Treatment Model Design and Use



06 April 2020

SNL Pandemic Modeling Team



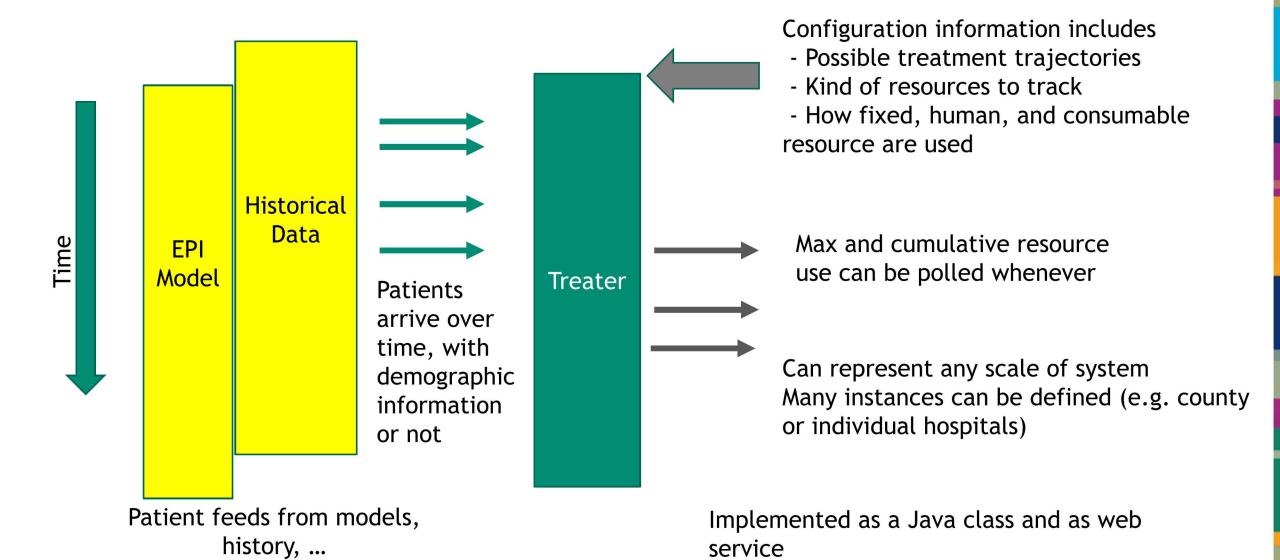
Sandia National Laboratories is a multimission laboratory managed and operated by National Technology & Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525.

SAND2020-3836 PE



Estimates maximum/cumulative resource use from patient flow data





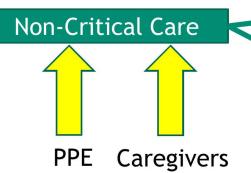
Treatment processes model processes and components

Patients take one of several possible paths, potentially based on demographics

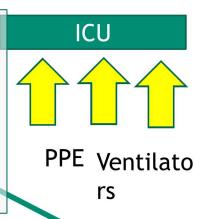
Patient

Each path is made of one or more stages

Each stage has minimum and maximum time Resource commitments (e.g. bgd).



Patients
transition to
other stages or
leave hospital
with some
probability



Each stage needs resources:

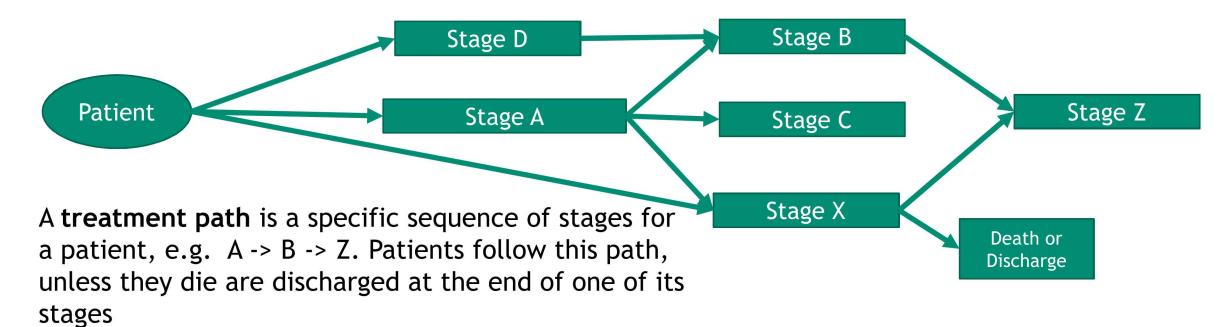
- specialists
- equipment
- resources per patient
- resources per practitioner

Death or Discharge

Treatment paths and patient fates

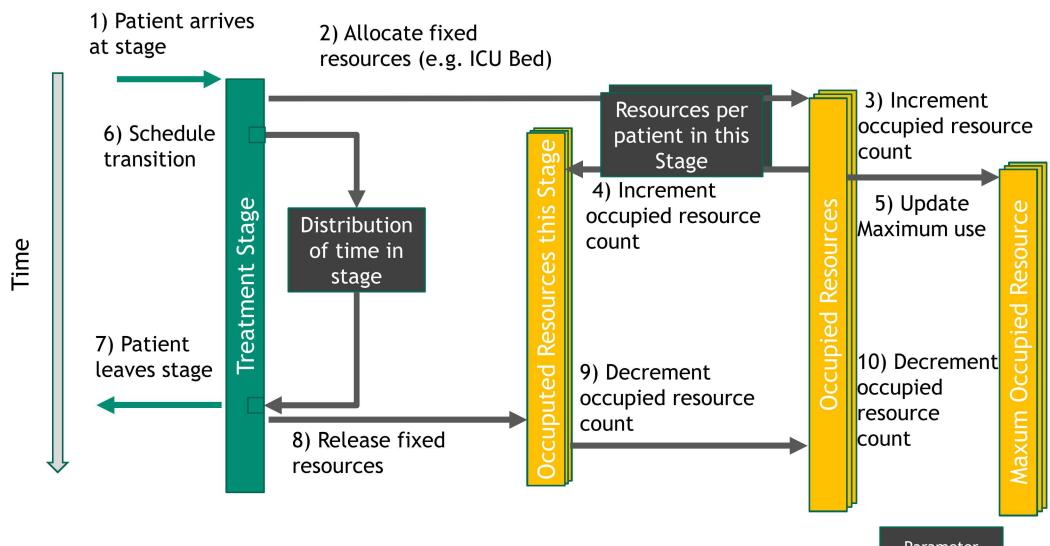
Stages model administration of a specific kind of treatment (e.g. ICU, ICU with Ventilation, General)

All resource consumption occurs in treatment *Stages*



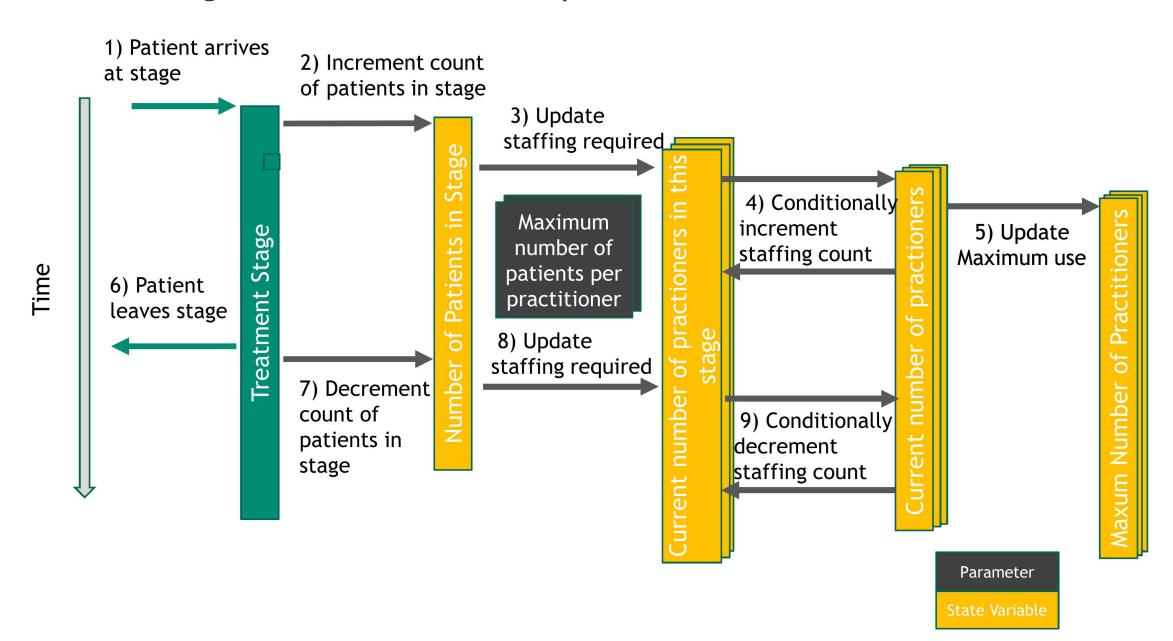
Fate is a set of rules that connect a patient's demographic characteristics to a set of possible paths with associated probabilities

Calculating resource burdens – re-useable resources

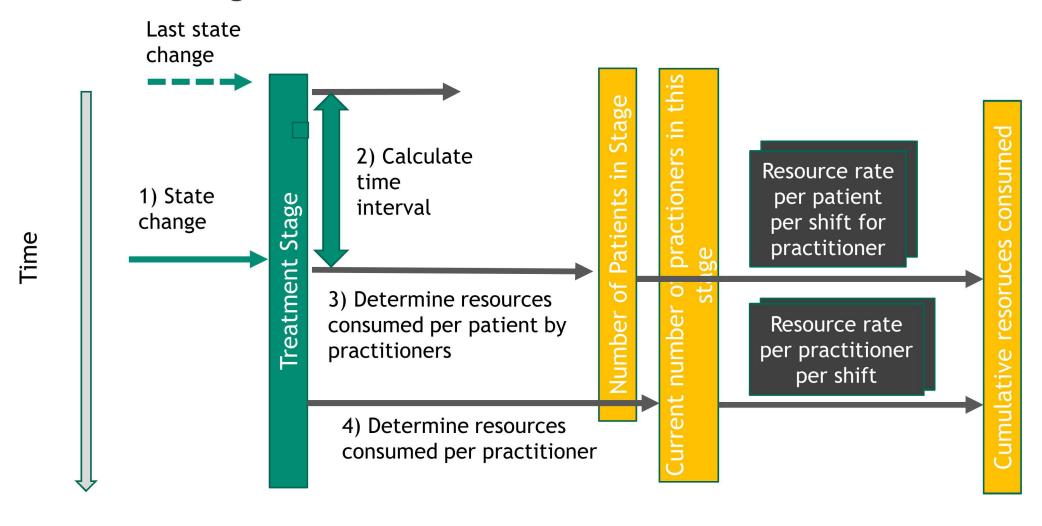


Parameter

Calculating resource burdens – practitioners



Calculating resource burdens – consumables



Parameters summary

Demographics

Age range
Gender
List of Conditions
(e.g. "COPD",
"Diabetes")
Fraction of population

If patients arrive with demographic data that is used. Otherwise their chosen randomly

Treatment stages are defined by their associated resource usage

Patients are assigned a course of treatment based on demographics.
Alternatives are probabilityweighted

Fates

Demographic rule Set of possible trajectories:

