MASSACHUSETTS HIGHTECHNOLOGYCOUNCIL

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The War on COVID-19

OCUMENT INTENDED TO PROVIDE INSIGHT AND BEST PRACTICES BASED ON CURRENTLY AVAILABLE INFORMATION FOR CONSIDERATION AND DOES NOT CONSTITUE SPECIFIC ADVICE

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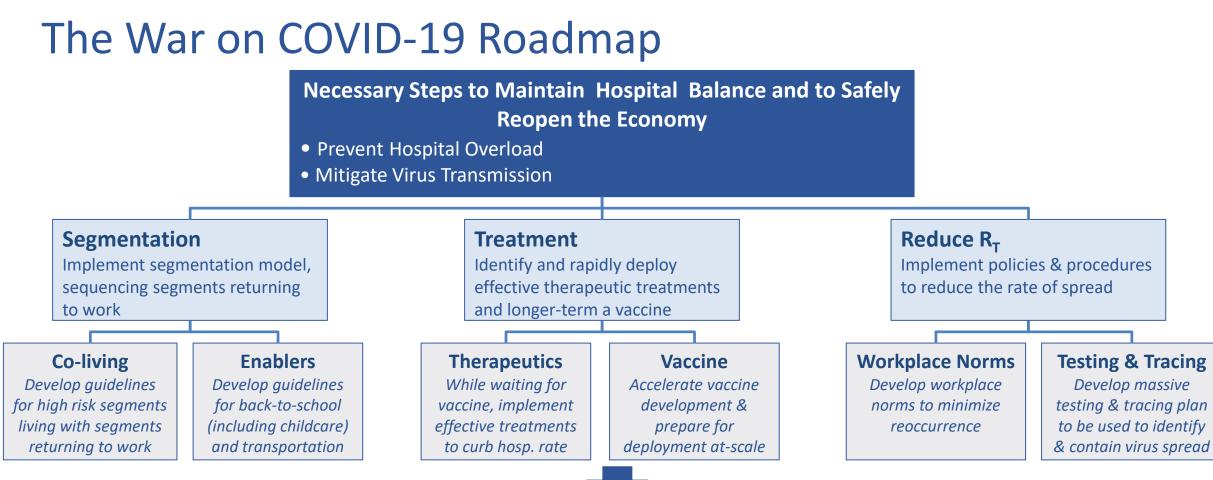
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Key Contributors

- Bill Acthmeyer, Founder and Senior Managing Director, EY-Parthenon
- Aron Ain, *CEO*, *Kronos*
- Chris Anderson, CEO of Massachusetts High Technology Council
- Mark Barnes, Partner, Ropes & Gray LLP
- Udit Batra, Ph.D., Executive Board Member, Merck KGaA Darmstadt, Germany & CEO, Life Science, MilliporeSigma
- Jasmine Burton, Associate, Bain Capital
- Thomas J. Cahill, M.D., Ph.D., Founder & MP, Newpath Management
- Marc Casper, Chairman and CEO, Thermo Fisher Scientific
- Benjamin Cravatt, Ph.D., Professor at The Scripps Research Institute
- Lynn R. Goldman, M.D., M.S., M.P.H., Professor at George Washington
- Megan Greenfield, Ph.D., Partner, McKinsey & Company
- Akiko Iwasaki, Ph.D., *Professor of Immunobiology at Yale University*
- Julie Jones, Chair, Ropes & Gray LLP
- Adam Koppel, M.D., Ph.D., Managing Director, Bain Capital Life Sciences
- Michael Z. Lin, M.D., Ph.D., Associate Professor at Stanford University
- David Liu, Ph.D., Professor at Harvard University

- Ed Mackey, EVP Global Operations, Boston Scientific
- Steve Pagliuca, Co-Chairman, Bain Capital
- Alex Panas, Senior Partner, McKinsey & Company
- Robert Reynolds, President and CEO, Putnam Investments
- Michael Rosbash, Ph.D., 2017 Nobel laureate in Physiology or Medicine, Chair in Neuroscience and Professor of Biology, Brandeis University
- Stuart Schreiber, Ph.D., *Professor of Chemistry at Harvard University*
- Edward Scolnick, M.D., former head of R&D at Merck
- Jonathan W. Simons, M.D., CEO & President, Prostate Cancer Foundation
- Navjot Singh, Senior Partner & Boston Managing Partner, McKinsey & Company
- Peter L. Slavin, M.D., President, Massachusetts General Hospital
- Michael Springer, Ph.D., Associate Professor at Harvard Medical School
- Jane Steinmetz, Boston Office Managing Principal, Ernst & Young
- Zane Stiles, Analyst, Bain Capital
- Upasana Unni, Associate Partner, McKinsey & Company
- David R. Walt, Ph.D., Professor at Harvard Medical School
- Ramnik Zavier, M.D., Ph.D., *Professor at Harvard Medical School*

