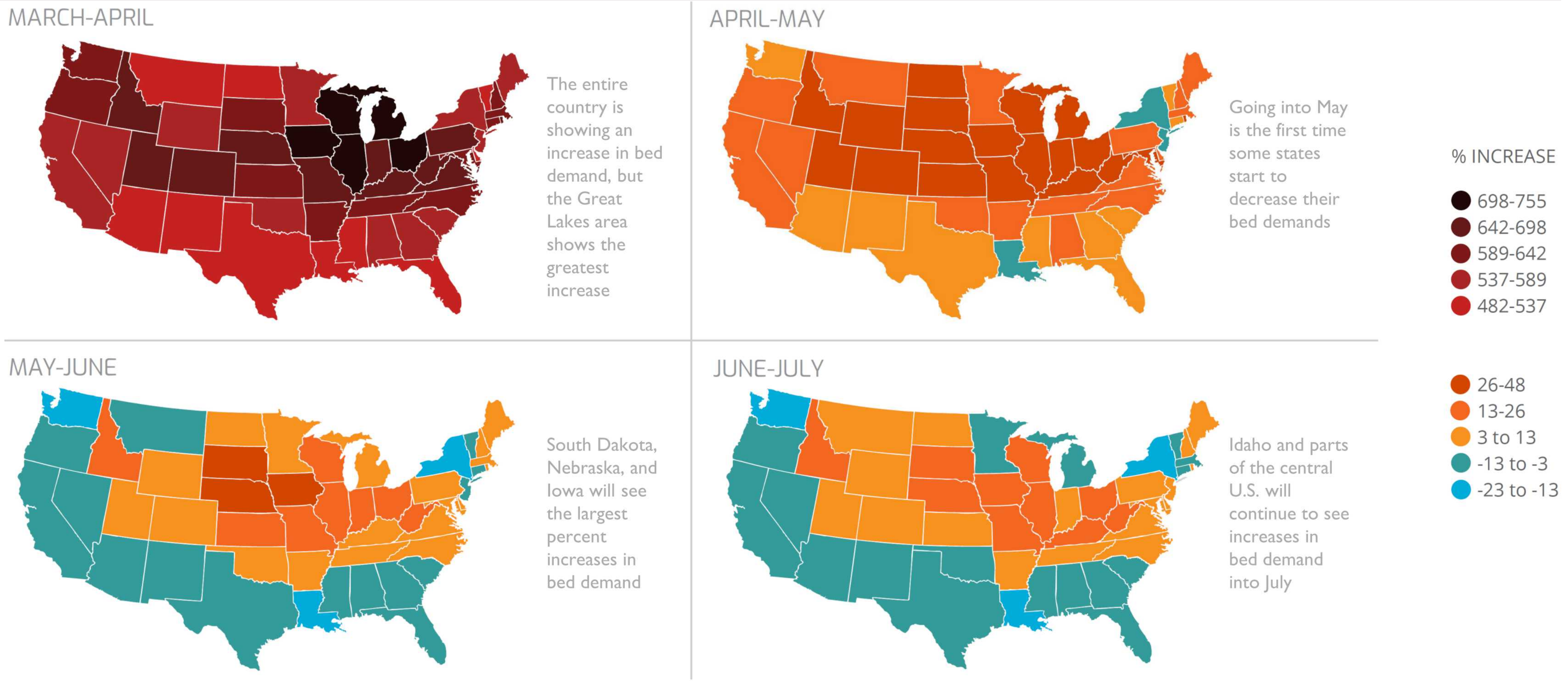
Note that with decreasing degree of social distancing (from left to right in above maps), the probability of exceeding capacity of ICU beds across the country increases significantly.

Resource utilization presented here is the mean value. This can be adjusted based on the level of acceptable risk tolerance.

Using EpiGrid patient streams, 4/26/2020 dataset
Analysis horizon: 3/3/2020 – 7/20/2020