- Probability of taking it
- Series of Treatment Stages

Treatment Stage

List of resources

Minimum time

Maximum time

Probability of death

Probability of transition to next stage

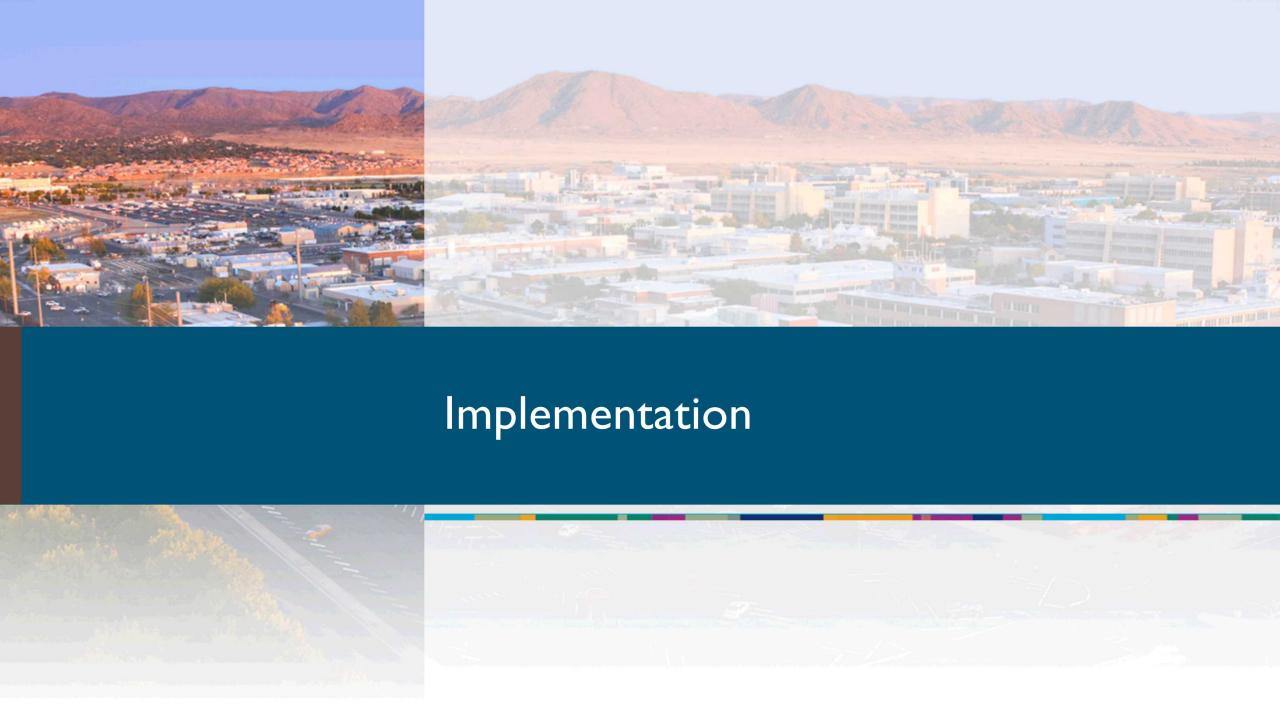
Types of caregivers required

for each type....

maximum number of patients they can handle

consumable resources per shift

consumable resources per shift per patient



Features

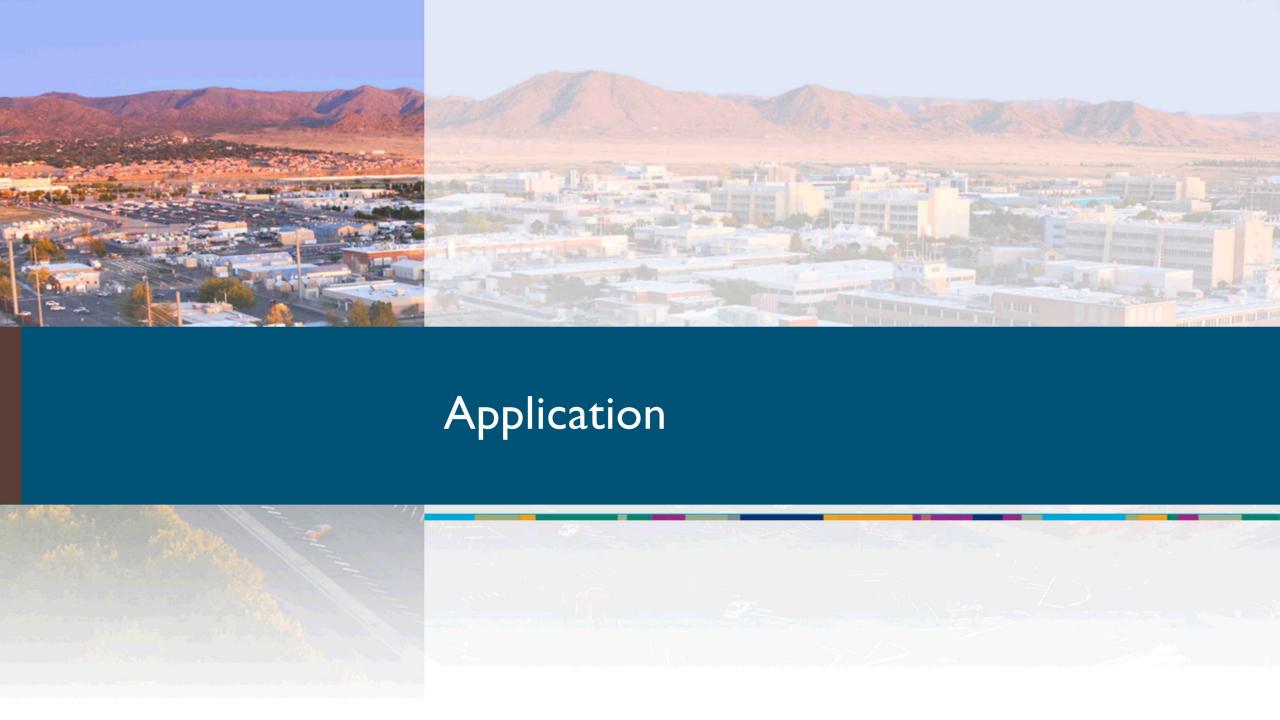
Configurable through input

- Treatment paths and probabilities
- Kinds of specialists and resources; requirements at different treatment stages

Reflects uncertainty about key inputs

Rapid updates as information and conditions change

Scalable to state, county, hospital



Outline

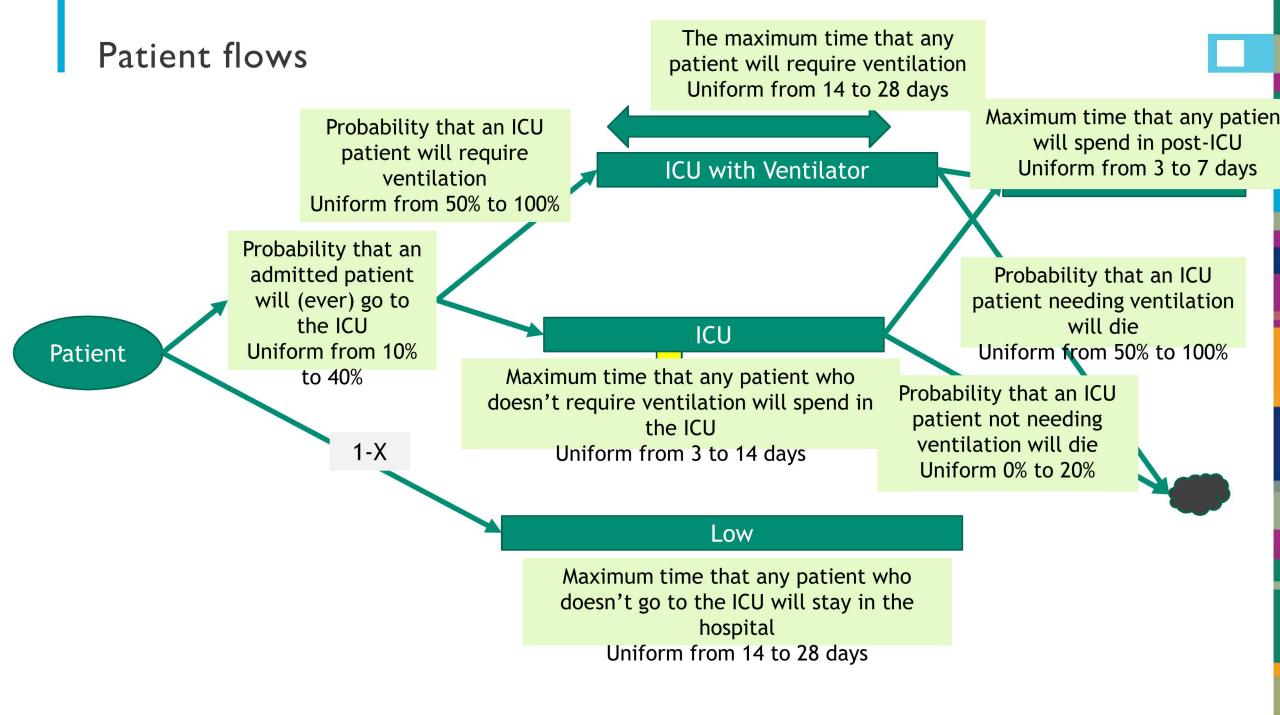
Model structure, parameters, and supporting data are common to two distinct analyses

Caveats

First analysis – possible resource needs for New Mexico considering uncertainty in epi forecasts, treatment characteristics, and use rates

- State-level analysis with three epi models
- County-level analysis with EpiGrid results for New Mexico

Second analysis – parametric study of resource demands as a function of patient curve acuity



Roles and resources

Roles:

- Physician
- FloorNurse
- ICUNurse
- RespiratoryTherapist

Committed Resources:

- Ventilator
- MeteredDoseInhaler
- ICUBed
- Bed

Treatments:

- General
- ICU
- SeverelCU

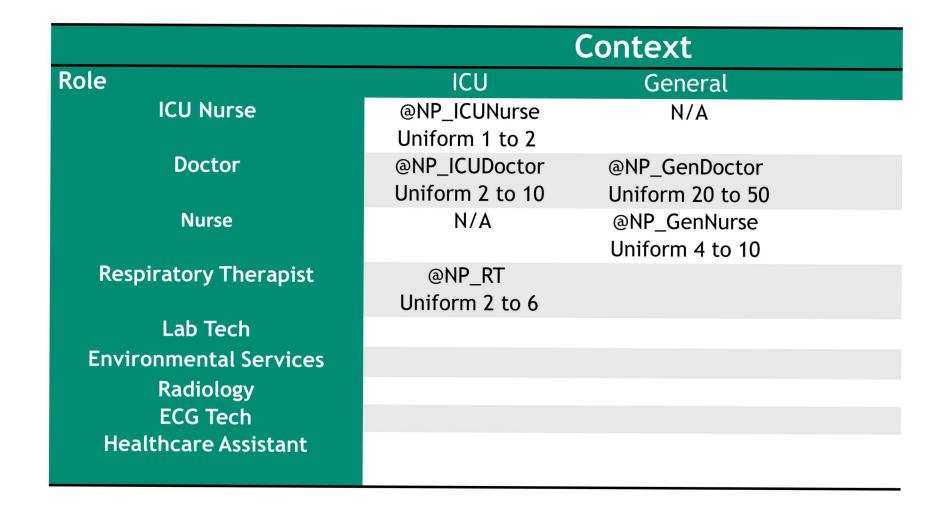
Consumable Resources:

- Gown
- N95
- FaceShield
- Gloves
- Sedatives

Notes

- Other resources that scale with ventilation (tubes etc.) are not tracked individually
- Sedatives are a surrogate for other drugs their cumulative demand is the total number of shifts that a patient is under ventilation

Staffing - Number of patients per practitioner



ICU							
Units used per shift							
Practiti oner	Gowns	N95 Mask	Gloves	Face Shield			
Floor Nurse		masik					
ICU Nurse	@NGown_ICU Nurse 2-4	@NMas k_ICUN urse 1-4	@NGloves_I CUNurse 4-12	@NShield_IC UNurse 1-4			
Doctor	@NGown_ICU Doc 1-2	1	@NGloves_I CUDoc 1-12	1			
RT	@NGown_ICU RT 1-2	1	@NGloves_I CURT 6-12	1			

General							
Units used per shift							
Practit ioner	Gowns	N95 Mask	Gloves	Face Shield			
Floor Nurse	@NGown_Ge nNurse 2-3	@NMask _GenNu rse 1-3	<pre>@Ngloves_Gen Nurse 3-12</pre>	1			
ICU Nurse							
Doctor	@NGown_Ge nDoc 1-2	1	<pre>@NGloves_Gen Doc 1-12</pre>	1			
RT							

References – treatment paths and outcomes

Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* doi: 10.1056/NEJMoa2002032

Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585

Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study.

Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y.

Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12-March 16, 2020 - CDC

Clinical Characteristics of Coronavirus Disease 2019 in China .Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., et al. doi: 10.1056/NEJMoa2002032; 10.1056/NEJMoa2002032; New England Journal of Medicine; Massachusetts Medical Society; 0028-4793; UR - https://doi.org/10.1056/NEJMoa2002032;2020/04/04

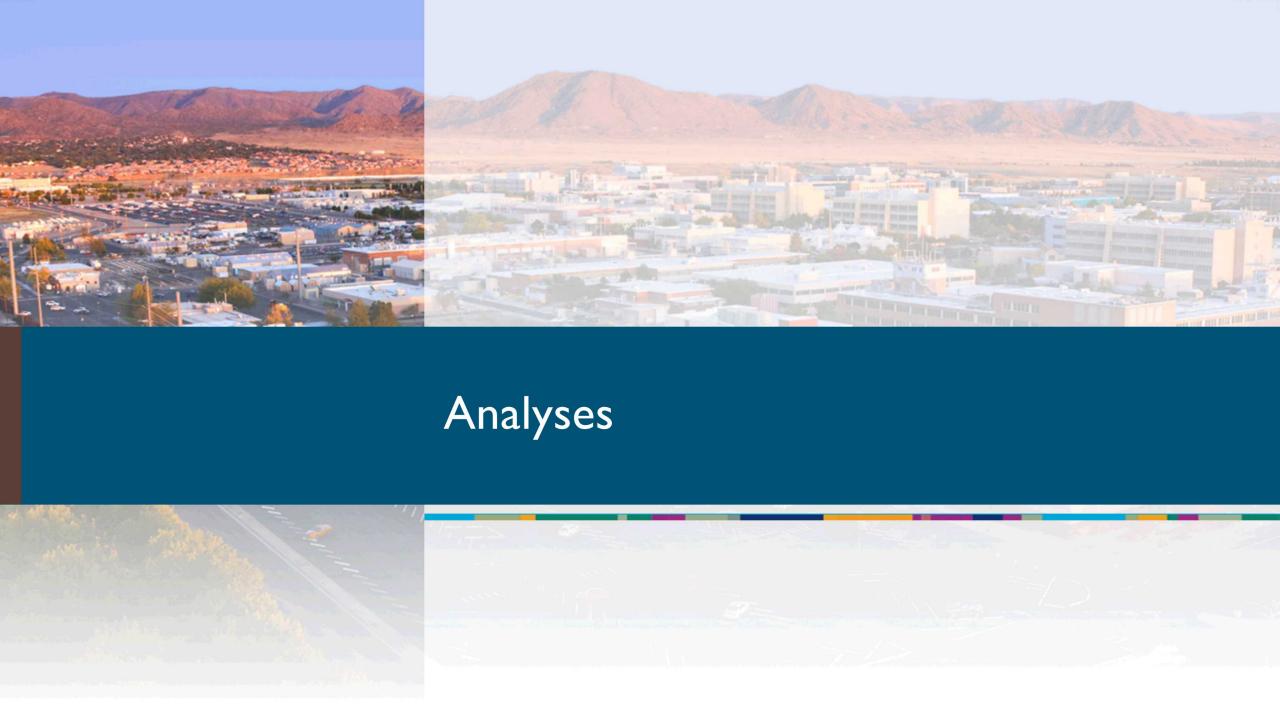
Preliminary Analysis of case data from Canada and New Mexico

References – usage rates

Planning estimates provided by a local New Mexico health service

Preliminary Analysis of hospital usage and staffing reports provided by NMHA

CDC guidance cited in: Potential Demand for Respirators and Surgical Masks During a Hypothetical Influenza Pandemic in the United States; Cristina Carias, 1,2 Gabriel Rainisch, 3 Manjunath Shankar, 3 Bishwa B. Adhikari, 3 David L. Swerdlow, 1,4 William A. Bower, 5 Satish K. Pillai, 3 Martin I. Meltzer, 3 and Lisa M. Koonin



Caveats

Model Framework

Practitioners have fixed roles and are dedicated to specific stages – possible overestimation of personnel

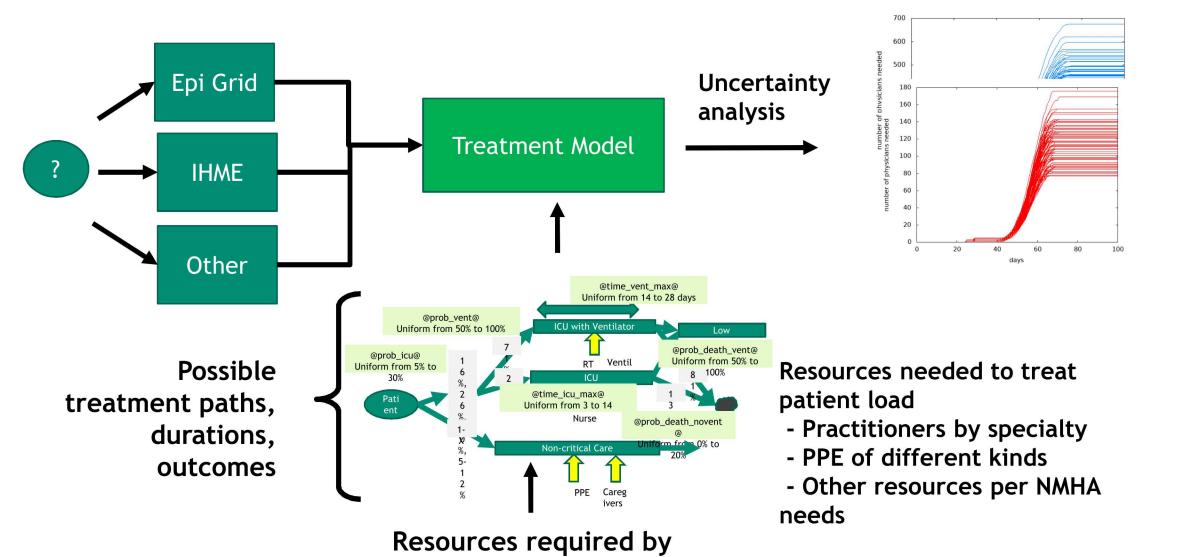
Model Implementation

• The code is simple and provides correct answer to a set of test cases; unit tests, documentation, and review are forthcoming

Configuration/Parameters

- Resource requirements from background medical services are not included
- Some categories of workers (e.g. Environmental Services) were not included
- PPE consumption rates in this context are not well characterized. Input reflects planning and recent practice
- Patient feeds from the epi models do not come with demographic characteristics; Treatment pathway probabilities are therefore not conditional on age, pre-existing conditions, etc.
- Relationship between inherent stochasticity (e.g. running model replications with the same parameters) vs. changing governing parameter (uncertainty) not yet characterized
- Initial results suggest output is dominated by scale of patient stream from epi model, but parameter uncertainty is also significant (e.g. the ratio of standard deviation to the mean is 0.3-0.4 for many response quantities, which results in wide uncertainty predictions). Properly accounting for epi scenario uncertainty vs. parameter uncertainty will be case-specific and is an important aspect of these studies.

Analysis Plan – Possible resource needs



specific practitioners and

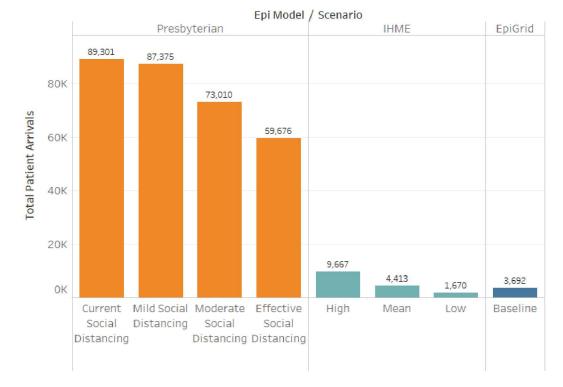
contexts

Analysis 1: Inputs

Goal: How does using a different epi input effect resource planning?

Three different epi models (each with different scenarios) are available for New Mexico All models and scenarios have very different projections for total patient arrivals





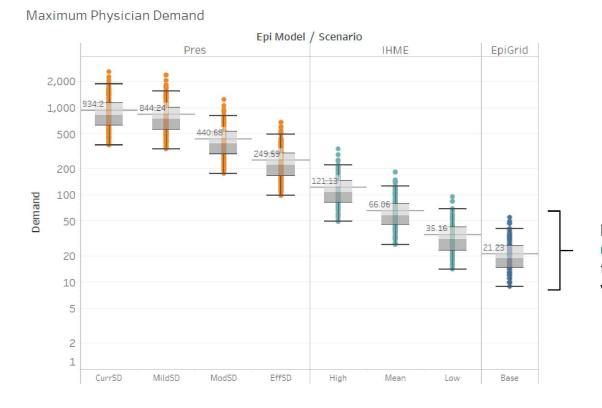
Results are presented in three ways:

- Dot plots that show range of maximum value for resource needs across all scenarios
- Table that shows mean values across all scenarios
- Time series with mean and 5th-95th percentiles

Analysis I: Results

Given the variation in possible patient arrivals, there is a wide range of resource demands as output from our model

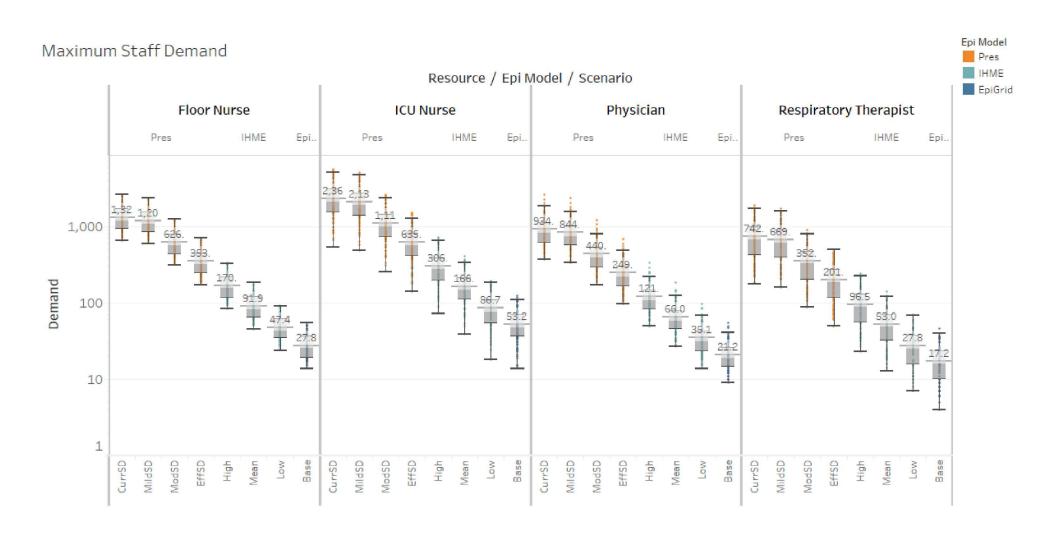
Example for Physician demand:



