Large-Scale Agent-Based Epidemiological Modeling

CLSAC 2020: Analytics for Pandemic Decision Support

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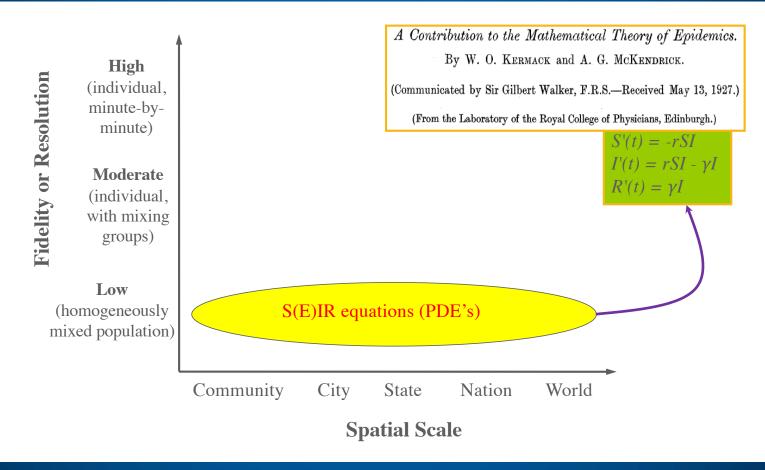
tcg@lanl.gov

October 6, 2020





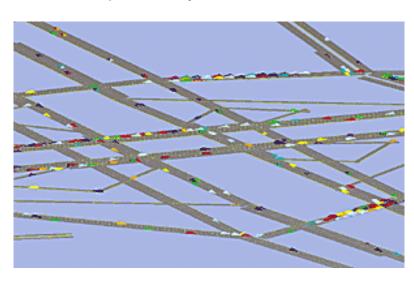
Oversimplified Epidemiological Model Landscape



LANL has a long history applying agent-based simulation to real-world issues

Transportation Simulation System (TRANSIMS)

 TRANSIMS is an event-driven agent-based simulation developed at LANL for simulating movement of people on the transportation system



The Epidemic Simulation System (EpiSimS) is derived from TRANSIMS

 EpiSimS is an agent-based simulation developed at LANL for simulating the spread of epidemics at the level of individuals



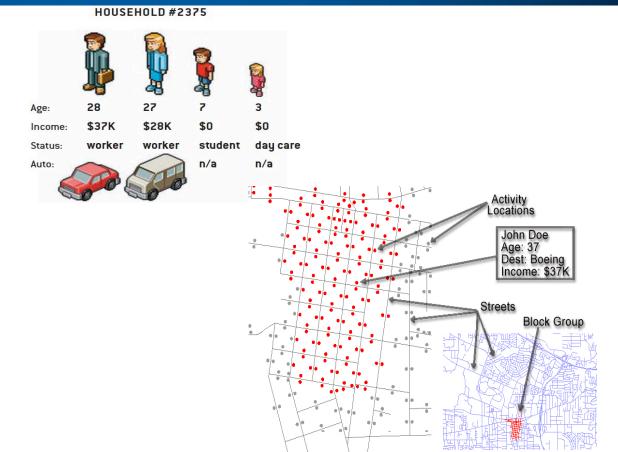
Epidemic Simulation System (EpiSimS)

Agent-based model to simulate disease spread in large regions

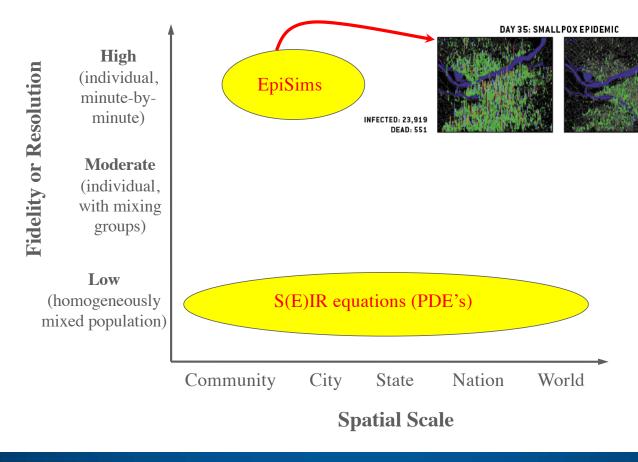
- Detail person-to-person contact on a minute-by-minute basis
- Workforce absenteeism by NAICS
- Explicit geography, demographics, social contact networks, and mitigations

Data Sources

- U.S. Census data
- Dun & Bradstreet business directory
- National Household Transportation Survey from U.S. DOT



Oversimplified Epidemiological Model Landscape



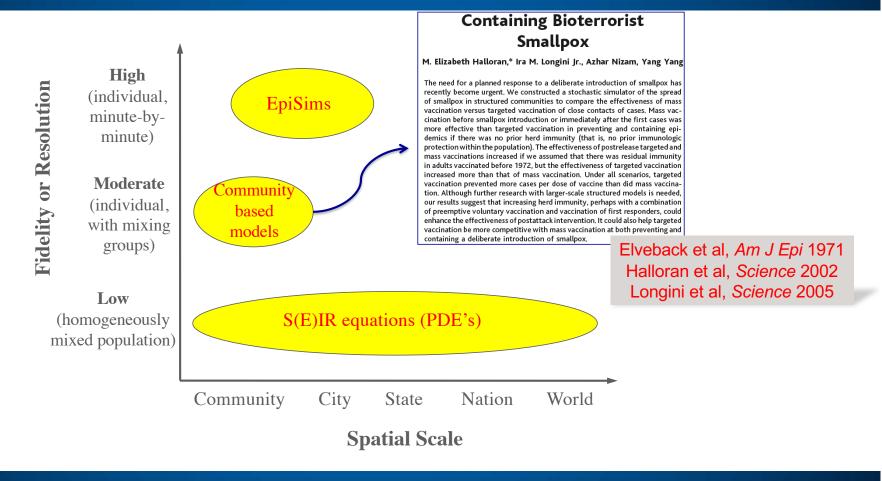
Scientific American
March 2005

INFECTED: 2,564 QUARANTINED: 29,910 VACCINATED: 30,560 DEAD: 312



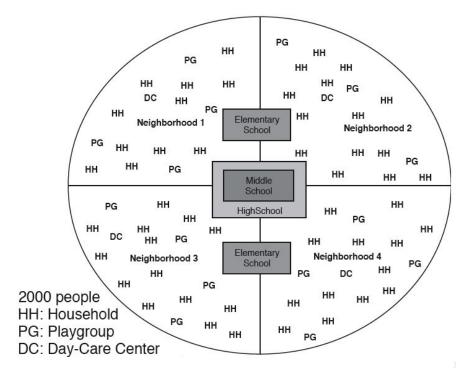


Oversimplified Epidemiological Model Landscape



Person-to-person transmission is represented via contact groups within a ~2000-person model community

Different cultures or modes of transmission may require different sets of contact (mixing) groups.