National Summary: Timeseries of Increase/Decrease in Demand

Month-to-month change in bed demand

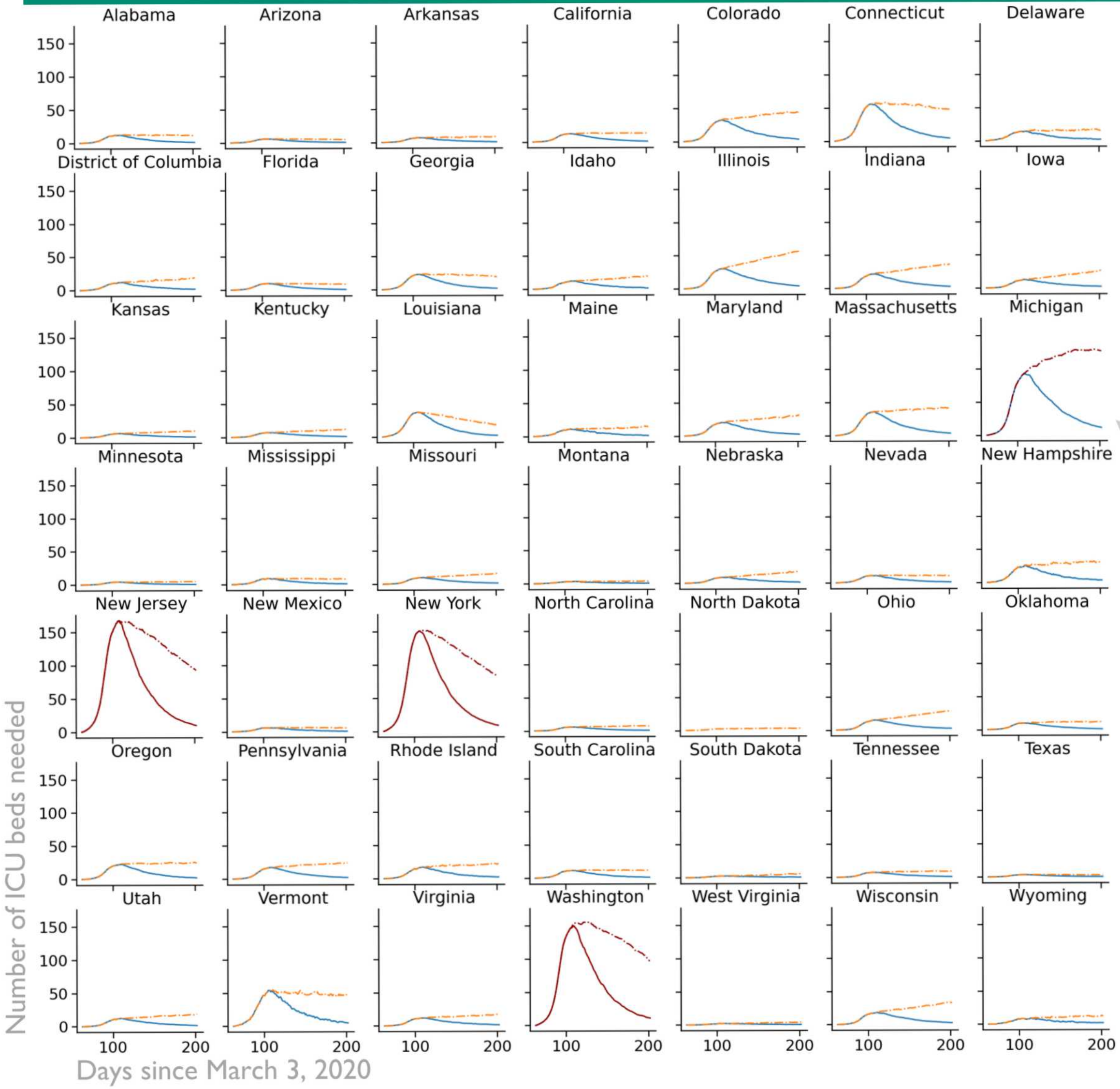


Resource utilization presented here is the mean value. This can be adjusted based on the level of acceptable risk tolerance.

Using EpiGrid patient streams, 4/26/2020 dataset, $\beta = 0.3$
Analysis horizon: 3/3/2020 – 7/20/2020

National Summary: Timeseries of State Patterns

Sparklines of ICU bed demand by state*, 3/3-7/20



	Maximum Social Distancing	*From 4/11/20 to the end of the simulation, likelihood of infections spreading is discounted 80% relative to doing nothing*
	Moderate Social Distancing	*From 4/11/20 to the end of the simulation, likelihood of infections spreading is discounted 70% relative to doing nothing*
	State exceeds ICU Bed capacity	

Enable quick visual indicators of differences in temporal patterns between states and impacts of social distancing scenarios

- Michigan, Illinois, Colorado, etc. experience very different ICU bed demand depending on extent of social distancing

*Contiguous 48 states plus Washington DC
Resource utilization presented here is the mean value. This can be adjusted based on the level of acceptable risk tolerance.

Using EpiGrid patient streams, 4/26/2020 dataset, β = 0.2 and 0.3
Analysis horizon: 3/3/2020 – 7/20/2020

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Integrated Medical Resource Supply/Demand Routing Model

Goal

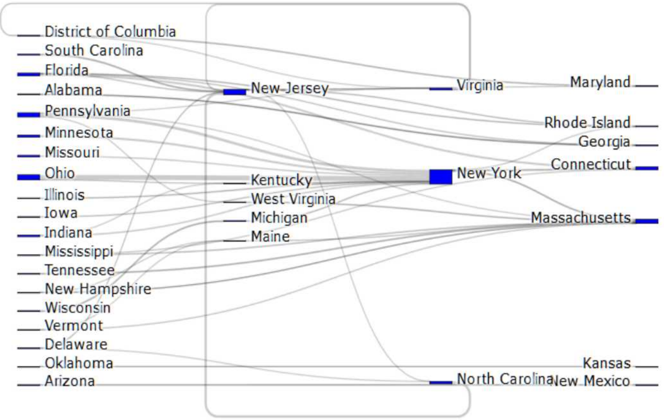
- Provide insights into the patterns and scale of routing recommendations to show the feasibility of specific routing strategies

Approach

- Use an optimization model which determines routing paths for medical resources to match supply with demand
- The model incorporates travel costs and seeks to minimize the number of regions with unmet demand

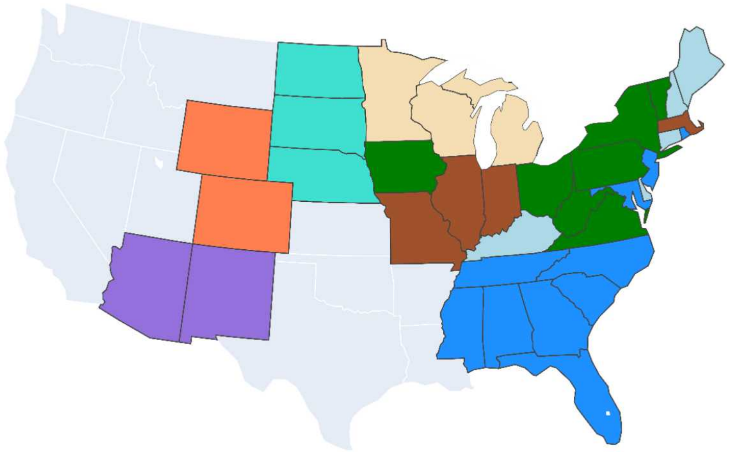
Results

Resource sharing feasibility to minimize shortfalls experienced by any state



Detailed routing recommendations at time points throughout the event

Integrated planning framework to combine multiple scenarios and assess uncertainty

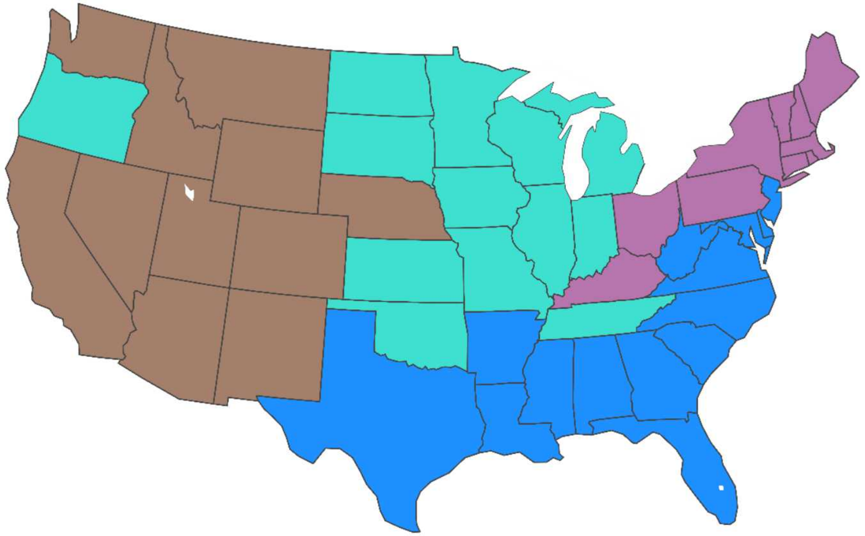


Resource Sharing Example Results

Ventilator Routing

Ventilator routing recommendations to minimize the shortfall experienced by any state for a single time point. Arrows represent the direction of resource flow, weighted by the magnitude of the shipment.