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

Analysis I: Results

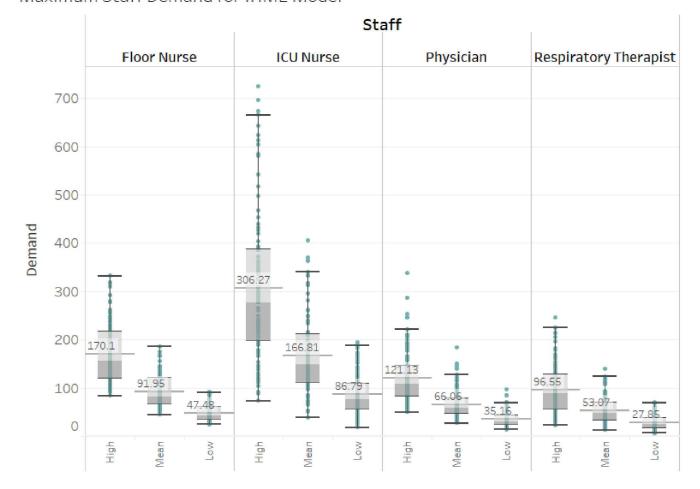
Compare staff demand across all epi models and scenarios



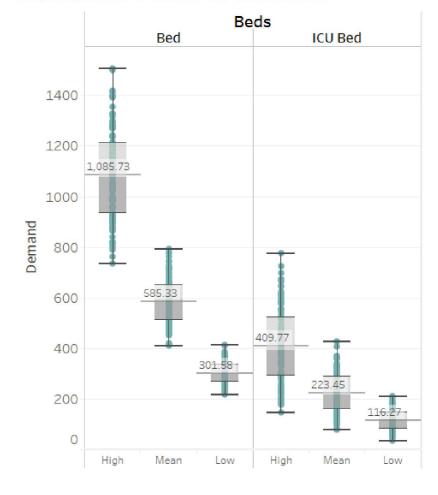
Analysis I: Results For IHME Patient Arrivals

Choose a subset of epi models to see all resource needs (slide 1 of 2)

Maximum Staff Demand for IHME Model



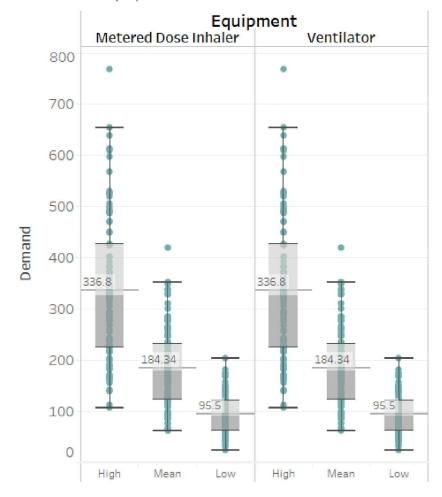
Maximum Bed Demand for IHME Model



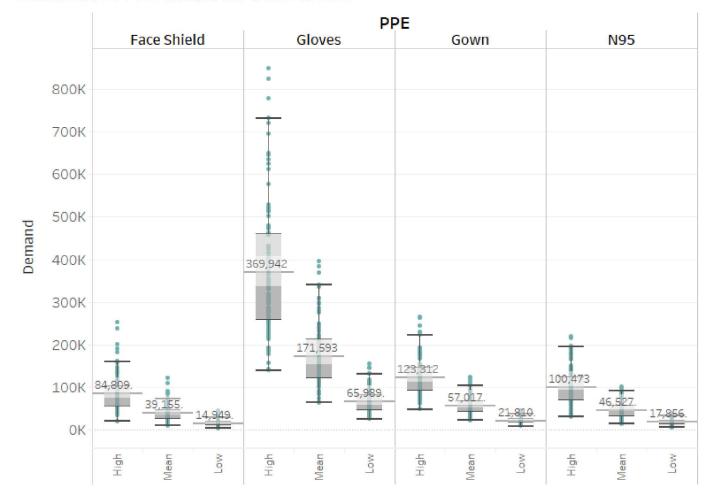
Analysis I: Results For IHME Patient Arrivals

Choose a subset of epi models to see all resource needs (slide 2 of 2)

Maximum Equipment Demand for IHME Model



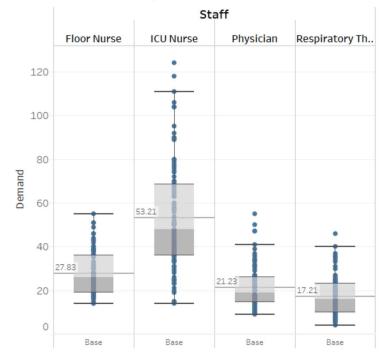
Cumulative PPE Demand for IHME Model



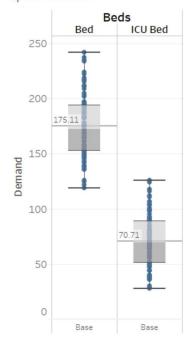
Analysis I: Results For EpiGrid Patient Arrivals

All resource needs for only the EpiGrid model

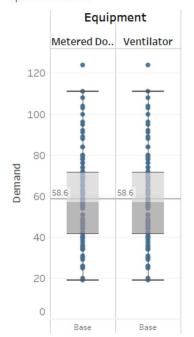




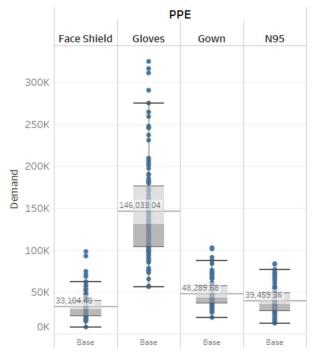
Max Bed Demand for EpiGrid Model



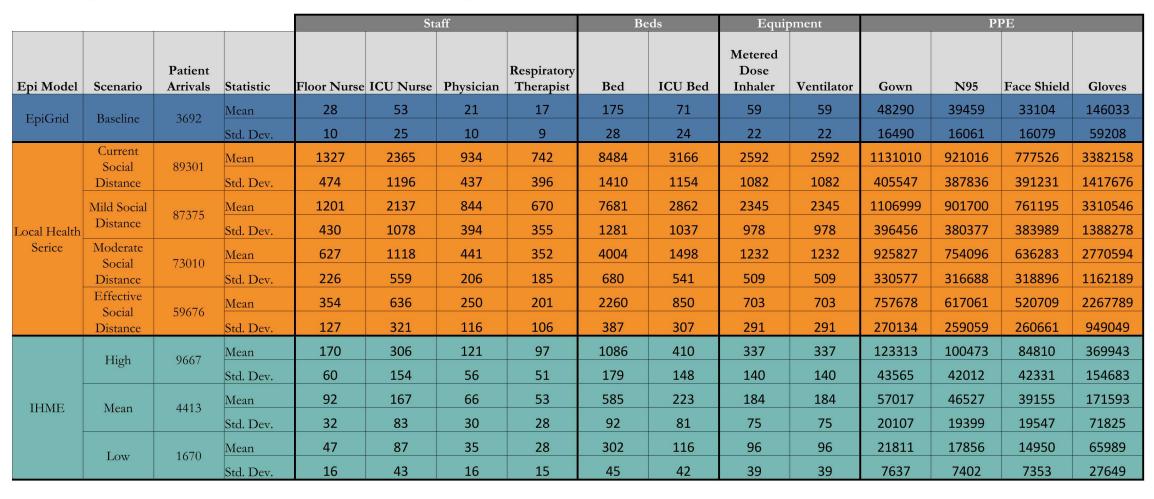
Max Equipment Demand for EpiGrid Model



Cumulative PPE Demand for EpiGrid Model

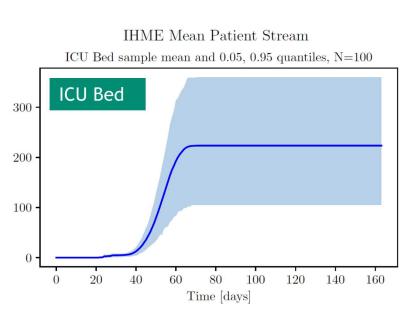


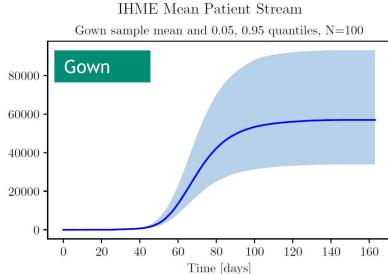
Analysis 1: Results, Summary Table

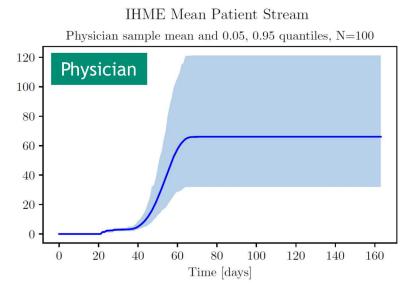


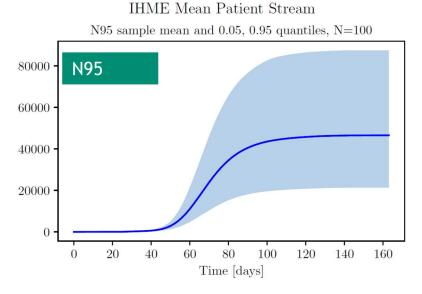
Analysis I: Results, Time Series for IHME Mean Patient Stream







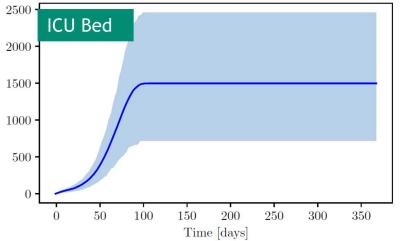




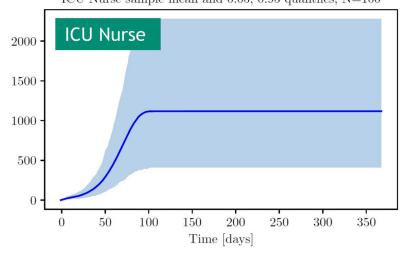
Analysis I: Results, Time Series for Patient Stream Forecast from a Local Health Service Model



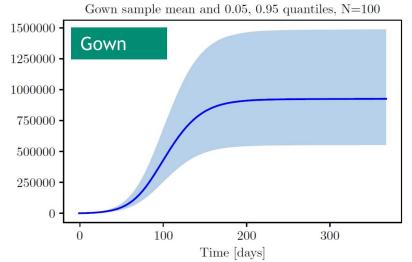
Presbyterian Patient Stream, Moderate Social Distancing ICU Bed sample mean and 0.05, 0.95 quantiles, N=100