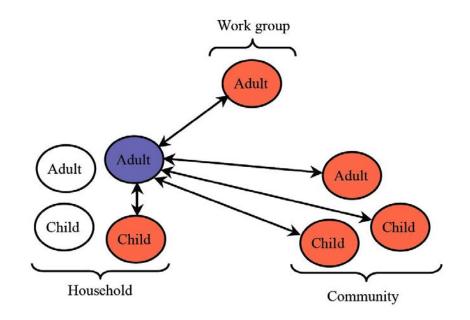
M. E. Halloran et al, Science 298, 1428 (2002);

I. M. Longini et al, Science 309, 1083 (2005).

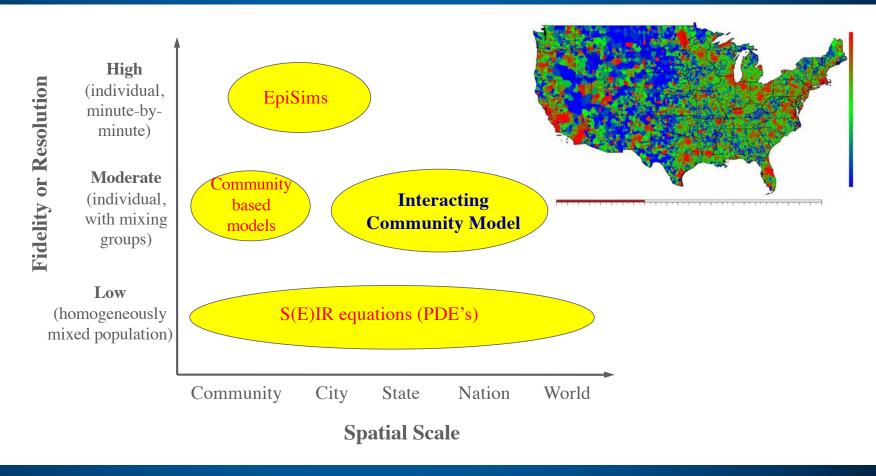
Stochastic Transmission with half-day timesteps

$$P = 1 - (1 - p_{HH}^{c \to a}) \cdot (1 - p_{WG}^{a \to a}) \cdot (1 - p_{Comm}^{a \to a}) \cdot (1 - p_{Comm}^{c \to a})^{2}$$

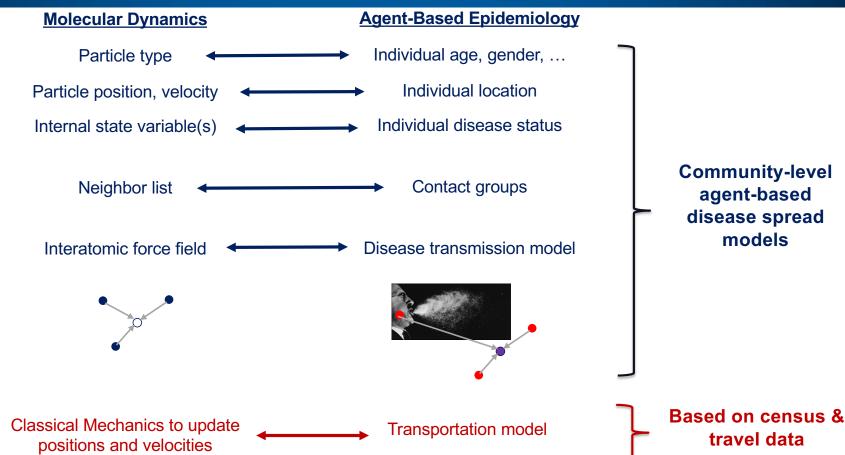
- Person-to-person transmission is represented via contact groups within a ~2000-person model community
- Each susceptible individual has a probability of becoming infected by infectious individuals in their contact groups during each 12-hour timestep
- These probabilities may be further modified if the infectious and/or susceptible individuals are adopting social distancing measures, taking antivirals, or have been vaccinated



Oversimplified Epidemiological Model Landscape

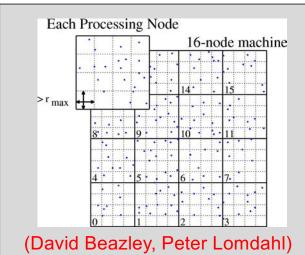


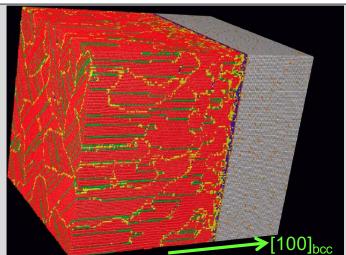
Agent-based epidemiological methods map directly to particle-based MD simulations



Scalable Parallel Short-range Molecular dynamics (SPaSM) is a high-performance code for studying large systems of interacting "particles"

- Finite-range (r_{max}) interactions $\Rightarrow O(N)$ computational scaling
- Spatial decomposition on shared and distributed memory architectures
- 1993 IEEE Gordon Bell Performance Prize (50 Gflop/s on LANL/Thinking Machines CM-5)
- 1998 IEEE Gordon Bell Price / Performance Prize (10 Gflop/s on Linux/Alpha Beowulf cluster, \$15/Mflop)
- 2005 IEEE Gordon Bell Prize Finalist (48 Tflop/s on LLNL/IBM BlueGene/L)
- 2008 IEEE Gordon Bell Prize Finalist (369 Tflop/s on LANL/IBM Roadrunner)
- Object-oriented scripting language with parallel visualization and analysis libraries (runtime "steering")





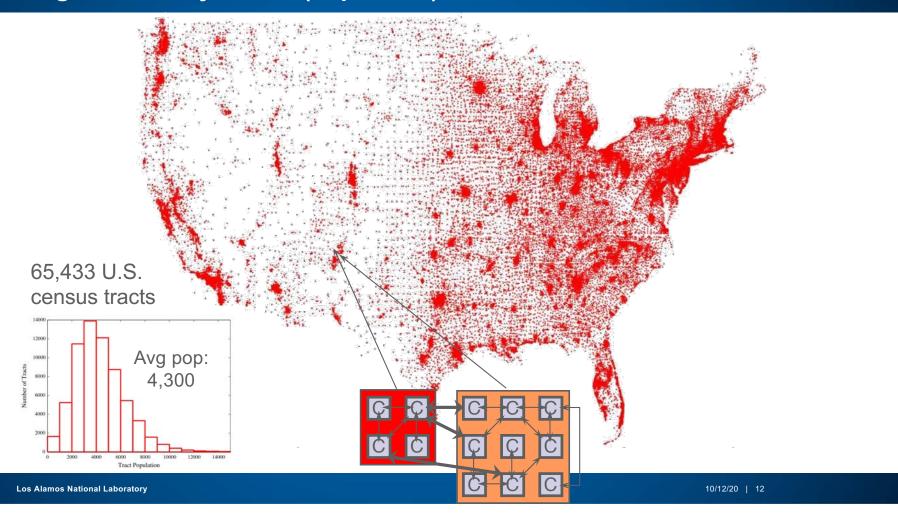
Microscopic View of Structural Phase Transitions Induced by Shock Waves