Communities that would benefit by sharing ventilators



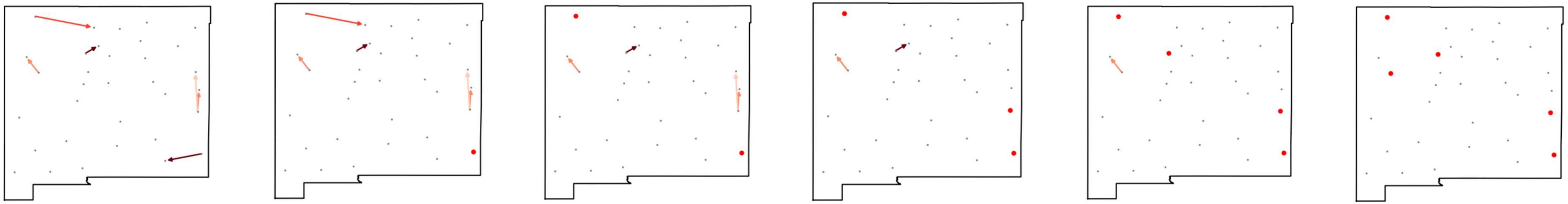
Communities detected for ventilator movements between states for a specific epidemiological scenario. States that belong to the same sharing community have the same color.

Provide insights into the patterns and scale of routing recommendations to show the *feasibility* of specific routing strategies, and to understand the implications of making policy based on specific forecasts

Resource Location Analysis

Example: where should ICU beds be placed to minimize patient travel within New Mexico?

With no added ICU beds	Choose 1 location to add ICU beds	Choose 2 locations to add ICU beds	Choose 3 locations to add ICU beds	Choose 4 locations to add ICU beds	Choose 5 locations to add ICU beds
	Lea	Lea; San Juan	Lea; Roosevelt; San Juan	Lea; Roosevelt; San Juan; Sandoval	Lea; Roosevelt; San Juan; Sandoval; Cibola
23 people must travel between counties	13 people must travel between counties	10 people must travel between counties	7 people must travel between counties	2 people must travel between counties	0 people must travel between counties



Arrows show direction patients must travel to overcome a shortfall in ICU beds (darker color = more travel)
Red dot shows optimal county to place more ICU beds

Evaluate feasibility of new resource placement incorporating uncertainty in patient needs

COVID-19 Modeling and Analysis Activities

Recovery Modeling
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Economics Analysis Overview

The COVID-19 pandemic could cause a loss in 2020 U.S. Gross Domestic Product (GDP)

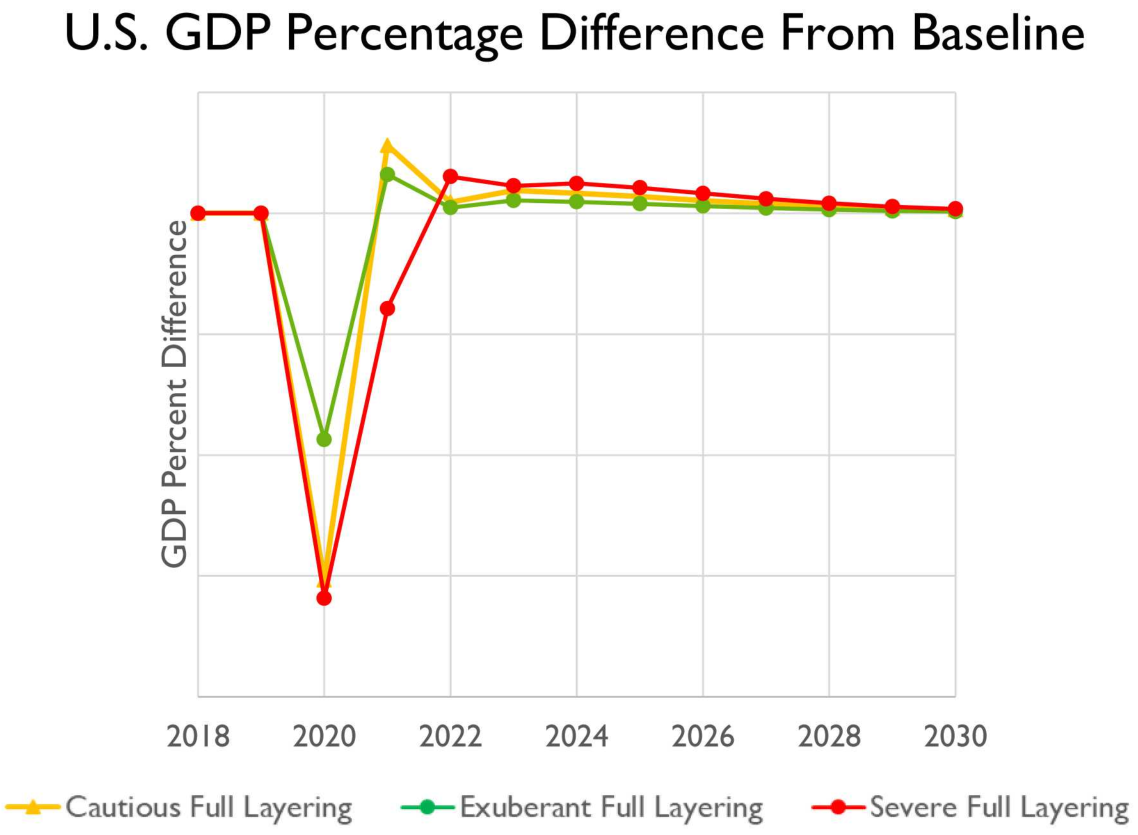
Our goal is to estimate the cumulative economic impacts of COVID-19 and recovery strategies.

Our approach is to generate a national baseline forecast with the REMI model, then modify the baseline to reflect national COVID-19 impacts, then examine response and recovery strategies.

The impact is sizeable, according to our analysis:

- Using data as of April 24th with assumptions about the duration of the COVID-19 event as projected now, combined with scenario assumptions about recovery, results vary
- Can provide percentage change from baseline and absolute values

Potential response and recovery strategies should be carefully examined for effectiveness.