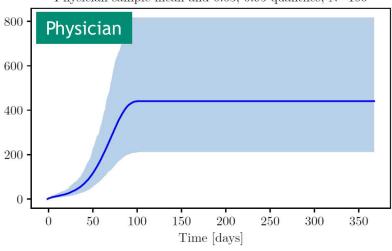
Presbyterian Patient Stream, Moderate Social Distancing ICU Nurse sample mean and $0.05,\,0.95$ quantiles, N=100



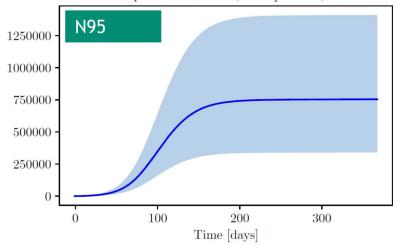
Presbyterian Patient Stream, Moderate Social Distancing



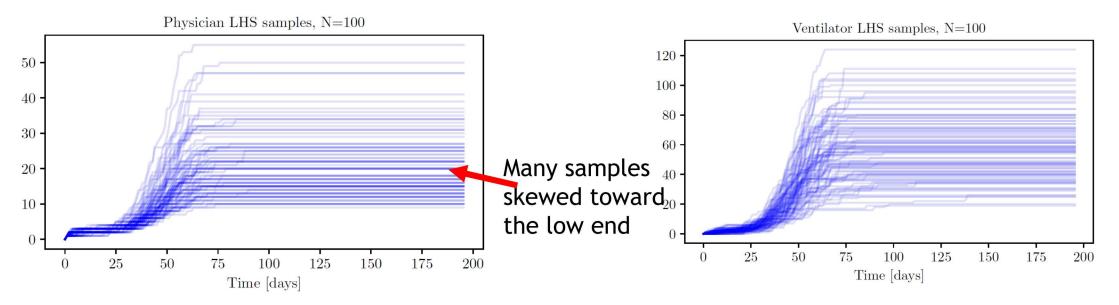
Presbyterian Patient Stream, Moderate Social Distancing Physician sample mean and 0.05, 0.95 quantiles, N=100

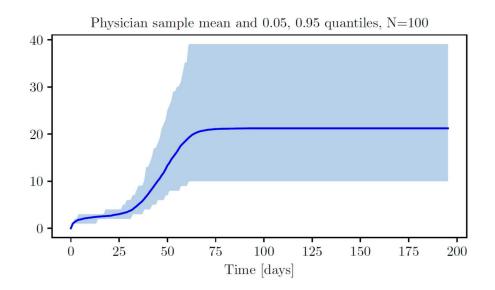


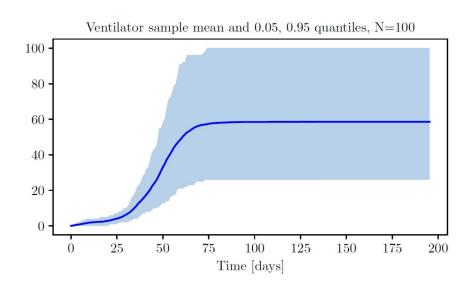
Presbyterian Patient Stream, Moderate Social Distancing N95 sample mean and 0.05, 0.95 quantiles, N=100



Analysis I: Results, Time Series for EpiGrid Patient Stream



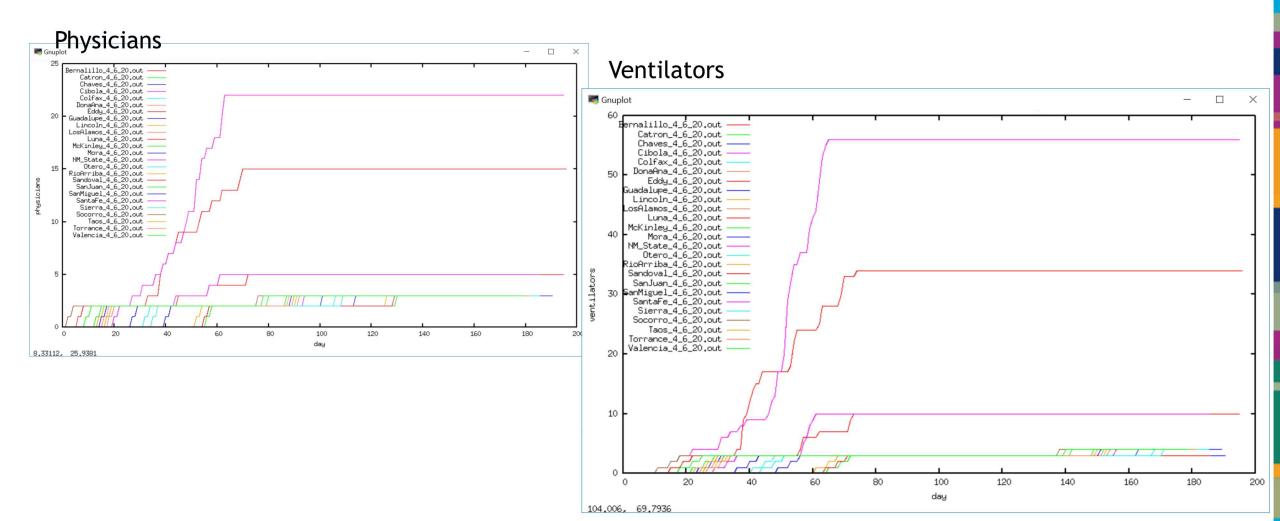




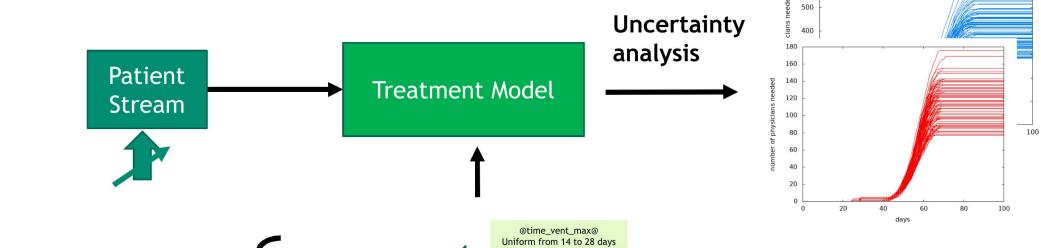
Analysis I: County-Level



Using EpiGrid county-level projections for New Mexico



Analysis Plan – Policy scanning



Possible treatment paths, durations, outcomes

@prob_vent@
Uniform from 50% to 100%

@prob_icu@
Uniform from 5% to
30%

Pati
ent

Pati
ent

Nurse

@prob_death_vent@
Uniform from 50% to
30%

Nurse

@prob_death_vent@
Uniform from 50% to
8 100%

**Nurse

@prob_death_novent
@
prob_death_novent
@

Resources required by specific practitioners and contexts

Resources needed to treat patient load

- Practitioners by specialty
- PPE of different kinds
- Other resources per NMHA needs

Bending the Curve

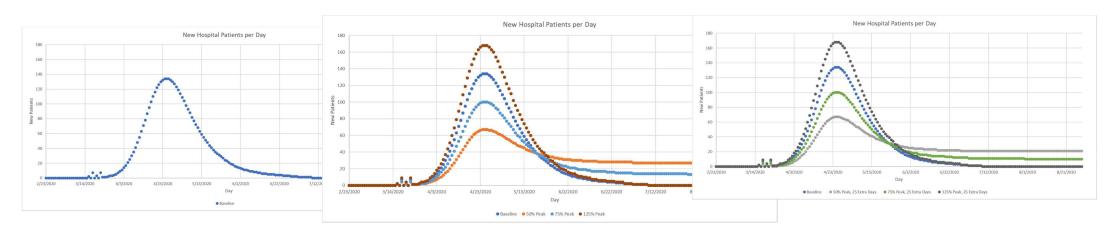
A process developed to synthetically modify patient curves to simulate changes to epidemiological results.

These do not represent epidemiological results of policies (social distancing, stay-at-home, etc.) but rather are notional examples of what the effects of "bending the curve" is on resource usage.

Patient curve modification can address multiple goals:

- Reducing peak but maintaining the same number of patients over time
- Extending the time horizon
- Matching the curve shape to a specific patient count

Example Using IHME Mean (number of patients kept constant)



2/23/2020

3/14/2020

4/23/2020

5/13/2020

6/2/2020

Day

• Baseline • 50% Peak • 75% Peak • 125% Peak

6/22/2020

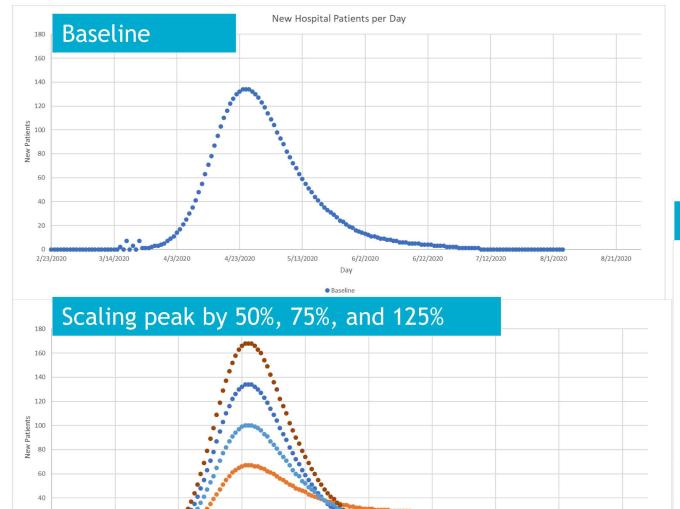
7/12/2020

8/1/2020

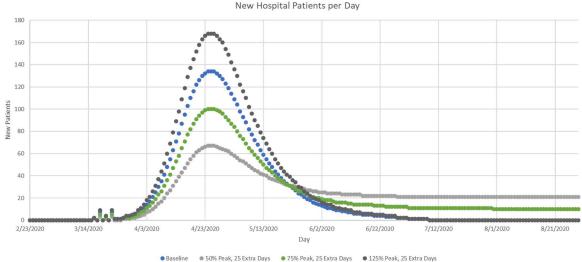
8/21/2020

Bending the Curve

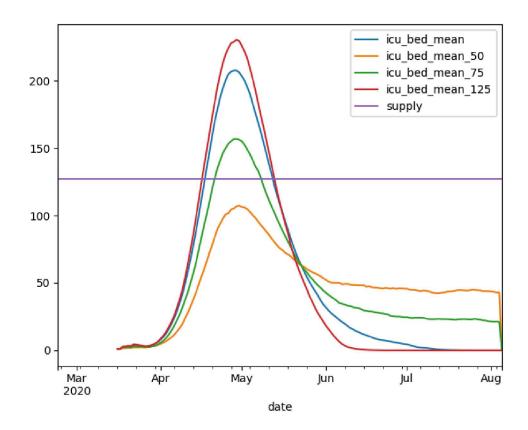
Example using IHME mean (number of patients kept constant)