Have assembled a team of experts to help operationalize the White House "Opening America" framework



Effective implementation of (1) segmentation, (2) treatment options and (3) a strategy to reduce R_T are necessary to dampen a second major reoccurrence until a universal vaccine is available

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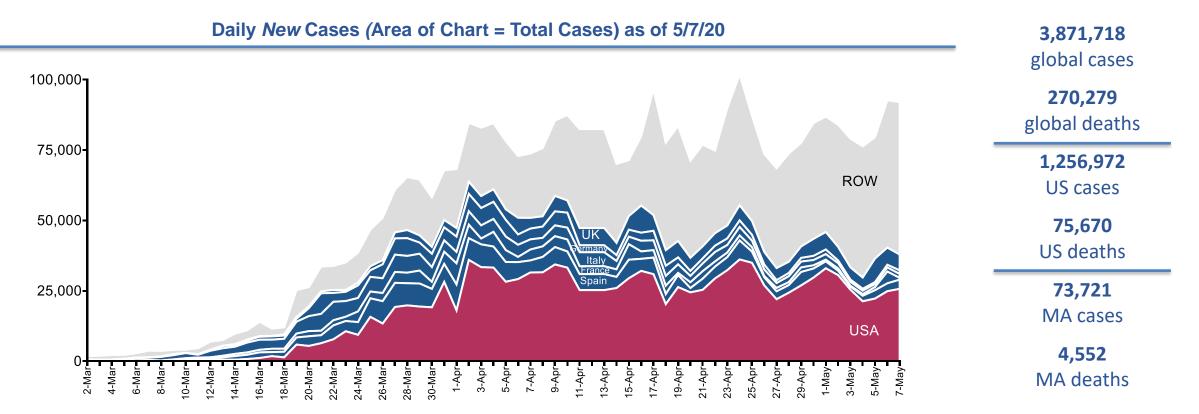
Contents

Summary COVID-19 History & Economic Impact

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- The Key Three Steps: *How* to Return to Work
- Timing: *When* to Return to Work

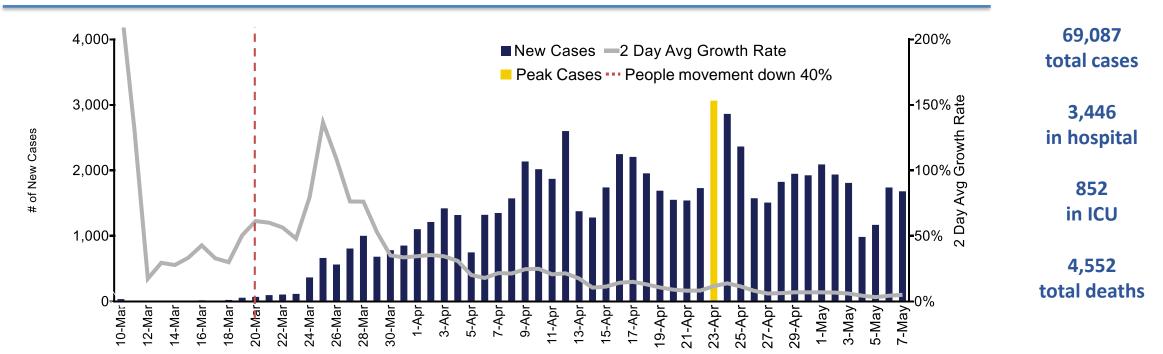
Global COVID-19 Cases Update



Global cases and deaths continue to rise. The US in early stages of "flattening" & Europe cases declining, but the rest of the world is still experiencing growth

Massachusetts COVID-19 Cases

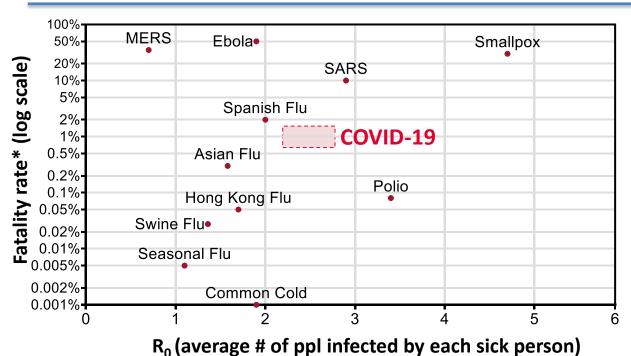
of new cases showing signs of flattening; growth rate has slowed since people movement slowed



MA growth rate has dramatically slowed since stay-at-home mitigation efforts, and new cases / day may be in early stages of declining

Note: There is day-to-day variability in cases reported by testing laboratories and no single day change in indicative of overall cases trends Source: Mass.gov; as of 5/7/20

Why is COVID-19 so serious?