Economics Methodology

Using the REMI code, modify a baseline national forecast to reflect national COVID-19 impacts

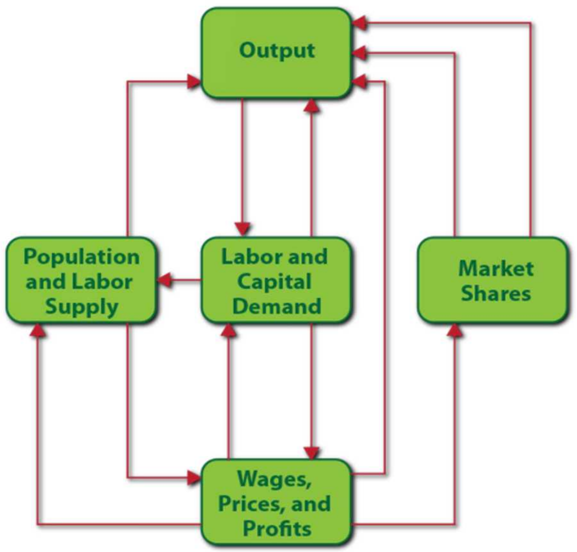
- Supply and demand shocks
- Results in new national COVID baseline forecast
- Slowdown or recession scenario

Test mitigation strategies

- Epidemiological
- Economic
- Resource model
- State and federal

Overall

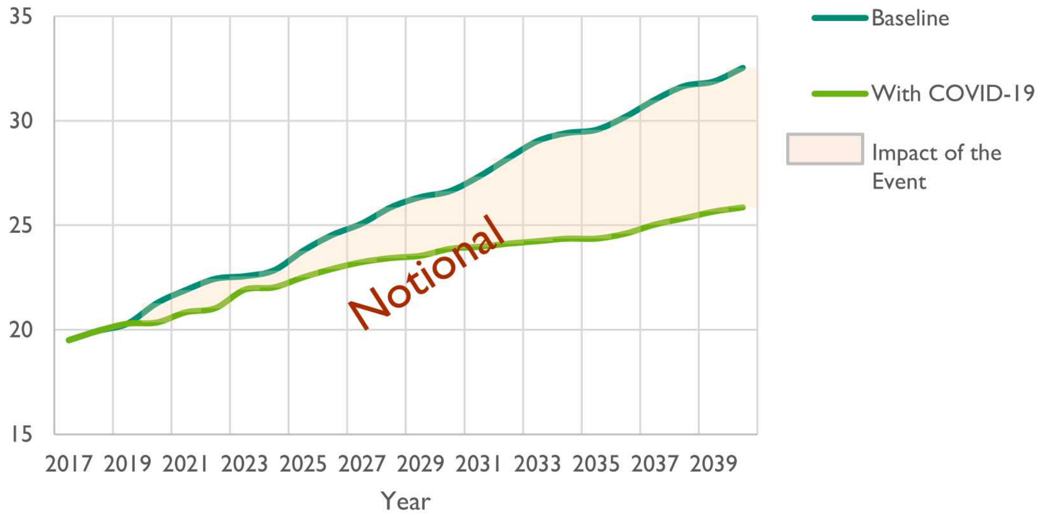
- All weekly, monthly, or quarterly data is scaled to annual
- Stimuli +/- will occur over the year at differing time intervals
- Base year in model for inflation is 2017
- Output will be reported in 2020 dollars
- Perform sensitivity analysis on principal parameter estimates or uncertainty quantification analysis



Representation of the circular nature of the economy which the model captures

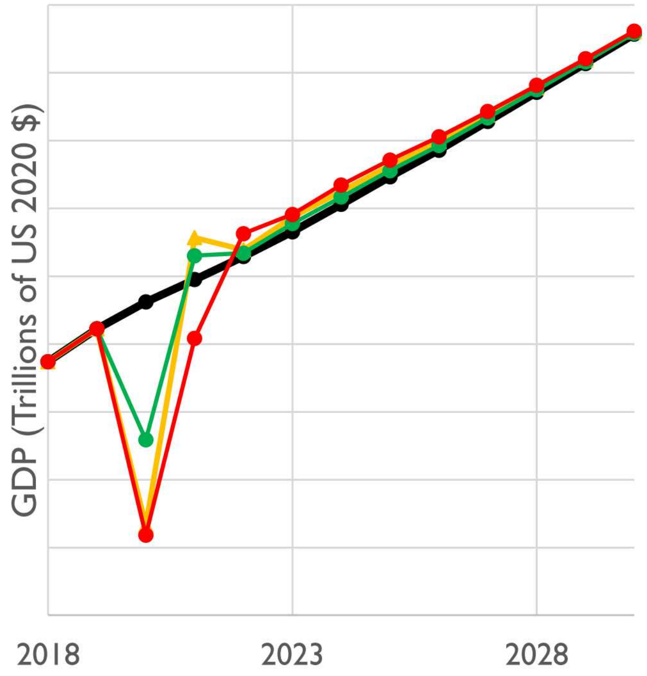
Example Output

GDP ($ trillion)

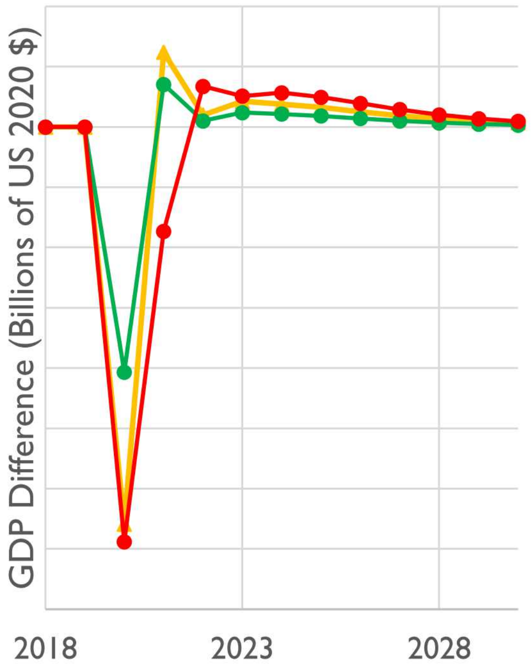


Results for Economic Scenarios
All categories combined, full layering approach applied