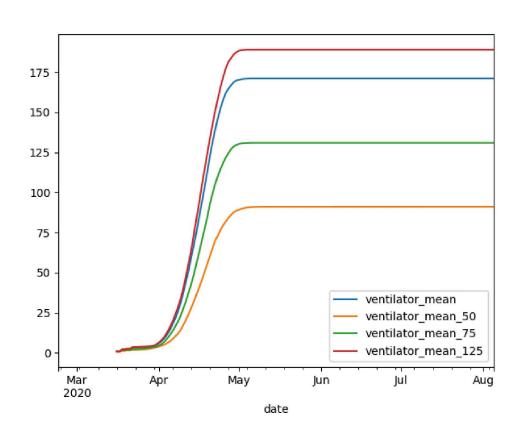
Scaling peak and adding 25 extra days



Results – Analysis 2 – Flatter curves require fewer re-usable assets

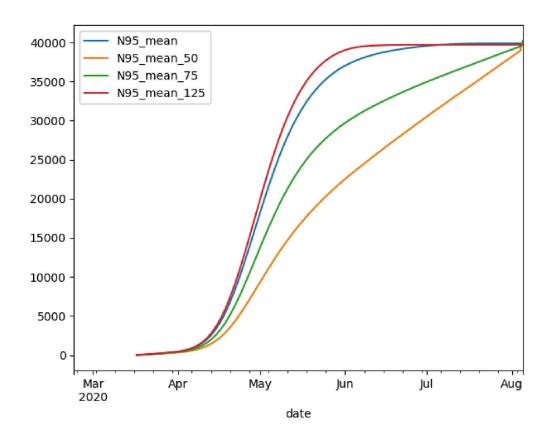


ICU Occupancy



Maximum Number of Ventilators

Results – Analysis 2 – Flatter curves lower required supply rates



Total Number of N95 Masks

Next steps

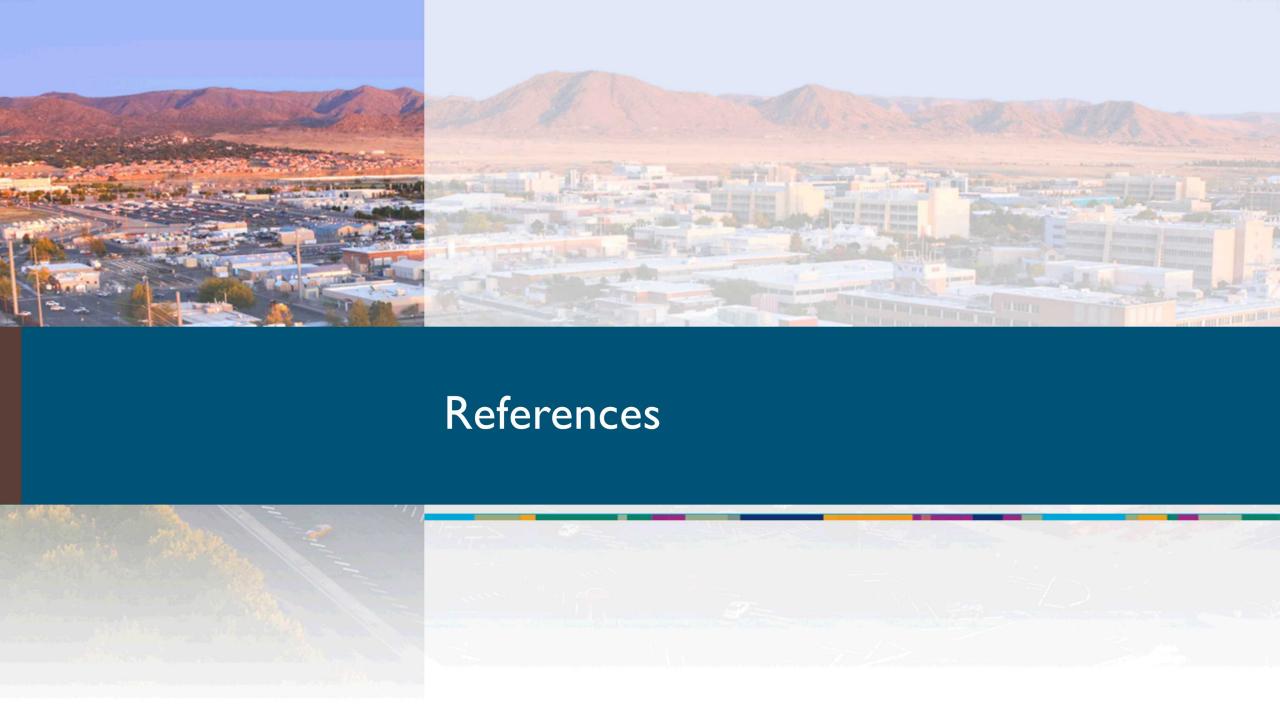
Application at national- or potentially hospital- scale. Prioritize regional analyses of New York, Chicago, Baltimore, DC, South Florida, New Orleans. Washington State, Los Angeles

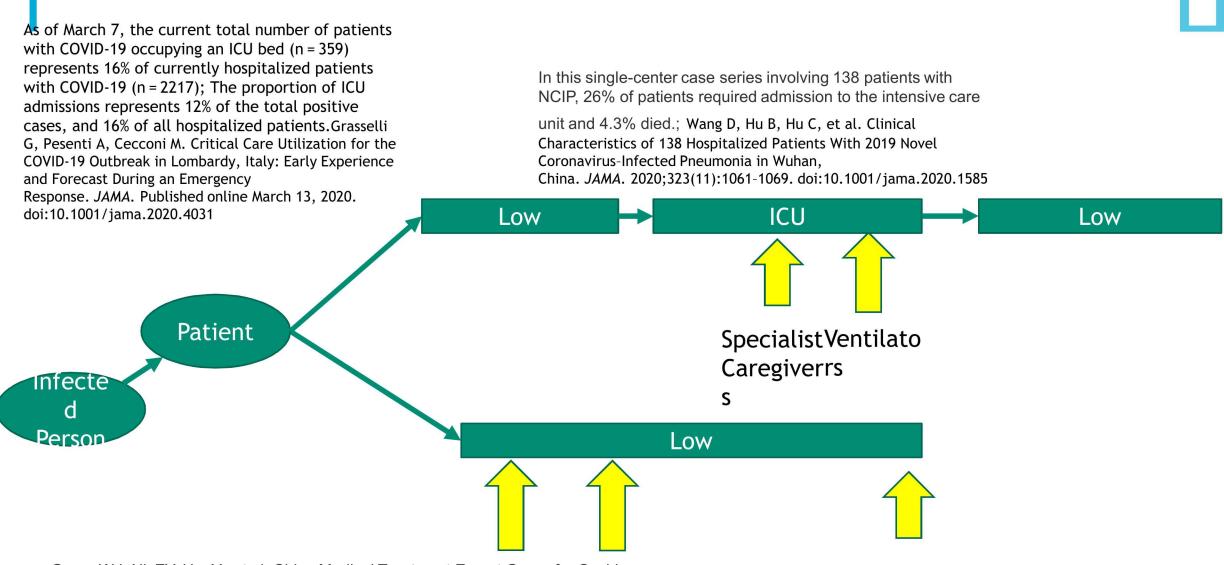
Assessing resource risk entails comparing demand and supply. Current databases estimate supplies of some critical assets (ICU beds, possibly staffing) at the hospital level, and larger-scale aggregate data are also available. Probability distributions of resource demands can be compared to these static estimates to derived resource-and time-dependent estimates of resource exhaustion.

Include simple models of resource dynamics (production, consumption, and redistribution). Use to refine resource exhaustion risk as well as the effectiveness of policies or endogenous processes like re-use and sharing in reducing exhaustion risk.

Case studies and hospital expansion plans can be reviewed to define concrete scenarios as well as estimating expansion time constants for more general modeling. Similarly, resource sharing can be studied using case studies as templates, as diffusive processes potentially constrained by political and institutional boundaries. I may also be approached as an optimization problem.

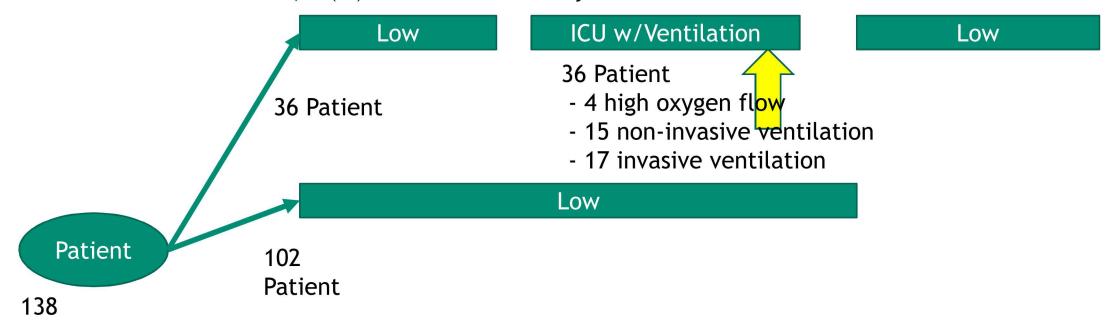
Resource dynamics modeling can help define the efficacy of policies designed to move resources from regions of large current need to regions of growing need. The UQ framework enables the robust evaluation given that the development path of outbreaks in different regions may be highly uncertain.





Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. doi: 10.1056/NEJMoa2002032

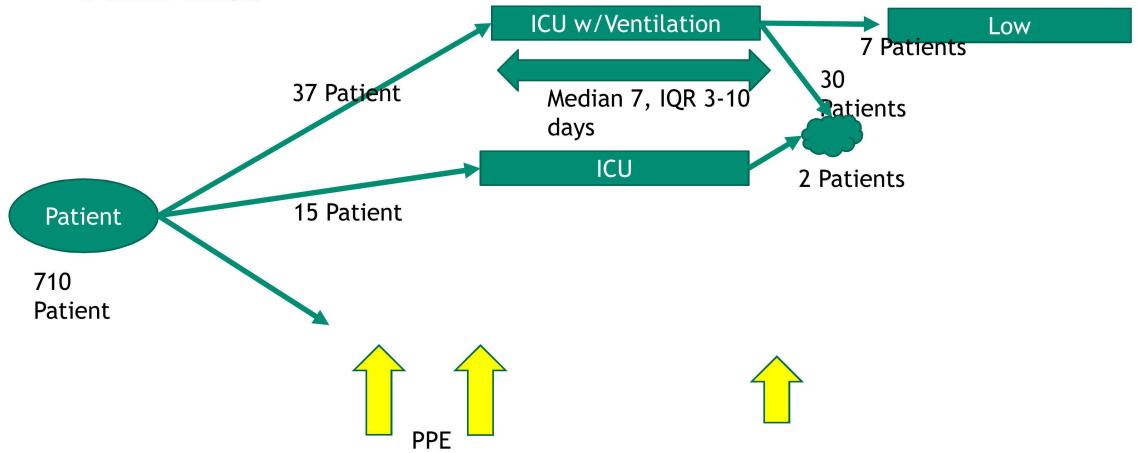
Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585



Patient Of 138 hospitalized patients with NCIP, the median age was 56 years (interquartile range, 42-68; range, 22-92 years) and 75 (54.3%) were men. Hospital-associated transmission was suspected as the presumed mechanism of infection for affected health professionals (40 [29%]) and hospitalized patients (17 [12.3%]). Common symptoms included fever (136 [98.6%]), fatigue (96 [69.6%]), and dry cough (82 [59.4%]). Lymphopenia (lymphocyte count, 0.8 × 10⁹/L [interquartile range {IQR}, 0.6-1.1]) occurred in 97 patients (70.3%), prolonged prothrombin time (13.0 seconds [IQR, 12.3-13.7]) in 80 patients (58%), and elevated lactate dehydrogenase (261 U/L [IQR, 182-403]) in 55 patients (39.9%). Chest computed tomographic scans showed bilateral patchy shadows or ground glass opacity in the lungs of all patients. Most patients received antiviral therapy (oseltamivir, 124 [89.9%]), and many received antibacterial therapy (moxifloxacin, 89 [64.4%]; ceftriaxone, 34 [24.6%]; azithromycin, 25 [18. Pp] Fand glucocorticoid therapy (62 [44.9%]). Thirty-six patients (26.1%) were transferred to the intensive care unit (ICU) because of complications, including acute respiratory distress syndrome (22 [61.1%]), arrhythmia (16 [44.4%]), and shock (11 [30.6%]). The median time from first symptom to dyspnea was 5.0 days, to hospital admission was 7.0 days, and to ARDS was 8.0 days. Patients treated in the ICU (n = 36), compared with patients not treated in the ICU (n = 102), were older (median age, 66 years vs 51 years), were more likely to have underlying comorbidities (26 [72.2%] vs 38 [37.3%]), and were more likely to have dyspnea (23 [63.9%] vs 20 [19.6%]), and anorexia (24 [66.7%] vs 31 [30.4%]). Of the 36 cases in the ICU, 4 (11.1%) received high-flow oxygen therapy, 15 (41.7%) received noninvasive ventilation, and 17 (47.2%) received invasive ventilation (4 were switched to extracorporeal membrane oxygenation). As of February 3, 47 patients (34.1%) were discharged and 6 died (overall mortality, 4.3%), but the remaining patients are still hospitalized. Among those discharged alive (n = 47), the median hospital stay was 10 days (IQR, 7.0-14.0).

Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study.

Yang X¹, Yu Y², Xu J², Shu H², Xia J³, Liu H¹, Wu Y², Zhang L⁴, Yu Z⁵, Fang M⁶, Yu T³, Wang Y², Pan S², Zou X², Yuan S², Shang Y⁷.



Of 710 patients with SARS-CoV-2 pneumonia, 52 critically ill adult patients were included. The mean age of the 52 patients was 59·7 (SD 13·3) years, 35 (67%) were men, 21 (40%) had chronic illness, 51 (98%) had fever. 32 (61·5%) patients had died at 28 days, and the median duration from admission to the intensive care unit (ICU) to death was 7 (IQR 3-11) days for non-survivors. Compared with survivors, non-survivors were older (64·6 years [11·2] vs 51·9 years [12·9]), more likely to develop ARDS (26 [81%] patients vs 9 [45%] patients), and more likely to receive mechanical ventilation (30 [94%] patients vs 7 [35%] patients), either invasively or non-invasively. Most patients had organ function damage, including 35 (67%) with ARDS, 15 (29%) with acute kidney injury, 12 (23%) with cardiac injury, 15 (29%) with liver dysfunction, and one (2%) with pneumothorax. 37 (71%) patients required mechanical ventilation. Hospital-acquired infection occurred in seven (13·5%) patients.

Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12-March 16, 2020 - CDC

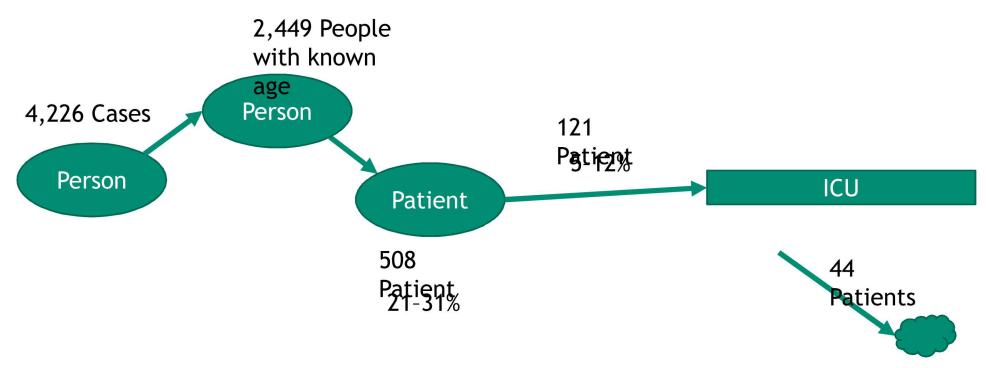
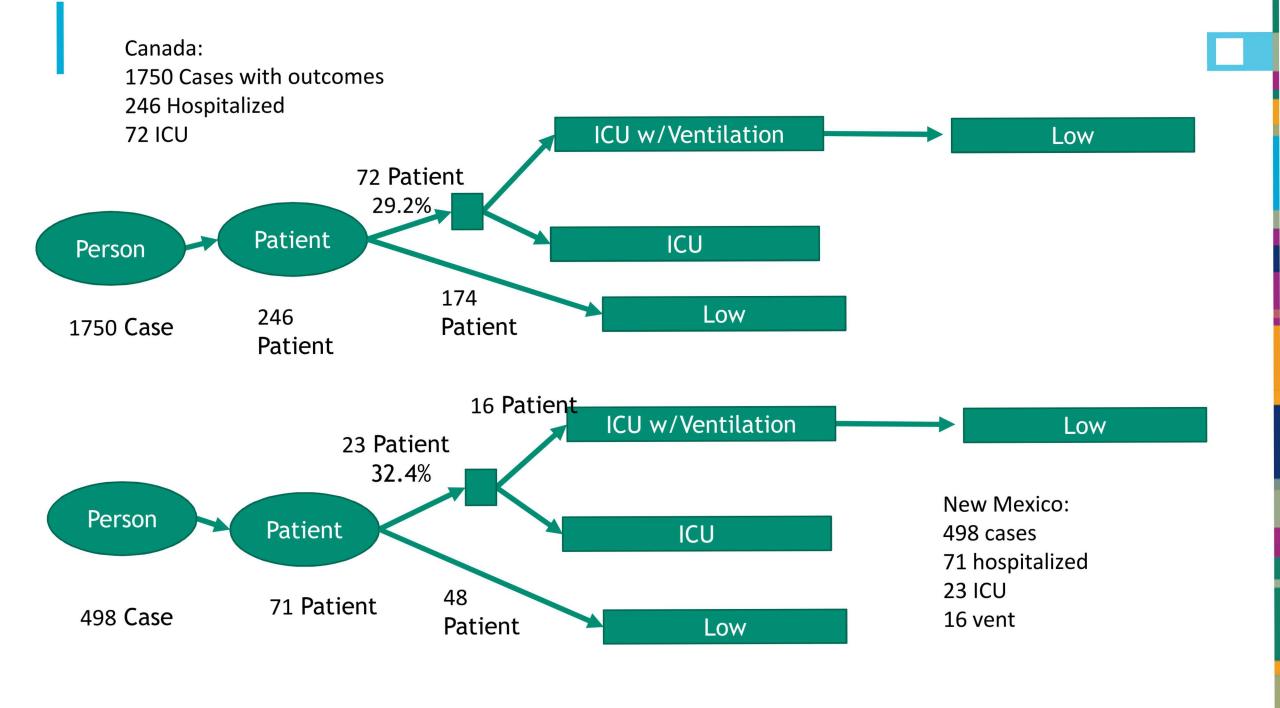
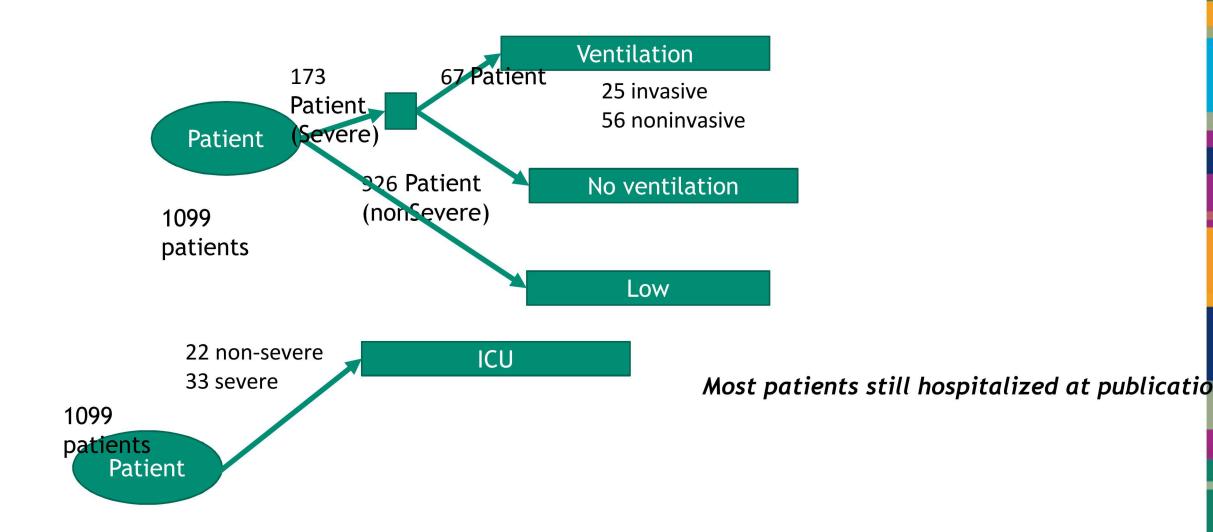


TABLE. Hospitalization, intensive care unit (ICU) admission, and case- fatality percentages for reported COVID-19 cases, by age group — United States, February 12-March 16, 2020 Age group (yrs) (no. of cases) %* Hospitalization ICU admission Case-fatality 0-19 (123) 1.6-2.5 0 0 20-44 (705) 14.3-20.8 2.0-4.2 0.1-0.2 45-54 (429) 21.2-28.3 5.4-10.4 0.5-0.8 55-64 (429) 20.5-30.1 4.7-11.2 1.4-2.6 65-74 (409) 28.6-43.5 8.1-18.8 2.7-4.9 75-84 (210) 30.5-58.7 10.5-31.0 4.3-10.5 ≥85 (144) 31.3-70.3 6.3-29.0 10.4-27.3 Total (2,449) 20.7-31.4 4.9-11.5 1.8-3.4 * Lower bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group; upper bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group with known hospitalization status, ICU admission status, or death.



Clinical Characteristics of Coronavirus Disease 2019 in China .Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., et al. doi: 10.1056/NEJMoa2002032; 10.1056/NEJMoa2002032; New England Journal of Medicine; Massachusetts Medical Society; 0028-4793; UR - https://doi.org/10.1056/NEJMoa2002032;2020/04/04



Estimates of the severity of coronavirus disease 2019:

a model-based analysis

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In the subset of 24 deaths from COVID-19 that occurred in mainland China early in the epidemic, with correction for bias introduced by the growth of the epidemic, we estimated the mean time from onset to death to be 18·8 days (95% credible interval [CrI] 15·7-49·7; figure 2) with a coefficient of variation of 0·45 (95% CrI 0·29-0·54). With the small number of observations in these data and given that they were from early in the epidemic, we could not rule out many deaths occurring with longer times from onset to death, hence the high upper limit of the credible interval. However, given that the epidemic in China has since declined, our posterior estimate of the mean time from onset to death, informed by the analysis of aggregated data from China, is more precise (mean 17·8 days [16·9-19·2]; figure 2).

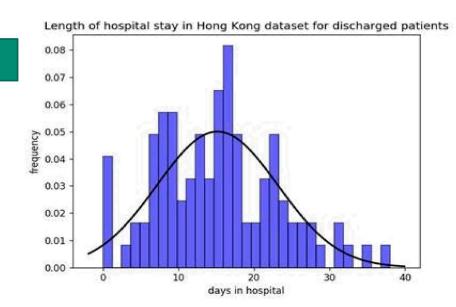
Using data on the outcomes of 169 cases reported outside of mainland China, we estimated a mean onset-to-recovery time of 24·7 days (95% Crl 22·9-28·1) and coefficient of variation of 0·35 (0·31-0·39; figure 2). Both these onset-to-outcome estimates are consistent with a separate study in China.