Fatality Rate v. R₀

• Fundamental issue: COVID-19 has a high fatality rate and a high R₀ (high rate of infection)

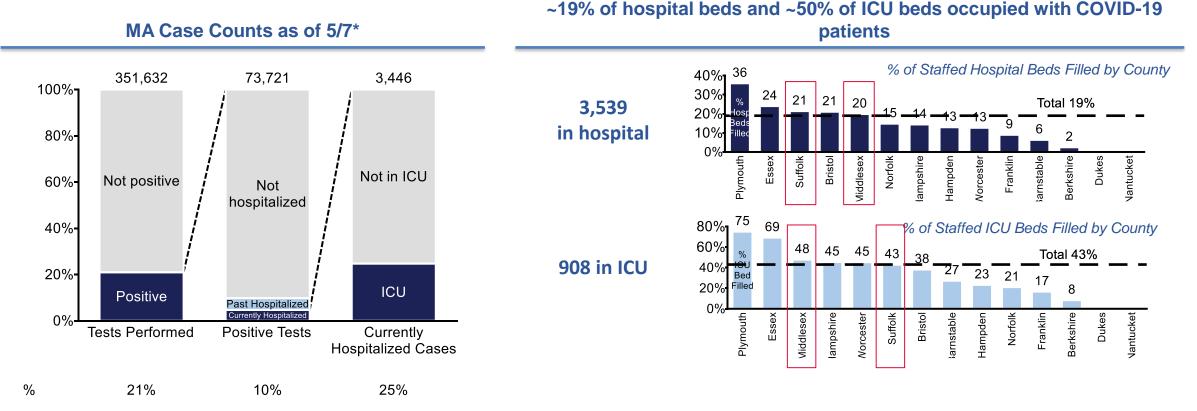
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- Additionally, COVID-19 has a high rate of hospitalization (~10%+), which combined with high rate of spread creates large tax on hospital capacity
- Finally, COVID-19 is **indiscriminate**, causing serious long term health consequences in all ages
- In order to return to work, need to adopt policies & procedures to reduce R_T

COVID-19 has a high spread & high rate of hospitalization / death – to return to work, need to adopt policies & procedures to reduce spread (R_T)

*Note: Infection fatality rate used where available, otherwise case fatality rate used to approximate IFR Sources: NY Times (https://www.nytimes.com/2020/02/18/learning/whats-going-on-in-this-graph-coronavirus-outbreak.html), World Health Organization, Institute for Disease Modeling, BMC Infectious Diseases

MA Hospitalization Rate & Capacity Data



Approximately ~10% of positive cases in MA hospitalized ~19% of hospital beds and ~43% of ICU beds are currently filled by COVID-19 patients

*Hospitalization rate does not include patients previously hospitalized but since discharged, so likely higher than demonstrated by existing data Source: Mass.gov H

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R_T Today

Massachusetts Estimated R_T Overtime



- Social distancing & mitigation efforts have successfully brought R_T down below 1, controlling the outbreak
- However, these efforts are having a significant impact on the economy
- Goal of a "back-to-work" program to put policies & procedures in place to keep R_T below 1 without as significant an impact on the economy

Today, MA's R_T has fallen below 1.0 – the virus is being contained. However, mitigation efforts are having a dramatic impact on the economy and thus are unsustainable

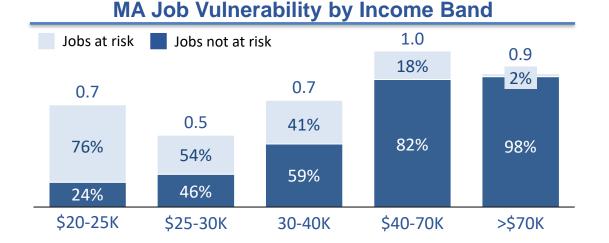
Economic Impact of Shutdowns

JP Morgan projecting US GDP to be <u>down 40%</u> QoQ in Q2; EU GDP to be <u>down 45-55%</u> QoQ