Kai Kadau, 1,2* Timothy C. Germann, Peter S. Lomdahl, Brad Lee Holian 1

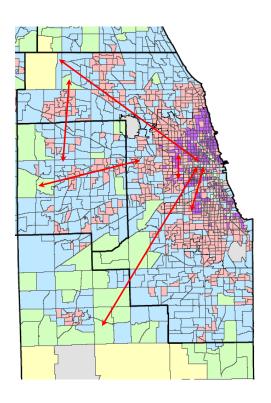
Multimillion-atom molecular-dynamics simulations are used to investigate the shock-induced phase transformation of solid iron. Above a critical shock strength, many small close-packed grains nucleate in the shock-compressed body-centered cubic crystal growing on a picosecond time scale to form larger, energetically favored grains. A split two-wave shock structure is observed immediately above this threshold, with an elastic precursor ahead of the lagging transformation wave. For even higher shock strengths, a single, overdriven wave is obtained. The dynamics and orientation of the developing close-packed grains depend on the shock strength and especially on the crystallographic shock direction. Orientational relations between the unshocked and shocked regions are similar to those found for the temperature-driven martensitic transformation in iron and its alloys.

Science **296**, 1681 (31 May 2002)

U.S. Census population & worker flow data are utilized to construct an interacting community model ("EpiCast")



Residential and workplace communities for synthetic population matches Census data



We use U.S. Census Bureau data on tract-level demographics and worker-flow, and Dept. of Transportation data on irregular long-range travel to assign fixed residential and workplace communities to each individual, in addition to infrequent visits to more distant communities.

1,344 Cook County (IL) census tracts



Irregular long-distance travel is modeled including three factors

1. Trip Generation: Which individuals/households make a long distance trip?

Use age-dependent average number of trips per year to determine the daily probability of making a long-distance trip, then roll the dice for each person every day.

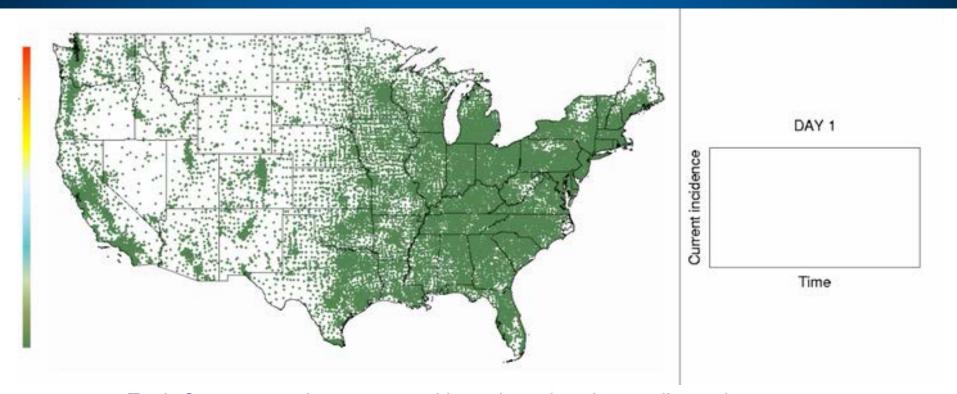
2. Destination Choice: Where do they go?

Simplistic gravity model: choose a random community within the simulation (either a 2,000-person residential or a 1,000-person workgroup-only community), without any distance dependence.

3. Trip Duration: How long do they stay there?

Use the national statistics on trip duration to choose a duration from 0-13 nights.

Baseline (unmitigated) pandemic, $R_0 = 1.9$



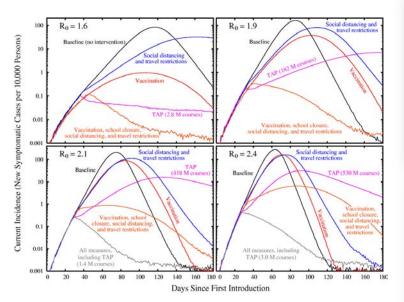
Each Census tract is represented by a dot colored according to its prevalence (number of symptomatic cases at any point in time) on a logarithmic color scale, from 0.3-30 cases per 1,000 residents.

Initial Application of the National EpiCast Model with Tract-level Resolution was to Pandemic Influenza

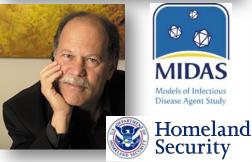
Mitigation strategies for pandemic influenza in the United States

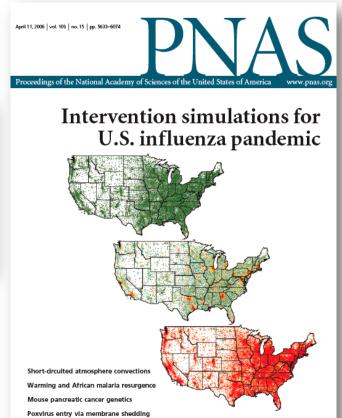
Timothy C. Germann*[†], Kai Kadau*, Ira M. Longini, Jr.[‡], and Catherine A. Macken*

*Los Alamos National Laboratory, Los Alamos, NM 87545; and [‡]Program of Biostatistics and Biomathematics, Fred Hutchinson Cancer Research Center and Department of Biostatistics, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98109









SPECIAL REPORT: PREPARING FOR PANDEMIC FLU IS ANYONE READY FOR THIS GLOBAL KILLER?

SCIENTIFIC AMERICAN

PANSPERMIA: Martian Cells Could Have Reached Earth

NOVEMBER 2005 WWW.SCIAM.COM

Pandemic Flu Hits the U.S.

A simulation created by researchers from Los Alamos National Laboratory and Emory University shows the first wave of a pandemic spreading rapidly with no vaccine or antiviral drugs employed to slow it down. Colors represent the number of sumptomatic flu cases per 1,000 people (see scale). Starting with 40 infected people on the first day. nationwide cases peak around day 60, and the wave subsides after four months with 33 percent of the population having become sick. The scientists are also modeling potential interventions with drugs and vaccines to learn if travel restrictions, quarantines and other disruptive disease-control



ABC's Good Morning America March 13, 2006









Nightline: March 14, 2006

The Economist April 8th 2006

Influenza

Just say "R"

Even a weak vaccine might be useful in an outbreak of influenza

ABRUTAL mathematics governs the spread of an infection. It is tied to what is known as the basic reproductive number, R_o. Whether the outbreak is of seasonal influenza, Ebola fever or bubonic plague, R_o tells you, for each person infected, how many others are likely to be infected later. The higher R_o is, therefore, the harder an infection is to control.