24.7 days (95% Crl 22.9-28.1)

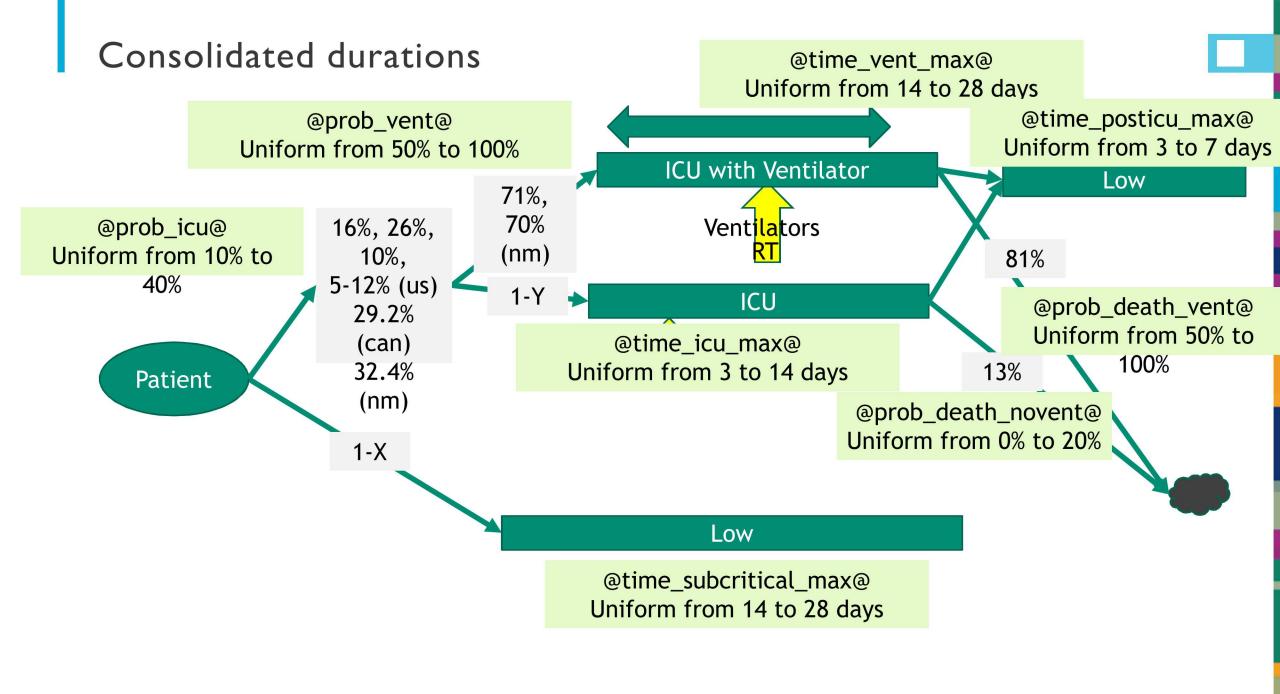
Onset to Recovery

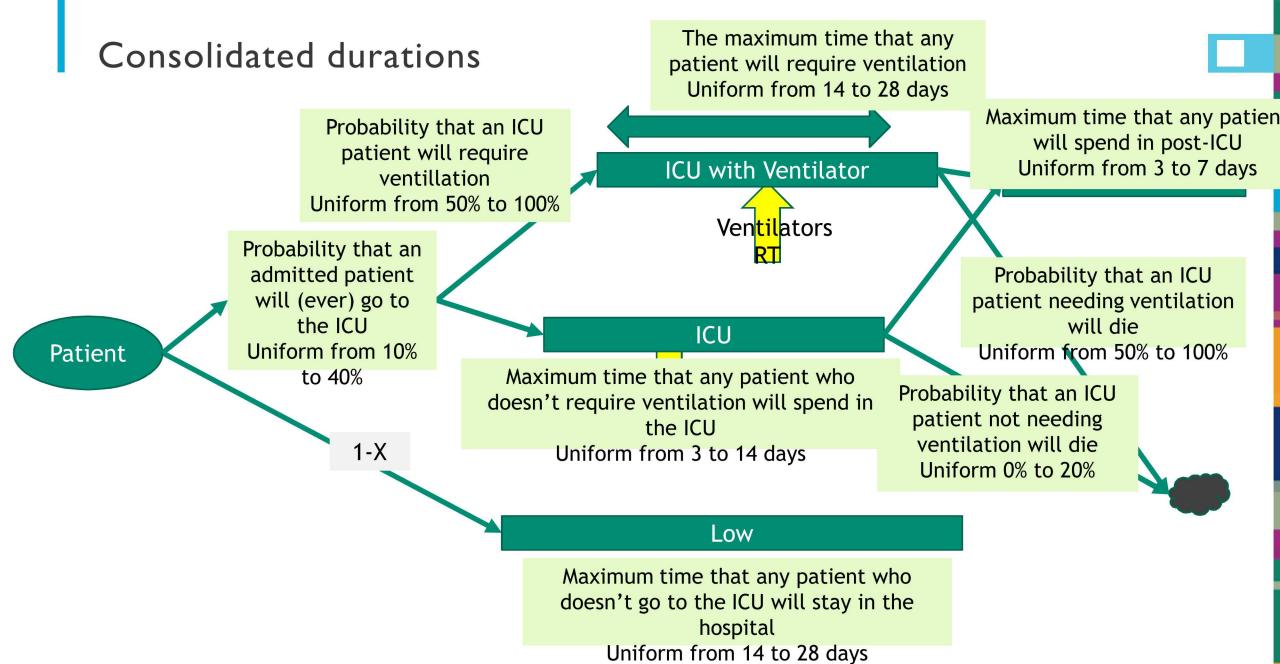
Onset to Death (mean 17.8 days [16.9-19.2]

Admission to Discharge



,	HOSPITAL_ICU_S TAY	TimeInHospit alm(D)
		, ,
	No	0
	No	0
	No	1
	Yes	2
	Yes	2
	No	2
	No	2
		3
	Unknown	3
	Yes	4
	No	4
		4
	Unknown	7
	No	8
	Yes	14
		19

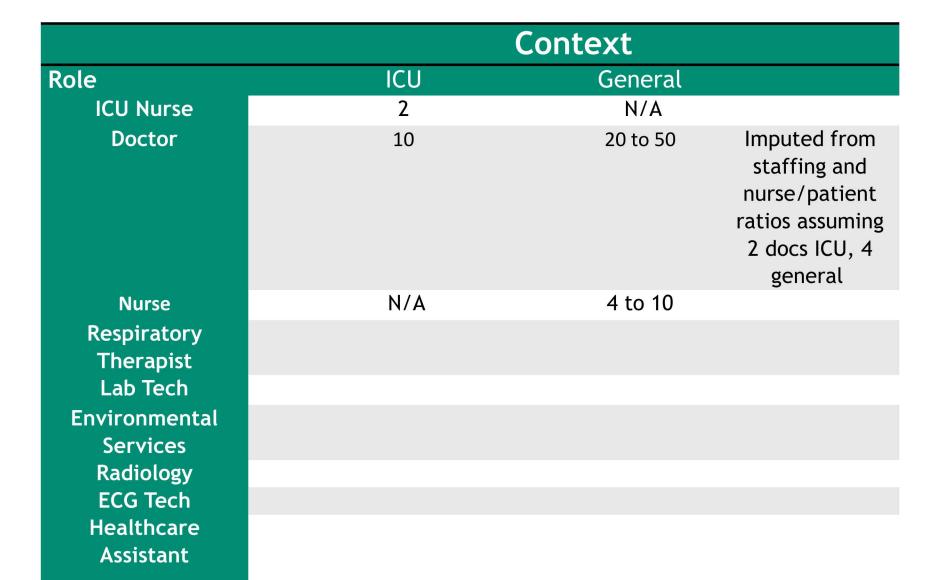




Resource Use

Local health service planning numbers

Staffing – Number of patients per practitioner



PPE

		ICU							Gen	eral		
Units used per shift						Units used per shift						
Practitioner	Go	N95	Gloves	Face		Practitione	r	Go	N95	Gloves	Face	
	wns	Mask		Shield				wns	Mask		Shield	
Floor Nurse	2	1	8	1		Floor Nurse	9	2	1	8	1	
ICU Nurse	2	1	12	1		ICU Nurse		2	1	12	1	
Doctor	2	1	12	1		Doctor		2	1	12	1	
Healthcare Assistant	2	1	8	1		Healthcare Assistant		2	1	8	1	
Environment	4	1	16	1		Environmer		4	1	16	1	
al Services		4	12	4		al Services			4	4.2	4	
Lab Tech	2	1	12	1		Lab Tech		2	1	12	1	
RT	2	1	8	1		RT		2	1	8	1	
Radiology	2	1	8	1		Radiology		2	1	8	1	
ECG Tech	2	1	8	1		ECG Tech		2	1	8	1	

Drugs



Review/Evaluation of NMHA data

Staffing – Number of patients per practitioner

		Context	
Role	ICU	General	
ICU Nurse	1 to 2	N/A	
Doctor	2 to 4	21	
Nurse	N/A	4 to 7	
Respiratory Therapist	4		
Lab Tech			
Environmental Services			
Radiology			
ECG Tech			
Healthcare Assistant			

PPE

		ICU							Gen	eral		
Units used per shift						Units used per shift						
Practitioner		N95 Mask	Gloves	Face Shield		Practitione	r		N95 Mask	Gloves	Face Shield	
Floor Nurse						Floor Nurse	е	3	3	3	1	
ICU Nurse	4	4	4	4		ICU Nurse						
Doctor	1	1	1	1		Doctor		1	1	1	1	
Healthcare						Healthcare	9					
Assistant						Assistant						
Environment						Environmer	nt					
al Services						al Services	5					
Lab Tech						Lab Tech						
RT						RT						
Radiology						Radiology						
ECG Tech						ECG Tech						

	Пки	T.C.						
				Supplies				
			Units used per patient per shift					
Н	ospital	Practitioner	Sedatives/drugs: Succinylcholine/ rocuronium Etomidate; Propofol Metered Dose Inhalers - Albuterol, (Ventolin); Azithromycin Plaquenil (hydroxychloroquine) Fentanyl; hydromorphine; IV fluids; TPN (Total Parenteral Nutrition) Lipids; dopamine		Conte	Drugs and routinely administered meds were separated out from equipment Some drugs are administered more often than others, while equipment may be just 1 per person until they need a new one		
	Cibola Grants	ICU Nurse	1- 4 (dose dependent)/patient; Maybe 6-8/patient (shortage)	1 or less/patient NA (IV pump)	ICU	4 bed ICU; 21 non-ICU beds		
	LLMC		1- 4 (dose dependent)/patient;	1 or less/patient	ICU	263 total beds;		

Additional Sources

ICU - 12 to 16 per patient per day
GW - 8 per patient per day

Per CDC cited in: Potential Demand for Respirators and Surgical Masks During a Hypothetical Influenza Pandemic in the United States

Cristina Carias, Gabriel Rainisch, Manjunath Shankar, Bishwa B. Adhikari, David L. Swerdlow, William A. Bower, Satish K. Pillai, Martin I. Meltzer, and Lisa M. Koonin. National Center for Immunization and Respiratory Diseases (NCIRD), JHRC, Inc, Division of Preparedness and Emerging Infections, National Center for Emer