		eal GDP				Real O				
	2019	er a year ag 2020	2021	4Q19	1Q20	2Q20	period, saar 3Q20	4Q20	1021	
	2010	2020	2021		1420		0420	1420		
United States	2.3	-7.7	6.2	2.1	-10.0	-40.0	23.0	13.0	12.0	
Canada	1.6	-6.9 L	1.9 J	0.3	-10.0 ↓	-30.0 L	12.0 [↑]	5.0	4.0	
Latin America	0.6	-4.5↓	2.4 1	-0.6	<u>-5.0</u> ↓	-24.4↓	12.0	4.2 T	3.0	1
Western Europe	1.3	-7.1↓	6.9 T	0.4	<u>-14.1</u> ↓	-46.6 ↓	81.3 T	7.8 ↑	4.4	t
Euro area	1.2	-7.1↓	6.7 ↑	0.5	-15.0	-45.0 L	75.0 ↑	7.0 [↑]	4.5	1
Germany	0.6	-6.61	6.8 1	0.1	-12.0 T	-45.0 J	75.01	6.0 T	5.0	t
France	1.3	-8.9 L	7.0 ↑	-0.2	-15.0	-55.0 L	100.0 ↑	8.5↑	4.0	1
Italy	0.3	-8.8↓	5.5 1	-1.2	-20.0	-40.0 J	55.0 T	8.0 1	4.0	Ť
Spain	2.0	-8.1 L	5.5 ↑	1.7	-15.0	-45.0 L	55.0 ↑	9.0 ↑	5.0	1
Norway	2.4	-4.4 1	6.6 ↑	0.7	-16.5 L	-33.2 L	68.1 ↑	5.3 ↑	3.3	t
Sweden	1.3	-4.0	5.5 ↑	0.6	-9.2 ↑	-33.2 ↓	50.8 ↑	5.1 ↑	5.6	1
United Kingdom	1.4	-8.0 L	8.0 1	0.1	-10.5 L	-59.3 L	119.9 [↑]	12.6 ↑	3.6	1

MA Unemployment approaching 2x+ '09 levels

'09 Peak	2/29/2020	3/7/2020	3/14/2020	3/21/2020	3/28/2020	4/4/2020	4/11/2020
5.7%	2.3%	2.1%	2.1%	2.3%	5.2%	8.7%	10.1%



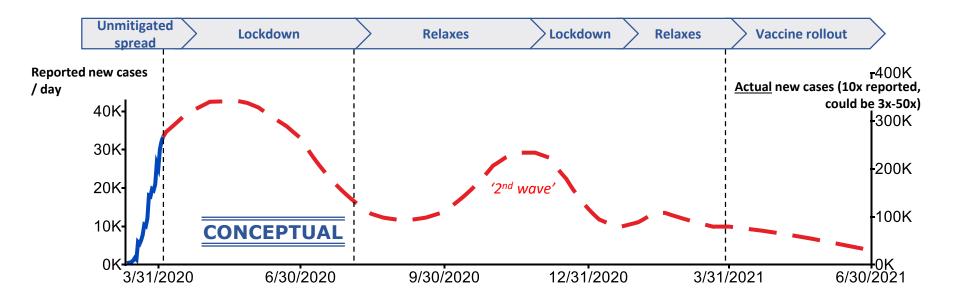
Mitigation efforts are having a significant impact on the economy, and impact is most severe in low income workers

Source: 4/17/20 JP Morgan Economic Outlook, US Department of Labor, LaborCUBE; BLS OES, Moody's, McKinsey Global Institute analysis Note: Analysis determines vulnerable jobs as a function of physical distancing policies and their immediate knock-on economic consequences – assumes maximum physical distancing (defined by shelter-in-place policy)

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Critical to "Avoid the W"

What we need to prevent:



Sub-optimal public health approach creates the bad/bad box of ineffective lockdowns and high burden on healthcare systems – creating wider, deeper "U" or "W" that only ends with vaccine

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COVID-19 History & Economic Impact: Summary

- Global cases and deaths continue to rise, but the US & Massachusetts are seeing evidence of "flattening"
- COVID-19 is particularly serious because of its high hospitalization & death rate and high rate of spread (R₀).
 Unmitigated spread can quickly overwhelm hospitals. MA managing hospital capacity well so far, with ICU beds only ~43% filled and total hospital patients declining the past week
- While mitigation efforts are contributing to the early curve "flattening," they will have a dramatic economic impact in the U.S., with some analysts forecasting Q2 GDP declines 2-3x that of the great depression. Workers earning less than \$40K/year and employed by small businesses are most vulnerable
- Need to reopen the economy, but critical to "avoid the W"

Mitigation efforts are working, but are also having a significant impact on the economy, and impact is most severe in low income workers. Need to focus on developing policies and protocols to enable a return to work while minimizing the risk of another lockdown