R_o is one of the many things scientists don't know about the virus that will cause the next pandemic of influenza, because that virus has not yet emerged. This is a problem, because it makes it hard to plan to minimise the impact of that outbreak.

One solution is to produce a virtual world in which various types of virus can be modelled. This is the approach taken by a team led by Timothy Germann, of the Los Alamos National Laboratory in New Mexico, and his colleagues. In a paper published in the Proceedings of the National Academy of Sciences, Dr Germann and his team describe a "virtual" population of 281m people distributed across a virtual version of the United States in accordance with census data. They have made assumptions about how often people mix with each other, where they mix (schools, workplaces and homes), and how often and how far they travel. This virtual world





Grim Scenario Predicted for Pandemic Flu

 $\underline{NPR.org}$, December 5, 2005 · Federal health officials meeting with state health authorities today are expected to paint a grim scenario of how a flu pandemic might unfold in America.

A federally financed study used supercomputers to predict what might happen if a virulent and easily spread new strain of flu entered the United States. The study was done by researchers at Emory University and Los Alamos National Laboratory.

They assumed the pandemic virus would leak into the country despite efforts to screen travelers for flu symptoms. If each infected person spread the virus to two others, large outbreaks of flu would occur all over the country within about two months after the virus began to spread. The national epidemic would peak around day 85, with about 4.5 million people falling ill that day. In the end, 122 million Americans may have gotten sick, more than four times the toll in a usual flu season. -- Richard Knox

We weren't prepared for how seriously policy-makers took our simulations....

5 days after the PNAS article:



... Many critical decisions remain to be made. Administration scientists are debating how much vaccine would be needed to immunize against a new strain of avian influenza, and they are weighing data that may alter their strategy on who should have priority for antiviral drugs such as Tamiflu and Relenza.

The new analysis, published in *Proceedings of the National Academy of Sciences*, suggests that instead of giving medicine to first responders and health-care workers, as currently planned, it might be wiser to give the drugs to every person with symptoms and others in the same household, **one senior administration official** said.

The approach offers "some real hope for communities to put a dent in the amount of illness and death, if we go with that strategy," a White House official said.

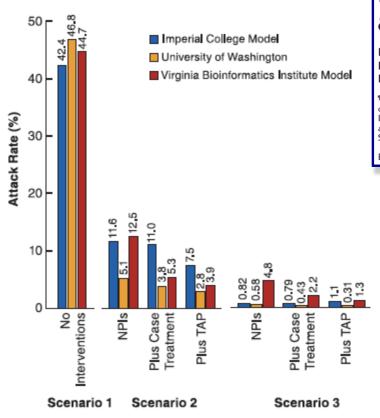
U.S. Plan For Flu Pandemic Revealed

Multi-Agency Proposal Awaits Bush's Approval

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Los Alamos National Laboratory 10/12/20 | 19 10/12/20 | 19

Cross-model Comparison of Community-based Targeted Layered Containment Strategies



Modeling targeted layered containment of an influenza pandemic in the United States

M. Elizabeth Halloran*†‡, Neil M. Ferguson⁵, Stephen Eubankⁿ, Ira M. Longini, Jr.*†, Derek A. T. Cummings⁵, Bryan Lewisⁿ, Shufu Xu†, Christophe Fraser⁵, Anil Vullikantiⁿ, Timothy C. Germannⁿ, Diane Wagener**, Richard Beckmanⁿ, Kai Kadauⁿ, Chris Barrettⁿ, Catherine A. Mackenゥ, Donald S. Burke⁺†, and Philip Cooley**

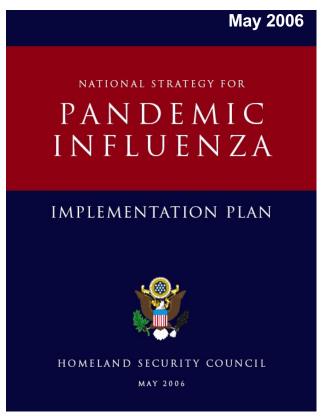
"Virginia Bioinformatics Institute, Virginia Polytechnical Institute and State University, Blacksburg, VA 24061; ^{††}Graduate School of Public Health, University of Pittsburgh, PA 15261; ^{**}Research Triangle Institute, Research Triangle Park, NC 27709; ⁵Department of Infectious Disease Epidemiology, Imperial College, London W21PG, England; "Los Alamos National Laboratories, Los Alamos, NM 87545; *Department of Biostatistics, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98195; and [†]Program in Biostatistics and Biomathematics, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA 98109

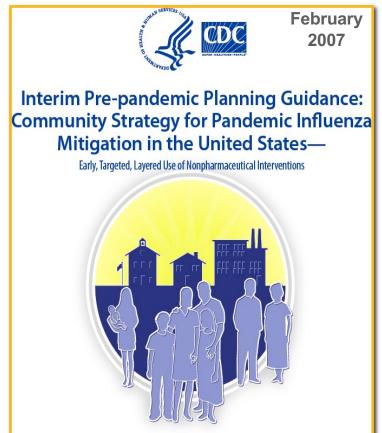
Edited by Barry R. Bloom, Harvard School of Public Health, Boston, MA, and approved January 15, 2008 (received for review July 23, 2007)

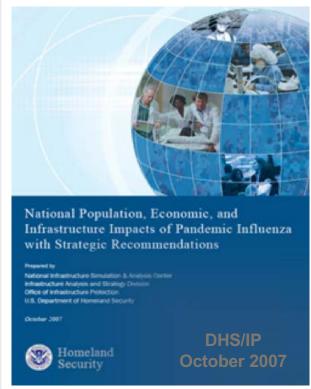
Table 3. Percentage of infections by place and scenario, $R_0 = 1.9$ (2.1) in the Chicago population

	Scenario 1. No intervention			Scenario 2			Scenario 3		
	Imperial	UW	VBI	Imperial	UW	VBI	Imperial	UW	VBI
Illness attack rates	42.4	46.8	44.7	7.3	2.8	3.9	1.1	0.31	1.3
Places									
Home	33.1	39.4	41.1	48.3	58	45.9	50.4	59	36.9
Work	21.8	14.5	28.6	12.9	10	27.8	13.5	10	18.7
School	16.0	18.8	23.3	11.7	11	9.6	9.0	11	2.7
Day care	-	1.1	-	-	0	-	-	0	-
Play group	-	0.8	-	-	0	-	-	0	-
College	_	-	3.3	_	-	12.3	_	-	40.0
Shopping	-	-	2.0	_	-	2.4	_	_	1.0
Neighborhood	_	17.7	-	_	15	-	_	15	-
Neighborhood clusters	-	7.7	-	-	5	-	-	4	-
Other/Community	29.0	0	1.7	26.6	0	2.0	23.8	0	0.8
Totals									
Primary Groups*	70.9	72.7	93.0	72.9	79	83.3	72.9	79	58.3
Community†	29.0	25.4	3.7	26.6	20	4.4	23.8	19	1.8