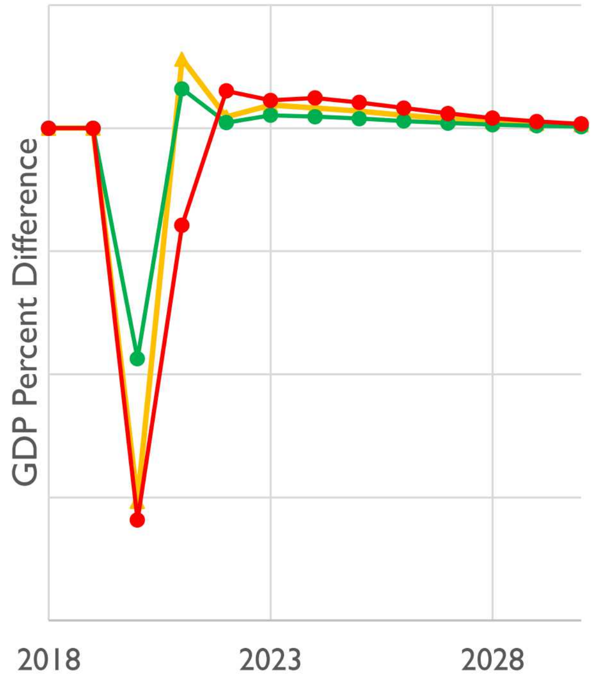
US GDP Levels



US GDP Difference from Baseline



US GDP Percentage Difference From Baseline



The pre-COVID baseline forecast is shown in red. "New COVID" baseline forecast is in purple. The interactions between supply and demand shocks, exogenous changes in economic transactions, and transfer payments are all captured in the purple result.

We are experiencing both demand and supply side shocks. It is the net of these effects that we are "experiencing" as economic losses. The economic situation will continue to evolve as either the event continues (i.e. healthcare spending) or mitigations (i.e. work from home; CARES Act) take a effect.

Depicted is the percent change from baseline. The shocks depress labor and commodity prices across the economy. Once the shock is gone it causes demand to more than bounce back in 2021. This expansion drives prices back up, creating a slow return to baseline in the years after 2021.

The Cautious Scenario results in a loss in 2020 U.S. GDP from the pre-COVID baseline.

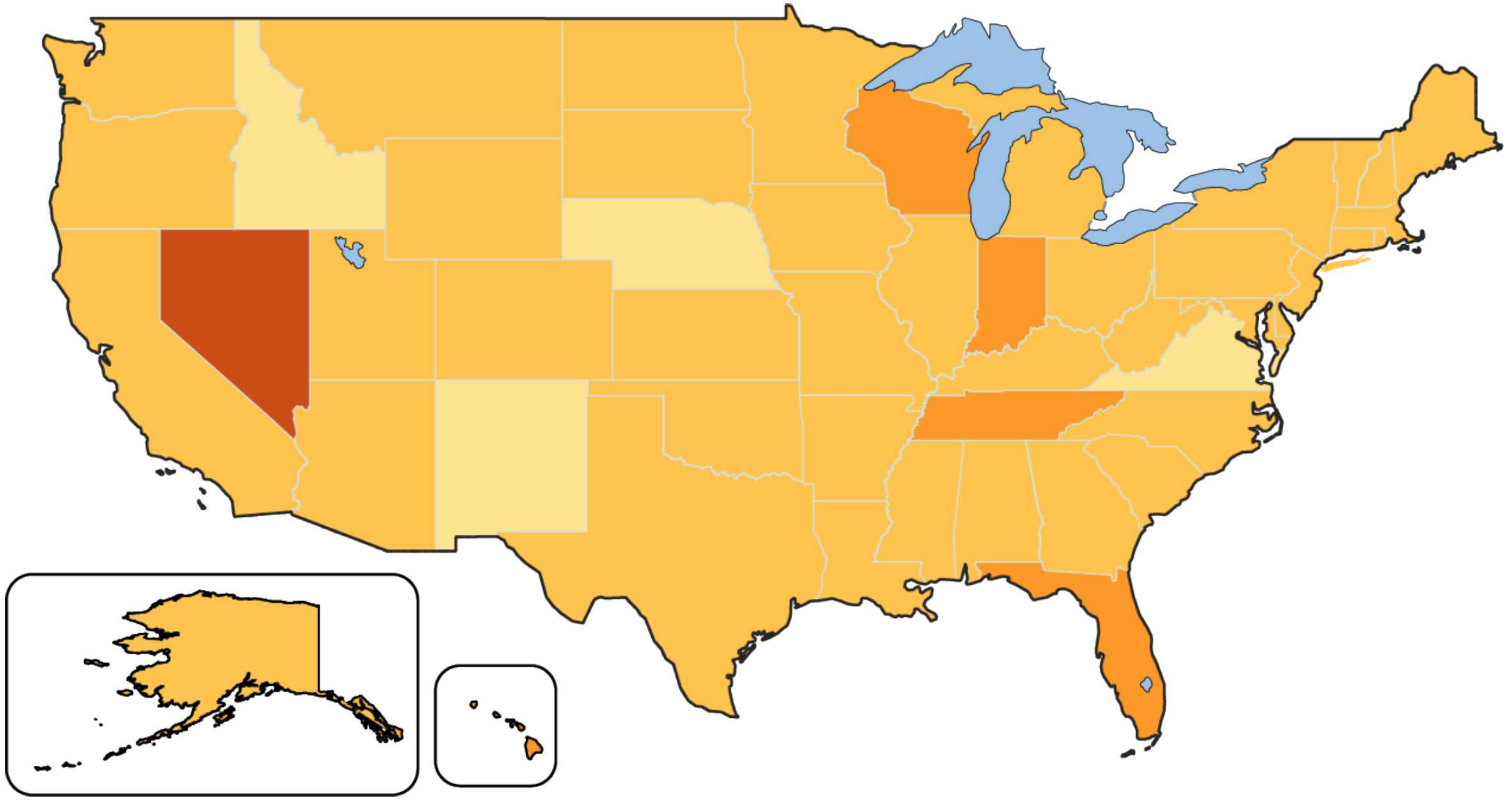
Cautious Scenario, this is a national scale event with possibly long-term negative economic impacts

Unprecedented event

- Unlike previous "disaster" events this is not a regional event
- Every state is negatively affected
- The longer the "event" continues the larger the economic impact

State-by-state impacts

- Overall closures to retail, food and drinking places, and entertainment affect all states
- Manufacturing closures are concentrated in specific states
- The energy sectors in every state are negatively affected due to declining demand



Decrease in state GDP in the cautious scenario

Every state is negatively affected.
States with diverse economies experience slightly less severe impacts.