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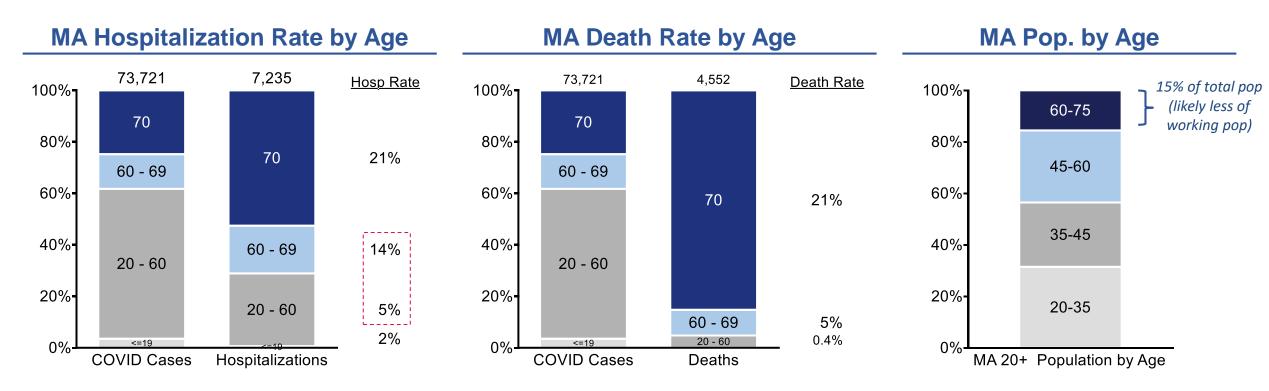
Segmentation: Sequence segments returning to work according to risk to lower hospitalization rate

Effective Therapeutics: While waiting for vaccine, implement effective treatments to curb hospitalization rate & fatality rate

Reduce R_T: Implement policies & procedures to reduce the rate of spread

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Age Segmentation



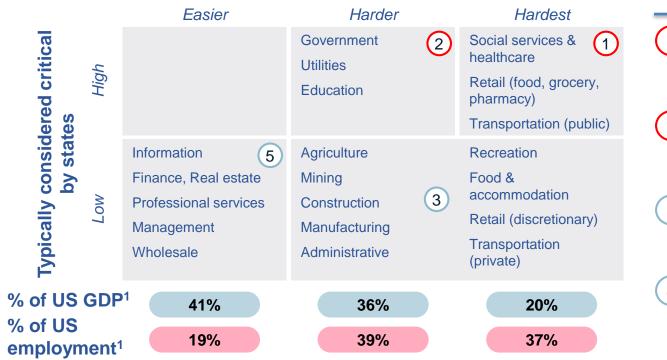
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Excluding those aged 60+ from initial return to work segment may greatly reduce the hospital burden without affecting a large portion of the working population

Segmentation

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Industry Segmentation



Ability to Work From Home

Need to Determine How To Group & Sequence Sector Reopening

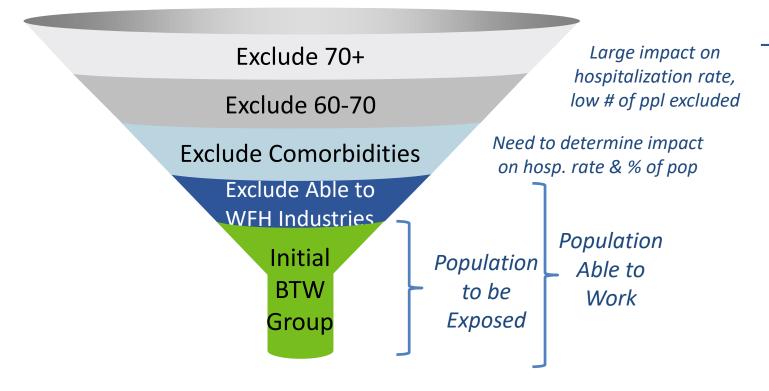
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- Critical sectors that cannot work from home will be harder to safeguard, but may need to be part of first wave
- 2 Critical sectors with some ability to WFH may be able to encourage portions to continue remote work
- 3 Less critical sectors that cannot work from home – Less critical, so possible to delay, but may need to be part of initial wave
- 4 Less critical sectors able to work from home encourage these sectors to continue working from home where possible

Possible to phase industries returning to work by criticality and ability to continue working from home

Segmentation

Comprehensive "Funnel Framework"



Other Considerations

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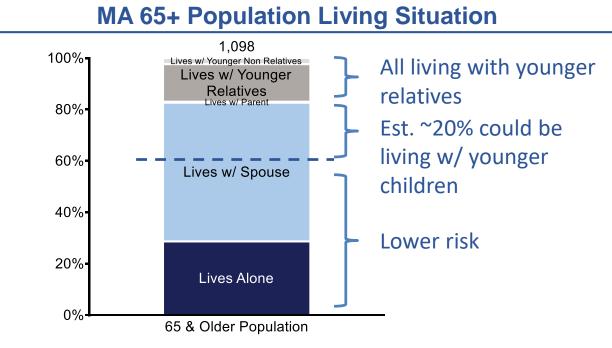
- Returning population's exposure to excluded population: how many excluded ppl will still be exposed by household members returning to work?
- Nursing Homes: how to deal with isolated high-risk populations interacting with workers?
- Workforce enablers: (childcare / education) – need enough capacity to support segment returning to work