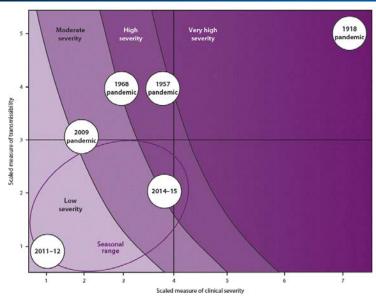
Large-scale Agent-Based Epidemiological Studies Have Directly Influenced the National Pandemic Planning Process





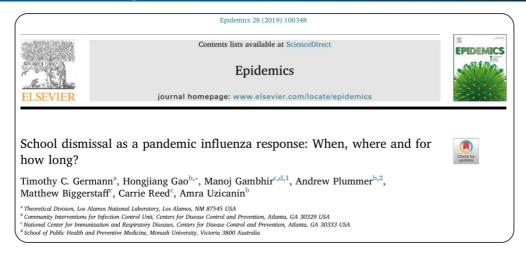


EpiCast Used to Assess School Dismissal Policies in the Context of the Pandemic Severity Framework



Adapted from C. Reed, M. Biggerstaff, L. Finelli, et al., *Novel framework for assessing epidemiologic effects of influenza epidemics and pandemics*, Emerg Infect Dis **19**, 85–91 (2013)

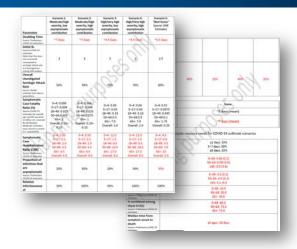




- In partnership with the CDC Community
 Interventions for Infection Control Unit (CI-ICU),
 we explored non-pharmaceutical interventions
 focused on school dismissal, specifically:
 - Threshold trigger: when to close
 - Geographic scale: where to close
 - Duration: for how long to close

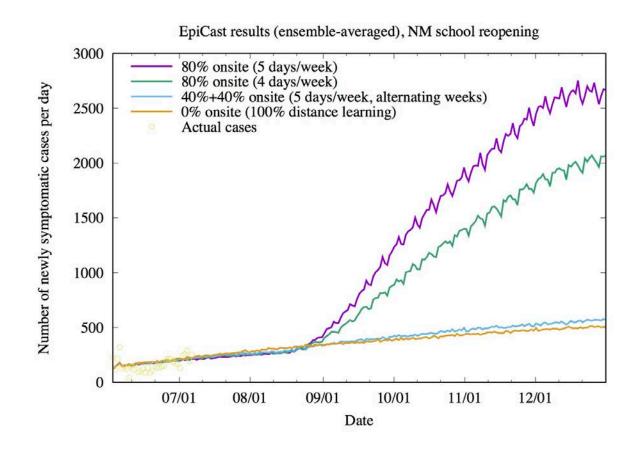
Adapting an influenza model to COVID-19

- Disease parameters from CDC's Planning Parameters for COVID-19 Outbreak Scenarios
- Initial conditions: Daily counts of diagnosed cases in each county from the NY Times database
- Mitigations
 - Schools are closed/children contacts reduced by 30% outside the household
 - Stay-at-home order is enacted on a county-by-county basis
 - Workplaces are assigned 3-digit NAICS codes, which determine whether they are open or closed, allow telework, shift schedules, etc.
 - Long-distance travel is assumed to be limited





The reported daily case counts in each county are used to calibrate the initial conditions (manually or automated*)



*See Peer-Timo Bremer's talk tomorrow on "Cognitive Simulations for COVID-19 Analysis, Exploration, and Scenario Planning" for more advanced multiparameter estimation techniques.

Initial EpiCast/COVID-19 national-level results: first report April 6

EpiCast COVID-19 simulation results - 6 April 2020

EpiCast team*, Los Alamos National Laboratory *Contact: Tim Germann, tcg@lanl.gov

NOTE: These are results based on *initial* models and parameters for COVID-19, which are being actively refined. Disease natural history and case hospitalization/ICU/ventilator/fatality rates are based on the "best guess" values in the March 20 *Planning Parameters for COVID-19 Outbreak Scenarios (PPCOS)*, and have not been updated to the more recent March 31 document. Contact rates are largely based on prior influenza modeling efforts [1-3], and no recently available mobility/contact data (e.g., through cell phone tracking) has been utilized. Data sources and assumptions are indicated below; suggestions are welcome.

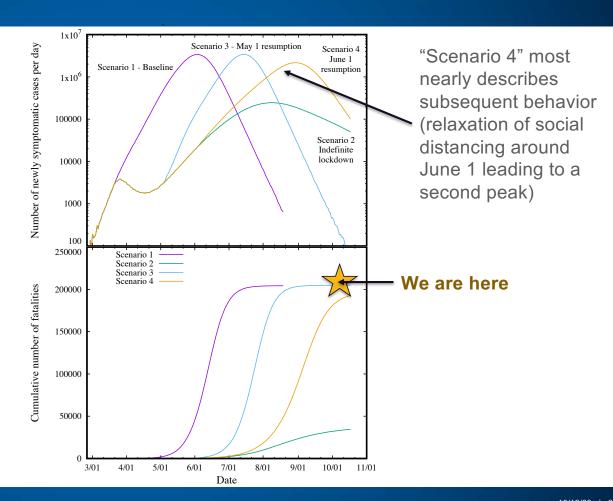
Disease model parameters

Parameter	Value	Source
Doubling time	6.5 days	March 20 PPCOS
Time to symptom onset	Mean ~5 days (range 2-8 days)	"
Serial interval	Mean ~8 days	"
Symptomatic duration	Mean ~6 days (range 3-9 days)	"
Proportion of pre-symptomatic transmission	35%	
Proportion of infections that are asymptomatic	50%	"
Relative infectiousness of asymptomatic individuals	100%	44
Pre-existing immunity	None	**
Symptomatic case hospitalization ratio (by age groups 0-4, 5-18, 19-29, 30-64, and 65+ years old)	1.25%, 0.5%, 1.25%, 1.5%, 16%	Adapted from March 20 PPCOS
ICU % among those hospitalized (by age)	15%, 20%, 15%, 17%, 15%	"
Ventilated % among those in ICU (by age)	35%, 30%, 45%, 47%, 45%	"
Symptomatic case fatality ratio (by age)	0.01%, .0075%, .045%, .072%, .1%	"

It is further assumed that seasonality (e.g., weakening of transmission in warmer and dryer summer months) effects are negligible and can be ignored.