Cautious Scenario, Impacts by State

Manufacturing

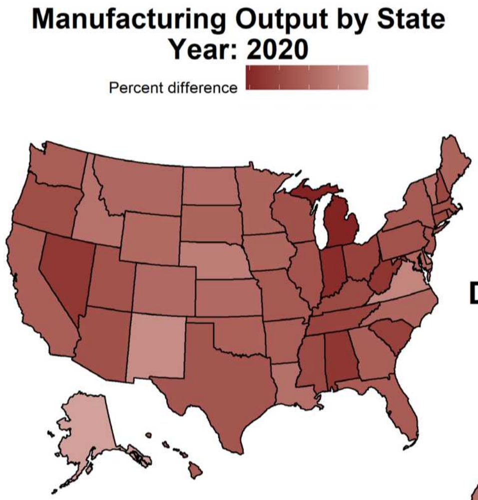
- Manufacturing is not a large industry in every state
- Makes up a significant portion of output in:
  - Michigan, Indiana, and Alabama
- Linked to automotive manufacturing sectors

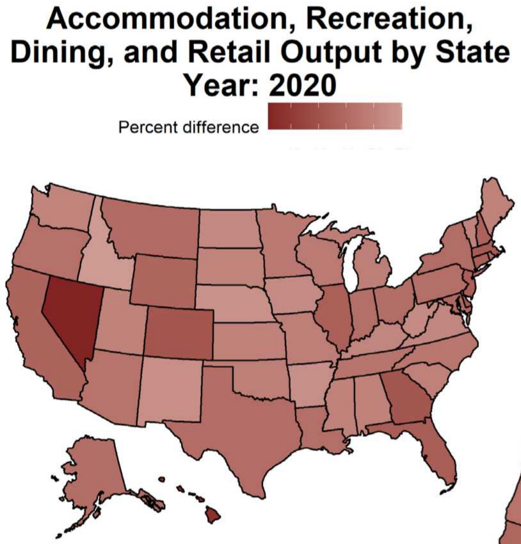
Accommodation, Recreation, Dining, and Retail

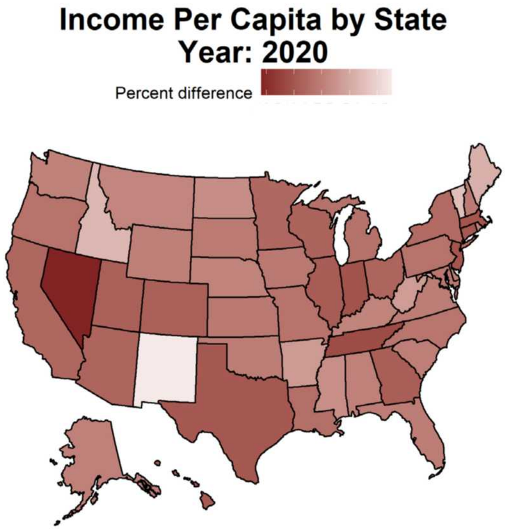
- These industries are a large source of jobs and output in every state
- The effect is very similar across almost all states
- Nevada is more reliant on tourism relative to other states

Income

- Nevada's loss in income is expected given the large concentration of labor in tourism-related industries
- New Mexico historically experiences economic downturns on a lag; overall is a very small economy







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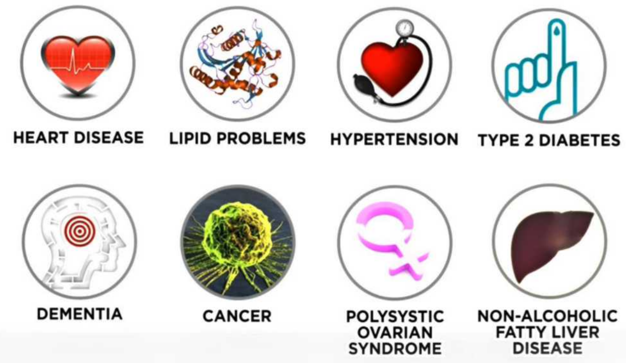
Comorbidity Analysis Overview

Machine learning and data science applied to electronic health record (EHR) medical data to improve risk prediction for severe COVID-19 symptoms

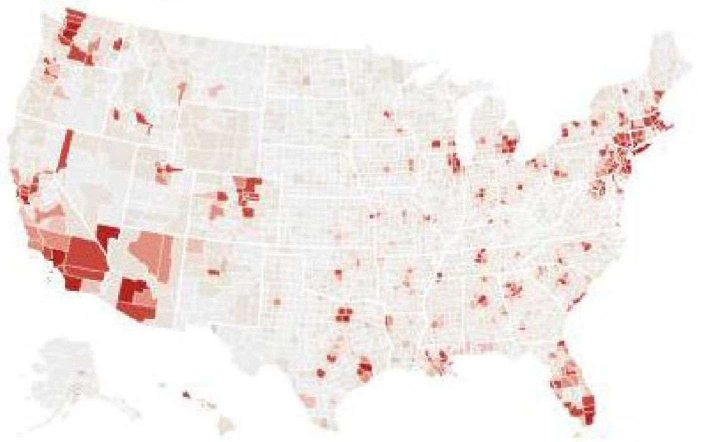
How do comorbidities affect infection severity?

- Our county-level model fits will reveal the effects of individual demographic and comorbidity features on infection outcomes



Which patients are most at risk?

- Longitudinal EHR analysis will train an improved deep Convolutional Neural Network/Recurrent Neural Network model to more accurately predict infection severity based on a patient's full medical history
- We will produce an interpretable model based on our findings for use in clinical settings



How will disease progression differ by US county?

- Local county-level models will be extensible to all US counties as broad demographic and comorbidity prevalence data is available
- Nuanced effects can then be incorporated into our epidemiological models

Exemplar - Regression to Parameterize Risk By Age

Data from public sources:

- China
- South Korea
- Hong Kong
- United States

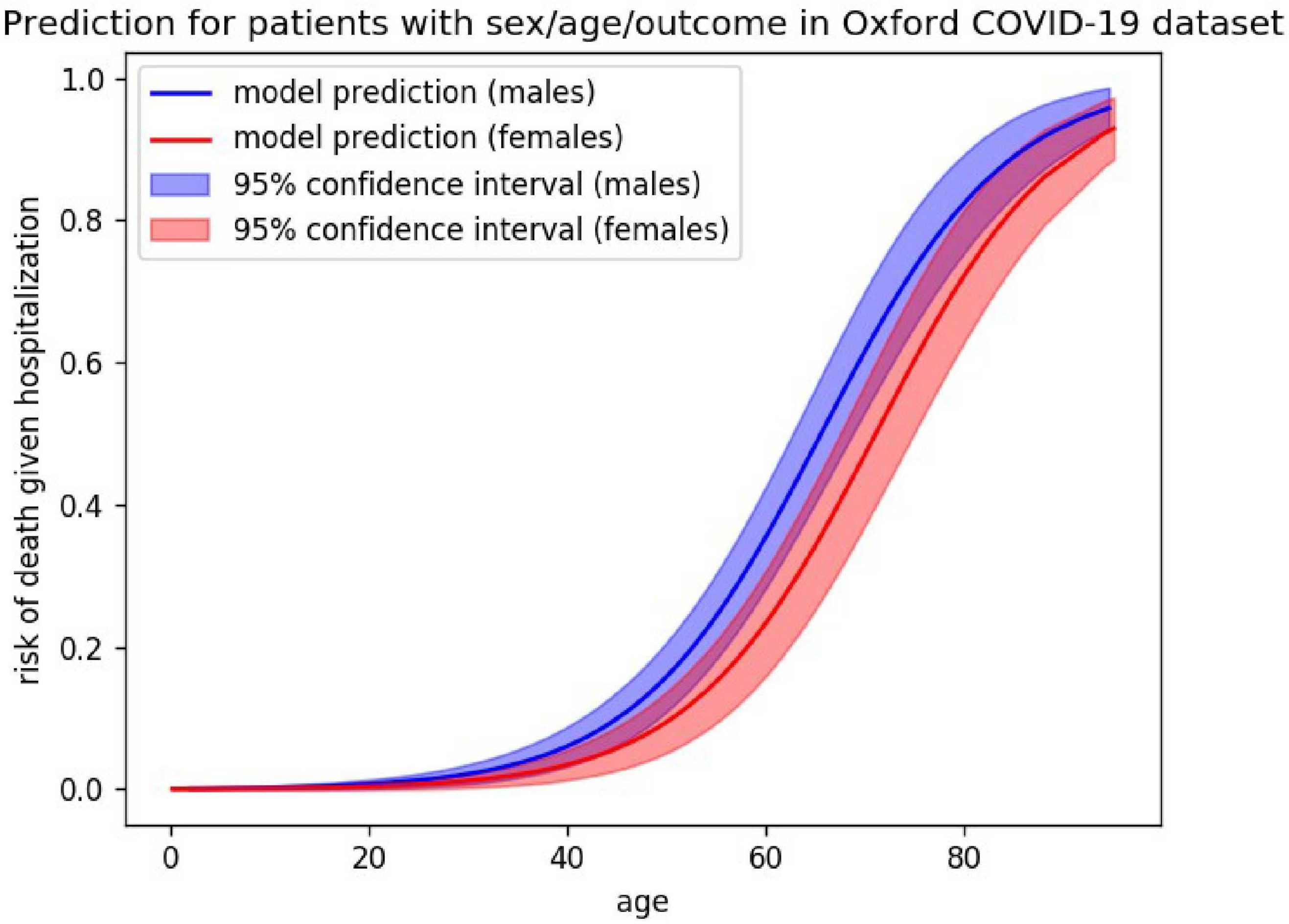
Logistic Regression Fit

- Reveals risk curves with uncertainty
- Also provides model parameters for use in other projections

Can be extended to explore comorbidity risk with additional data

Analysis Conclusion:

- Mortality risk increases with age
- Men at higher risk than women



Characterize mortality risk based on patient demographics and history to potentially discover unknown risk factors

Preliminary Results – Socio-Economic Status Proxy Predicts County Mortality Growth

Using California health survey data, we trained a model with all available features to fit the COVID Mortality growth rate.

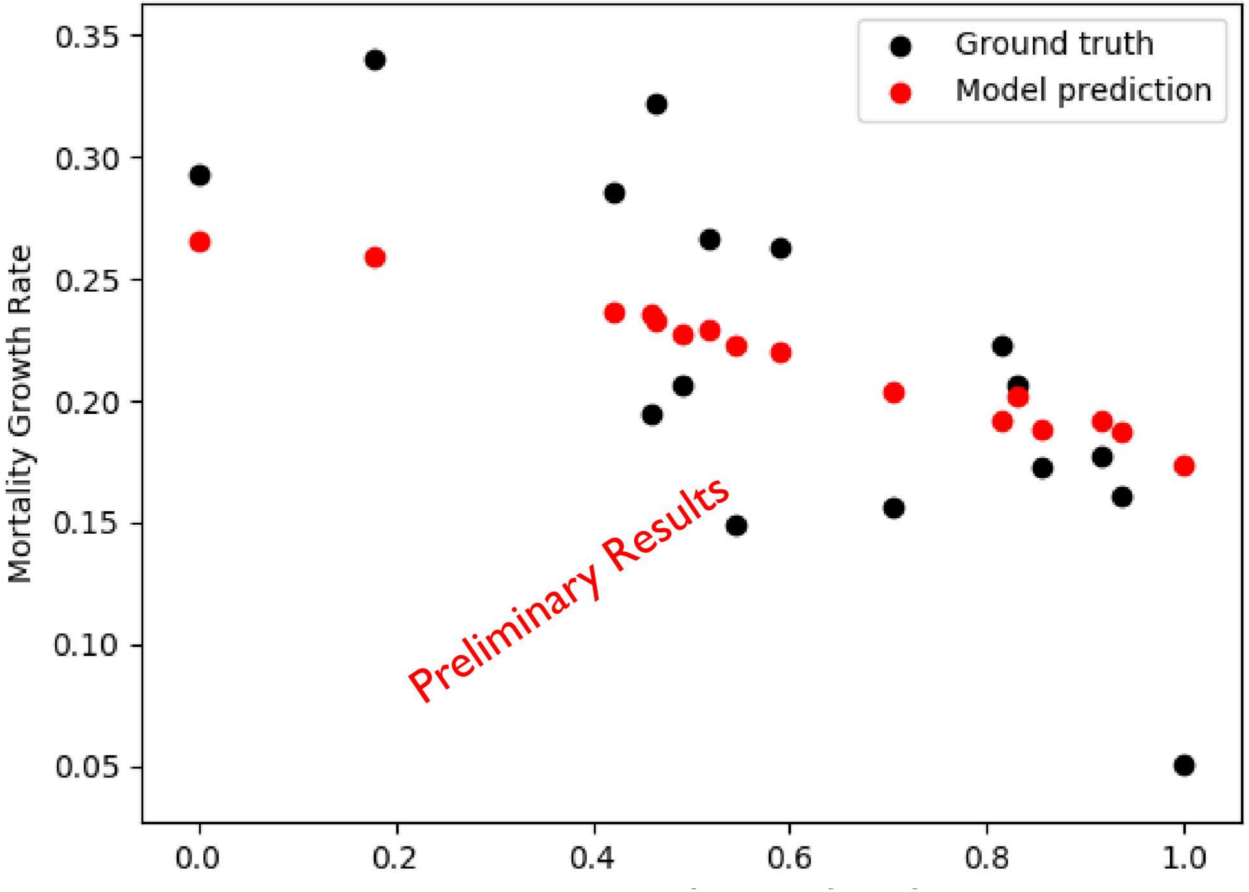
Over 16 training examples:

- Training R^2 Score: 0.43
- Training Mean Absolute Error: 0.045
- Cross Validation Mean Test Error: 0.061 +/- 0.040
- Cross Validation Mean Train Score: 0.45 +/- 0.07

This figure shows the relationship between ***the most significant feature*** in the model (the highest coefficient in the trained model) to the outcome.