A handful of key segmentation decisions can greatly reduce the hospitalization rate while still enabling large portions of the economy to restart

Segmentation



Other Considerations: Families with At-Risk Relatives

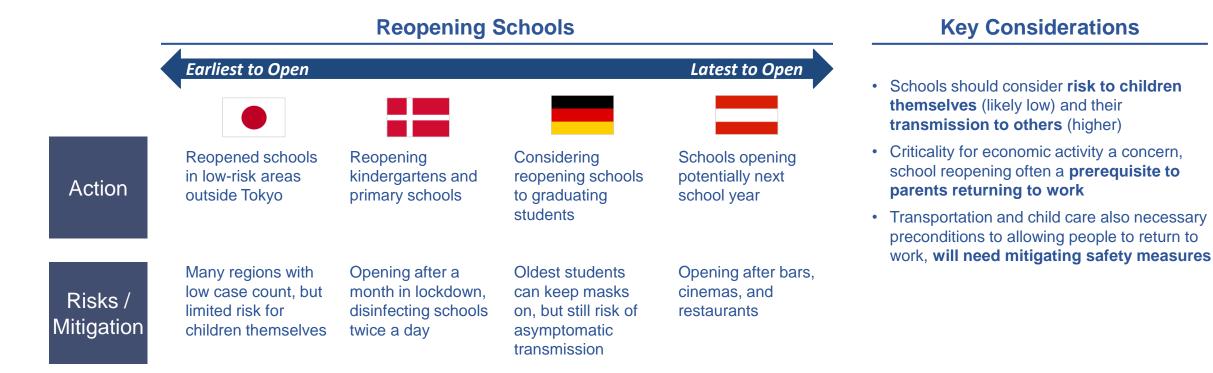


Strategies for At-Risk Individuals with Family Members Returning to Work

- Encourage workers living with at-risk individuals to strictly adhere to all policies and procedures
- In hot spots, could consider setting up alternative housing for at-risk individuals

Up to ~40% of 65+ population could be living with individuals returning to work. To manage these atrisk populations, may need to set up alternative living arrangements in hot spots

Other Considerations: Education



Reopening schools and child care precondition to returning to work, but carries key risks. Will also need plan for other key enablers (e.g., transportation)

Segmentation

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The Key 3 Steps to Achieve Hospital Balance & Worker Safety

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Types of Solutions & Timeline

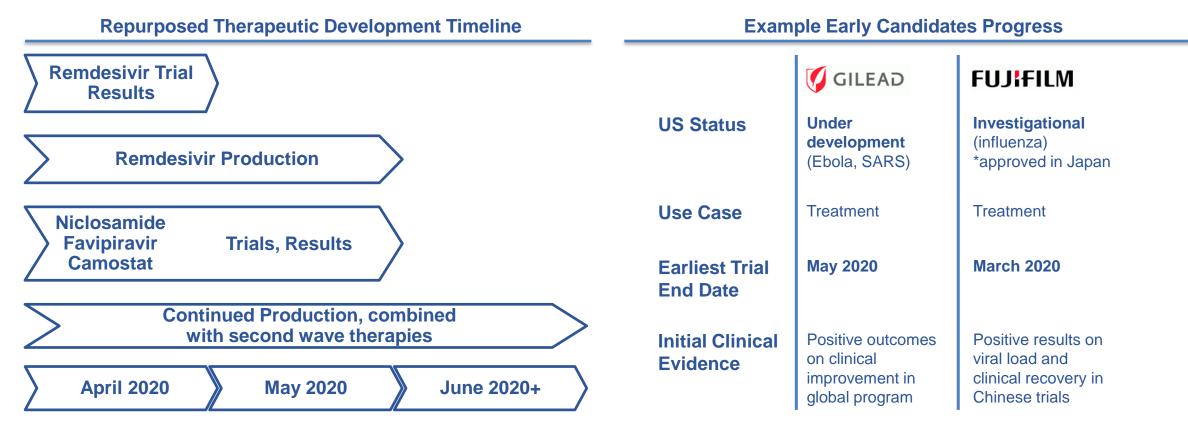
	First Wave "Repurposed" Therapeutics	Second Wave New Therapeutics	Third Wave Vaccines
Use Case	Acute remediation	Prevent and treat	Long-term prevention
Drug Candidates	 Remdesivir Niclosamide Favipiravir 	 Human antibodies Monoclonal and polyclonal New compounds targeting essential viral proteins 	 Inactivated virus particles Live-hybrid viruses RNA-based vaccines Moderna, CureVac, BioNTech
Challenges	 Dose likely higher than existing use cases, supply limited 	• FDA approval timelines are usually 30 days for testing, 3-6 months for approval	 Unknown if vaccines will need to be seasonal (like influenza) or durable long-term (like measles)
	April-June 2020	July-September 2020	April 2021-April 2022+