Simulation Details

EpiCast is an individual-based model, with daily contacts between people in household, workplace, school, neighborhood, and community settings. The primary data source is U.S. Census demographics at the tract level (the –65,000 tracts are subsets of the ~3000 counties, with typically a few thousand people in each tract), and Census tract-to-tract workerflow data (i.e., how many people live in tract A and work in tract B). This is used to construct a model population with tract-level age and household size demographics, and realistic daily workflow pattern, which captures most of the short-range mobility. In addition, occasional long-distance travel is possible. A 12-hour timestep is used, so (unless on travel) individuals spend the night-time at home and day-time at school or workplace, if they belong to one (and they are open). Additional details are provided in the Supporting Information of [1]. In the original model [1,2], the individual age- and context-specific contact rates that account for the duration and closeness of interactions between pairs of individuals in different settings (home, school, workplace, neighborhood, community, etc.) were uniform across the U.S. In our recent school dismissal study [3], we allowed for different communities to decide to close their schools at different times, depending upon the current local disease incidence. In our ongoing COVID-19 work, these local policies have been extended to all community mitigation measures: school dismissal, workplace closure, shelter-in-place and other social distancing.



Effects we can model (that most others can't)

- Impact of heterogeneous mixing patterns
- Impact of school/workplace closures by school district, county, or state level
- Impact of workforce impacts by NAICS
- Non-pharmaceutical interventions differentiation by spatial or demographic factors



EpiCast has been used to evaluate school reopening scenarios for the state of New Mexico

Scenario 1: Distance Learning

- All household contacts are increased by 40%
- Daycares are assumed to be closed
- Workplaces are partially opened (consistent with Phase 1)

Scenario 2: Partial Onsite Learning

- Students are stratified into two non-overlapping groups
- Students are assumed to go to school for only 2 days a week
- Workplaces are partially opened (consistent with Phase 1)

Scenario 3: Onsite Learning

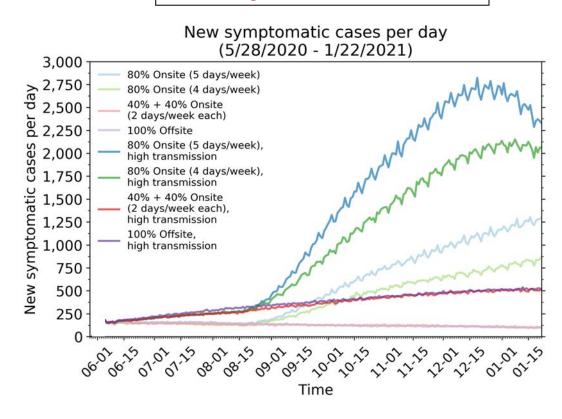
- Schools are assumed to be opened 5 days a week
- Transmission is reduced by 50% to account for social distancing measures, facemasks, mixing groups, etc.
- Workplaces are partially opened (consistent with Phase 1)

LANL PI: Sara Del Valle (A-1)

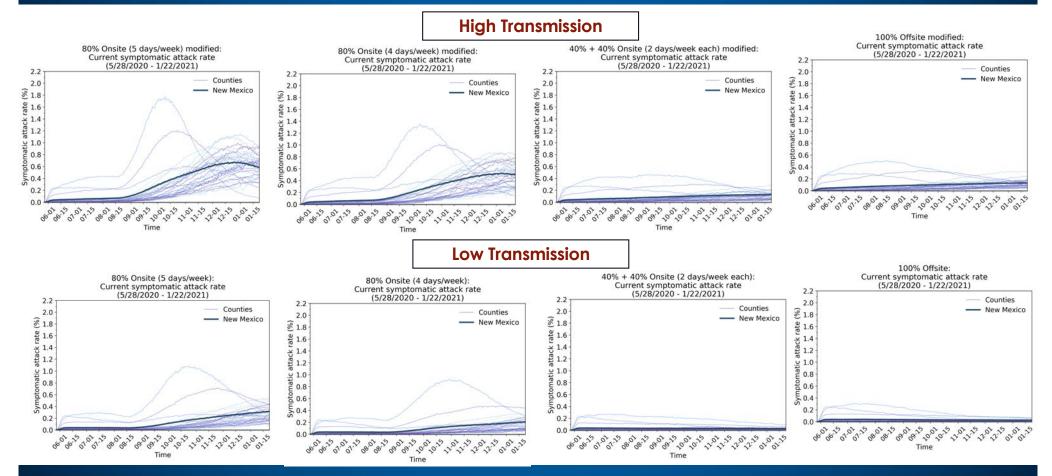
EpiCast Results – Overall Trends

- Lower transmission leads to less cases
- Reducing school attendance by 1 day (4-day scenario) has a significant impact
- Two non-overlapping groups of students 2 days a week leads to less cases and results in similar results as the offsite scenario due to assumed interactions outside school

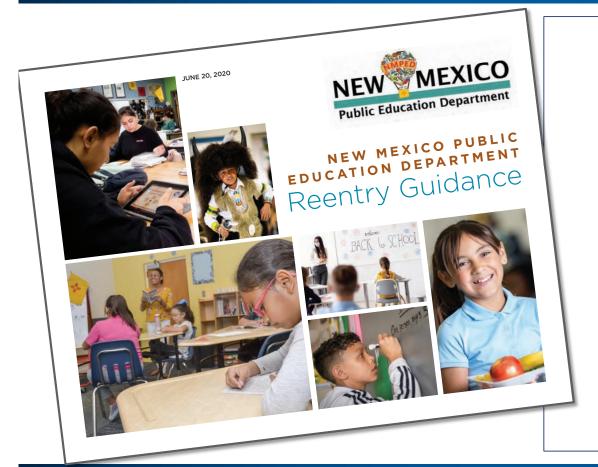
Low & High Transmission Scenarios



County-level Trends



LANL simulations (including but not limited to EpiCast) are informing NM policy-makers



Using Data to Drive Decisions



In partnership with Los Alamos National Laboratory (LANL), the state is using the most up-to-date epidemiological models to assess current virus threat level.

A phased entry approach will allow the state to collect and analyze data on the impact of a controlled start on the spread of the virus. This information will be essential to ensure that the state is able to move toward the goal of returning all children to a full school schedule as soon as it can be safely accomplished.

In addition, the phased entry approach will enable New Mexico to use the latest and best data on the impact of reopening in nearby states, as well as to base decisions on emerging, peer-reviewed research on virus transmission rates in children.