Lasso regression merges similar features into one, **it is likely that the feature shown is representative of the % of county residents with employment based insurance.**

Model Predictions vs. Most Significant Feature



% Children Covered by Employment Health Ins.

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COVID-19 Forecasting via COVID-19 Modeling and Bayesian Forecast (COMBO)

Model Purpose:

- Short-term forecasts of expected COVID-19 case counts from readily available public datasets

Method:

- Collect daily COVID-19 cases from public data sources (e.g. JHU or NYT)
- Use case-count data to determine latent infection curve
- From latent infection rate curve, forecast future case counts and uncertainty

Pros:

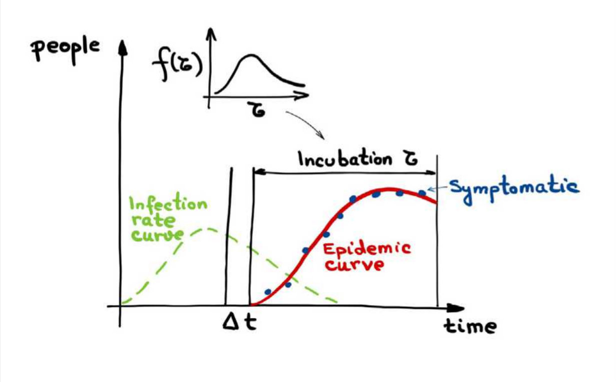
- Unlike traditional epidemiological models, doesn't rely on detailed knowledge of a region's population, healthcare system performance, or public health policies.
- Purely data-driven; minimum of modeling assumptions
- Method allows us to provide uncertainty bounds on forecasts
- Can apply to county, region, state and national scales

Cons:

- Limited to short-term forecasts (7 to 10 days)
- Forecasts depend on accurate datasets
- Assumes sufficient testing capability – often not the case

Technical details:

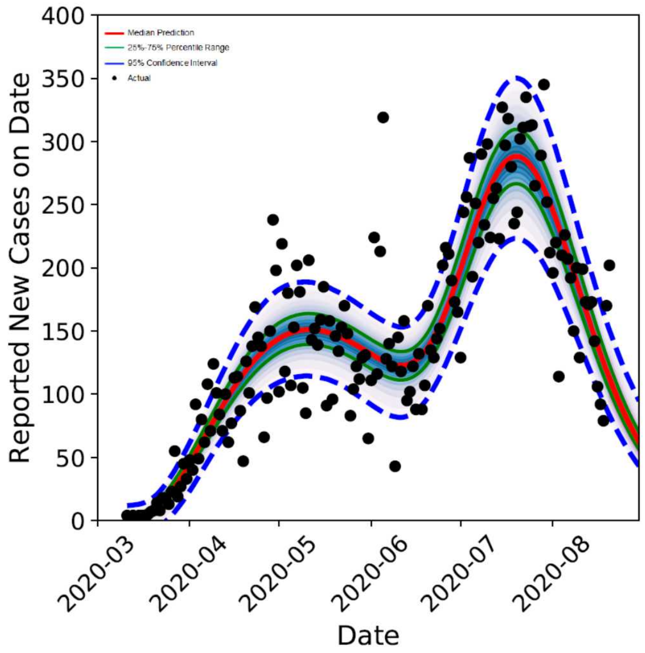
- Infected cases observed on a given day are a consequence of people infected at an earlier time coming out of incubation and presenting symptoms
- The incubation period is drawn from COVID19 incubation period distribution
- Infection rate model is a parameterized curve



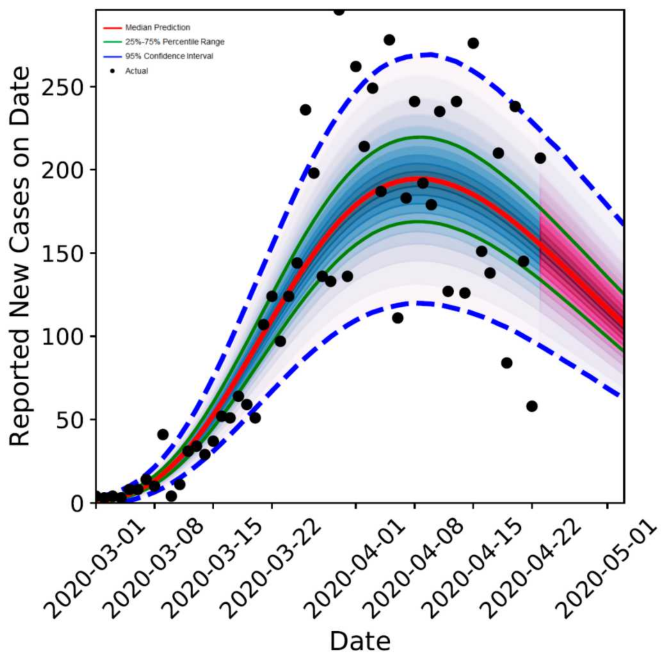
Provide 10-day forecast of new cases from inferred infection curve based on case data

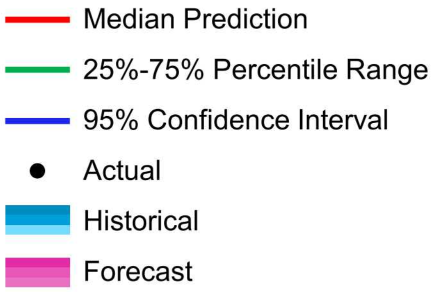
Example State and Regional Results

New Mexico New Case Forecast 8/20/20



San Francisco Bay Area New Case Forecast 4/23/20





- Forecast new cases at country, state and regional scales
  - Technique uses Bayesian inference; always true to data/evidence
  - Uncertainty quantification built into the model
- Detects/infers ”flattening” of the infection curve due to countermeasures
  - Changes forecasts accordingly & automatically; no special calibration/model change needed
  - Infers effect of countermeasures when signal is evident in data (time-lag ~1.5x incubation period)

Team

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