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Therapeutics in development, but vaccine 18+ months away

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First Wave – "Repurposed" Therapeutics

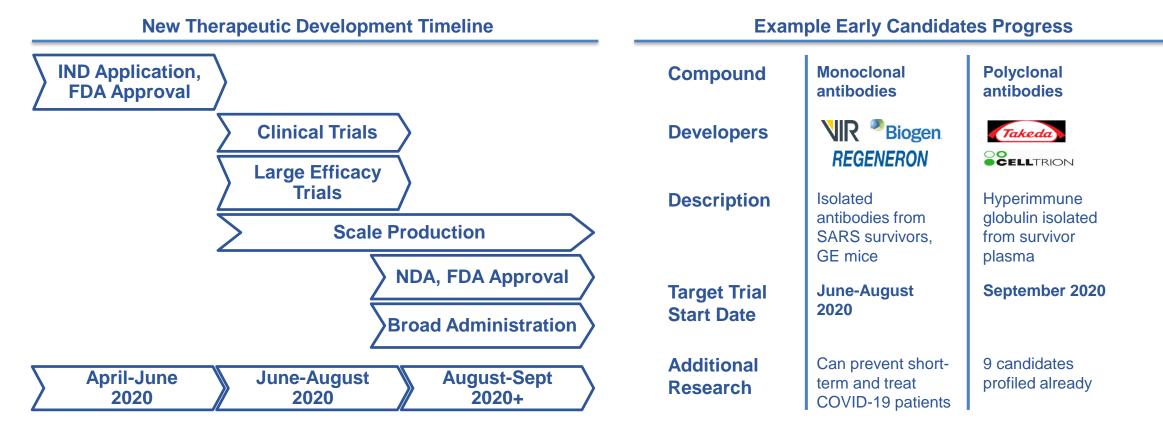


With rapid FDA approval and ramped production will be available in next six to nine weeks, but limited to acute remediation

Effective Therapeutics

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Second Wave – New Therapeutics

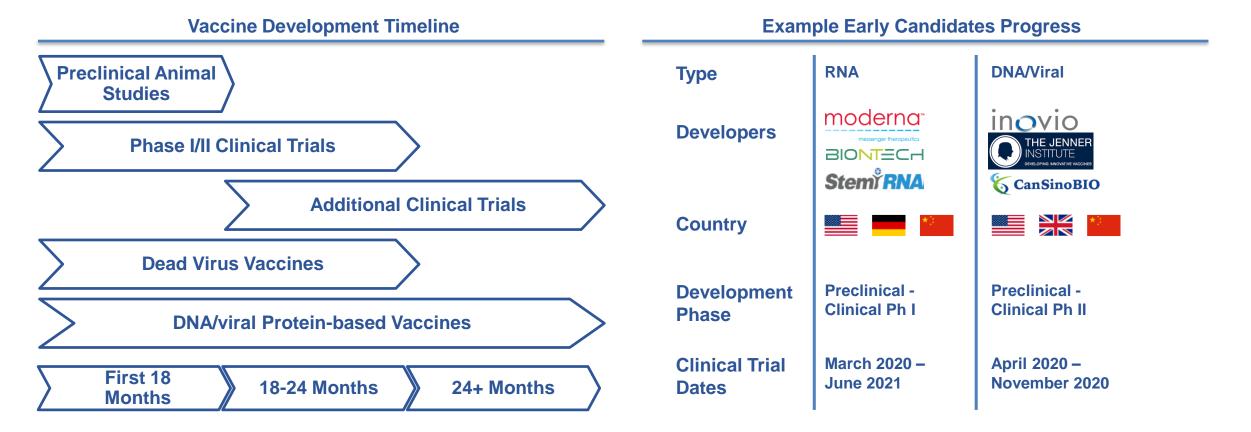


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With regulatory flexibility and ramped production, may be available by late summer 2020, but still not a cure T Di