National School Reopening Studies

- In collaboration with the CDC, our goal is to assess different school reopening scenarios at a regional and national scales under different phase assumptions using an agent-based simulation.
- In previous EpiCast models, school mixing groups accounted only for transmission between students; teachers and staff were not explicitly included.
- For this work, we associate a workplace with NAICS Subsector Code 611 (Educational Services) with each school, and account for mixing between the teachers, staff, and school children.
- Where necessary, additional workplace(s) are added to achieve an average 14:1 student-toteacher/staff ratio in each school (based on data from the National Center for Education Statistics).
- Two scenarios were considered, roughly corresponding to "Opening Up America Again" Phases 2 ("Fewer Workplaces") and 3 ("More Workplaces")

	Working Status				Reduction due to socia	Long Distance Travel	
Workplace Assumption	Full Time	Part-time or Shift	Telework Take-up	Laid Off	Workplace	Other non- household	
Fewer Workplaces	44%	32%	20%	16%	10%	50%	50%
More Workplaces	52%	32%	15%	8%	10%	25%	75%

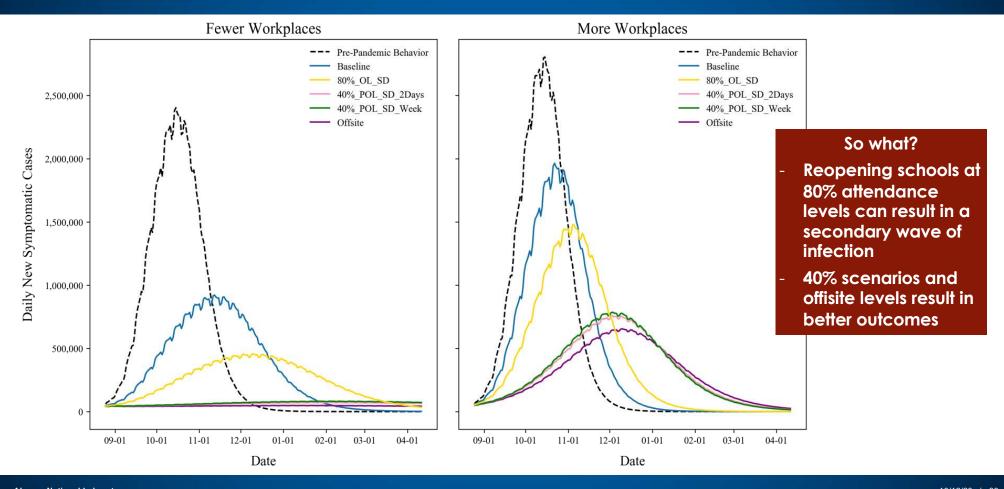
NAICS Sector	NAICS 2-Digit Code	Ability to Telework (Median)	
Agriculture & Mining	11	8.1%	
Utilities & Construction	21-23	32.7%	
Manufacturing	31-33	41.0%	
Wholesale	42	26.5%	
Retail	44-45	26.5%	
Transportation & Warehousing	48-49	32.7%	
Information	51-52	80.4%	
Finance, Insurance, & Real Estate	52-53	81.1%	
Professional and Business Services	54-56	71.6%	
Education	61	47.9%	
Health & Social Services	62	47.9%	
Leisure & Hospitality	71-72	20.3%	
Other Services	81	39.9%	
Government & Administration	92	57.0%	

Several reopening scenarios were considered

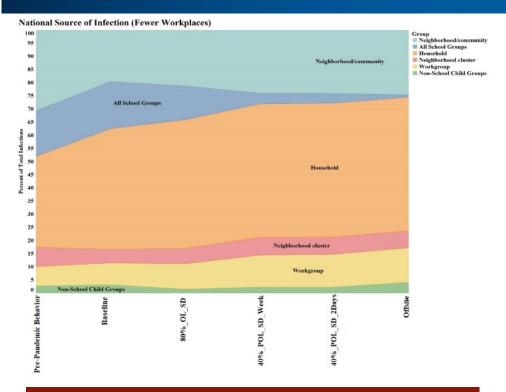
- 10-20 sets of alternative school schedules and assumptions were considered, using regional (New Mexico and Chicagoarea) models to identify the most important factors.
- Some surveys indicated that even if schools were open, a significant fraction of parents (~20%) would opt for distance learning or home schooling.

Scenario Name	Scenario Code	Scenario Description			
Pre-Pandemic Behavi	or Pre-Pandemic Behavior	No mitigations, all businesses completely open.			
Baseline	Baseline	All students physically in school with some social distancing.			
80% Onsite Learning v	vith				
Reduced Social	80%_OL_LessSD	All students physically in school.			
Distancing					
80% Onsite Learning v	vith 80%_OL_SD	All students physically in school.			
Ideal Social Distancia	ng – –				
80% Partial Onsite		Two non-overlapping cohorts of students – 40% of the students attend one week and the other 40% attend the next week.			
Learning – Alternation	40% POL LessSD Week				
Week with Reduced	d 1075_1 SE_ESSE_WEEK				
Social Distancing		12.5 12.12 11.01.01			
80% Partial Onsite		Two non-overlapping cohorts of students – 40% of			
Learning – Alternation	ng 40% POL LessSD 2Day	the students attend for two days/week (Mon/Tue) and			
Days with Reduced	I 4070_1 OL_LessSD_2Day	the other 40% attend for two days (Thu/Fri).			
Social Distancing		Wednesday off for disinfection.			
80% Partial Onsite		Two non-overlapping cohorts of students – 40% of			
Learning – Alternation	ng 40% POL SD Week	the students attend one week and the other 40% attend			
Weeks with Ideal Soc	cial 1070_10E_SB_Week	the next week.			
Distancing					
80% Partial Onsite		Two non-overlapping cohorts of students – 40% of			
Learning – Alternation	ng 40% POL SD 2Days	the students attend for two days/week (Mon/Tue) and			
Days with Ideal Soci	ial 40/0_10L_3D_2Days	the other 40% attend for two days (Thu/Fri).			
Distancing		Wednesday off for disinfection.			
100% Distance Learni	ing Offsite	No students physically in school.			

National Model Results

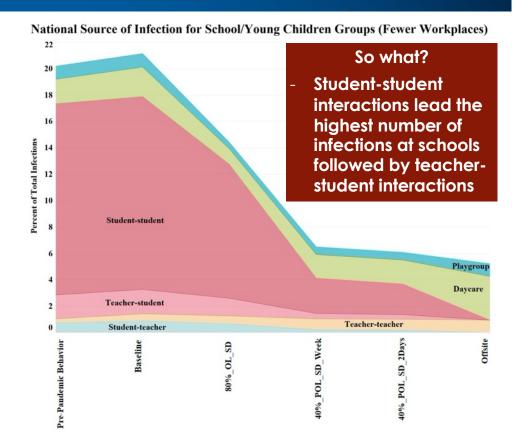


Source of Infection ("Fewer Workplaces")

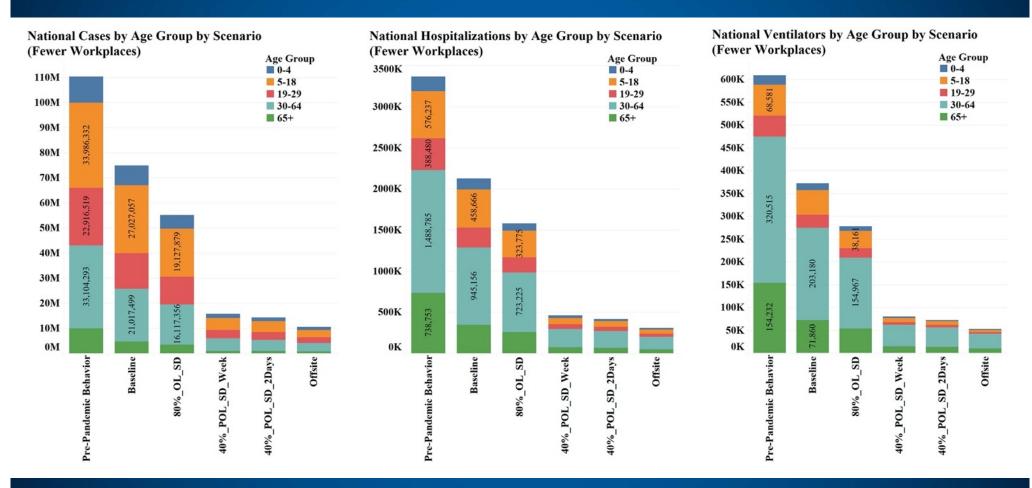


So what?

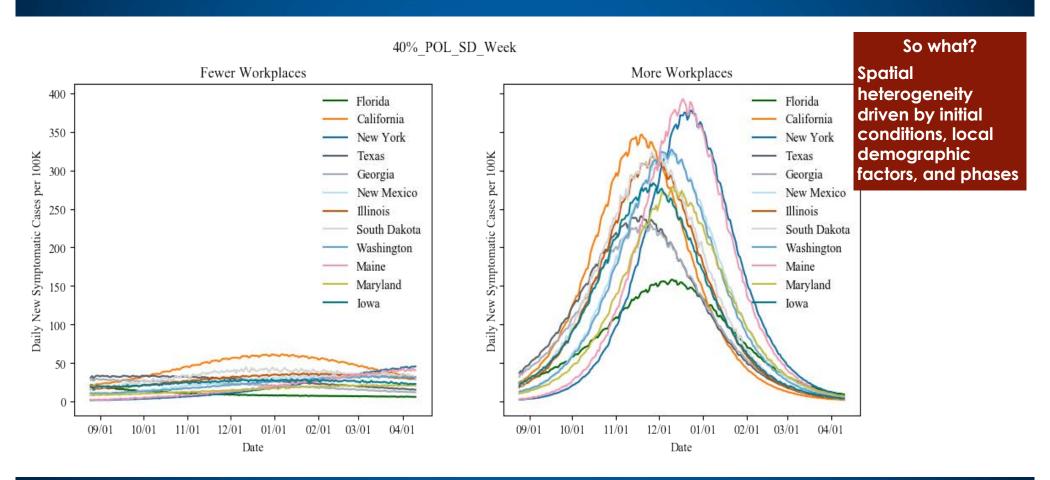
The majority of infections are generated at home followed by neighborhood/community



Case, hospital, and ventilator usage by age group ("Fewer Workplaces")

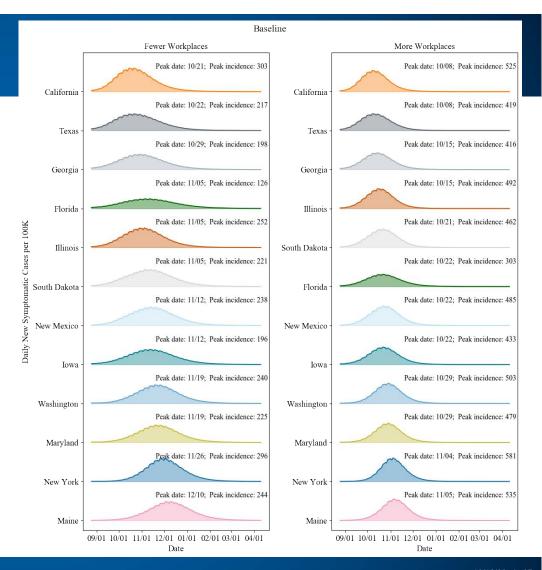


Spatial heterogeneity



Spatial heterogeneity

- For the baseline with Fewer Workplaces, the peak date ranges from October 21st (California) to December 10th (Maine).
- The timing of the peak for each state is dependent on:
 - 1. The current transmission levels; states with active community spread will reach their peak sooner; and
 - 2. Announced school reopening dates, which vary from August 3 (Arizona) to September 6 (New York).

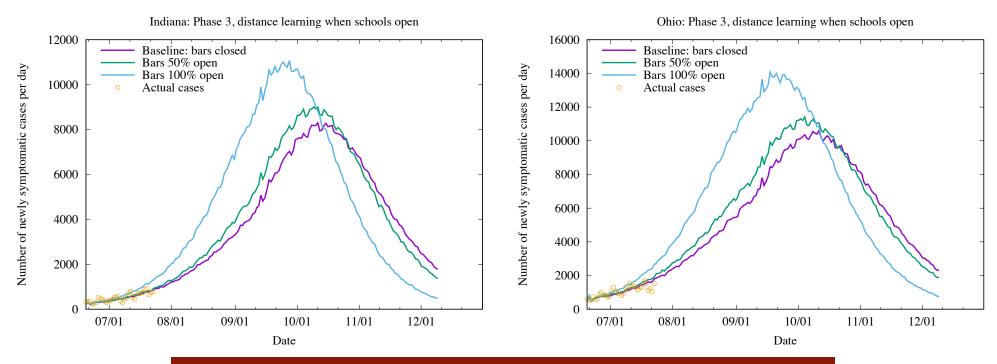


Assumptions: Bars and Restaurants



- Transmission in large social settings (bars, restaurants, birthday parties, college fraternities, ...) is important and a key target of policy guidance
- Various pre-COVID studies suggest that ~1/3 of adults visit bars/restaurants at least once a month, with one stating that "34% said at least once a month; 19% said at least once a week; 3% said every day"
- Data on the % of bar industry revenue across different age groups closely matches (perhaps surprisingly!) the population of those age groups
- We assume that in the "normal" situation with fully open bars and restaurants, a 3% of adults will participate in this mixing group each day
- Transmission in bars is assume to be similar to inside household
- The following results assume **Phase 3** business and social distancing practices, and a **regular 5-day work week** (for open businesses) with maximum telework

Results: Bars and Restaurants



So what?

The effect of opening 50% of bars is small relative to the overall transmission, however opening 100% can lead to significantly larger clinical attack rate

Some key limitations (which are being addressed by ongoing work)

- Identical policies (e.g., workplace restrictions and school schedules) uniformly across all states.
- Testing and contact tracing were not explicitly modeled.
- Uniform policies and behavior (e.g., compliance) assumed throughout the pandemic duration (simulations are through the end of March 2021).
- The model population in EpiCast is based upon the 2000 U.S. Census data, to take advantage of the tract-to-tract work flow data that was last compiled then.
- Epidemiological parameters are assumed to be constant throughout the simulation, but in reality may have spatial and temporal variability during the course of the COVID-19 pandemic.
 - -Local weather (e.g., humidity) may affect not only human behavior, but also the dynamics and lifetime of droplets, spray, etc., which affect the transmissibility.
 - –As more is learned about the disease course and effective treatments, the case fatality ratio has dropped.

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