Third Wave - Vaccines



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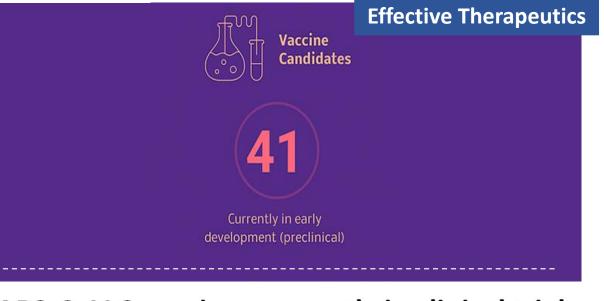
Vaccine likely to take 18+ months to develop

VACCINES

Vaccine	Company	Platform	Stage	Description	Location
1. mRNA-1273	Moderna Moderna	RNA	Phase I-First Patient Dosed	First to dose a human in the US. Vaccine consists of a synthetic strand of mRNA designed to elicit an immune response to produce antibodies against SARS-CoV-2	٩
2. Ad5-nCoV	🌀 CanSino Bio	Non-Replicating Viral Vector	Phase I	Benefits from previous success in the Ebola virus (time to market -3 years). The vaccine being developed is based on viral vectors (adenoviruses) to deliver antigens to express the SARS-CoV-2 spike protein	٩
3. ChAdOx1 nCoV-19	University of Oxford	Non-Replicating Viral Vector	Phase I/II	Enrolling 500+ inviduals to test its vaccine candidate, which uses a non-replicating virus to deliver RNA into cells.	*
4. LV-SMENP-DC	Shenzhen Geno-Immune Medical Institute	Lentiviral	Phase I/II	Begun early testing of its vaccine candidate. The vaccine uses a lentiviral vector to deliver Covid-19 minigenes to modify dendritic cells and activate T cells.	
5. BCG Vaccine	Research Group, Netherlands	Live Attenuated Virus (LAV)	Phase II/III	Repurposing the BCG vaccine, orginally for TB, to fight SARS-CoV-2 in healthcare workers at high risk of infection. 1,000 individuals will be enrolled across 8 hospitals to receive the vaccine or placebo.	0
6. BCG Vaccine	Murdoch Children's Research Institute		Phase II/III	The BRACE trial will conduct a randomized, multi-center study of the TB vaccine in 4,000 healthcare workers across Australia.	٢

Vasudev Bailey, PhD Zoe Guttendorf

♥ @vasudevbailey @zoeguttendorf



SARS-CoV-2 vaccines currently in clinical trials

Entity	Vaccine	Clinicaltrials.gov#	Stage	Phase
University of Oxford	ChAdOx1 nCoV-19	NCT04324606	Recruiting	Phase I
CanSino Biologics Inc.	Ad5 Vectors	NCT04313127	Active, not recruiting	Phase I
CanSino Biologics Inc.	Ad5 Vectors	NCT04341389	Recruiting	Phase II
Sinovac	Inactivated virus vaccine	NCT04352608	Recruiting	Phase I/II
Symvivo Corporation	Bifidobacterium vector	NCT04334980	Not yet recruiting	Phase I
NIAID	mRNA-1273	NCT04283461	Recruiting	Phase I
Inovio	DNA	NCT04336410	Recruiting	Phase I

How to Accelerate Therapeutic Development

	Investigational New Drug Review	New Drug Application (NDA)	Commentary
Rapid FDA Approval	 <i>Issue:</i> Companies must wait 30 days after submission to implement trials Solution: FDA should ask relevant questions before receiving IND, allow trial initiation immediately 	 <i>Issue:</i> FDA review of an NDA typically takes 3-6 months Solution: FDA communicate daily with relevant companies, complete NDA review within 1 week 	Government action can turbo charge vaccine and therapeutic development & deployment
	Purchase Guarantees	Test and Trace Funding	What we can do to help:
Government Funding	 <i>Issue:</i> Insufficient PPE including gloves, gowns, masks, and N95s Solution: Provide companies financial guarantees above market prices, regulatory relief 	 <i>Issue:</i> Hospitals, others lack supplies to conduct fastest tests Solution: Provide funding guarantees for viral testing and serological test to detect antibodies 	 Encourage frequent communication between FDA & companies & push for rapid FDA approval
	Scaling Existing Production	Free Up U.S. Plant Capacity	 Provide financial stability to companies scaling production
Scale Production	 <i>Issue:</i> Individual companies cannot produce enough of emerging therapies Solution: Facilitate manuf. of promising candidates by other U.S. drug cos 	 <i>Issue:</i> Need capacity to scale treatments prior to approval Solution: FDA should approve new plants for the production of other medicines 	Help U.S. plants be ready and able to produce therapeutic candidates

New therapies and vaccines months to years off,

but targeted government action can accelerate development

Effective Therapeutics



The Key 3 Steps to Achieve Hospital Balance & Worker Safety

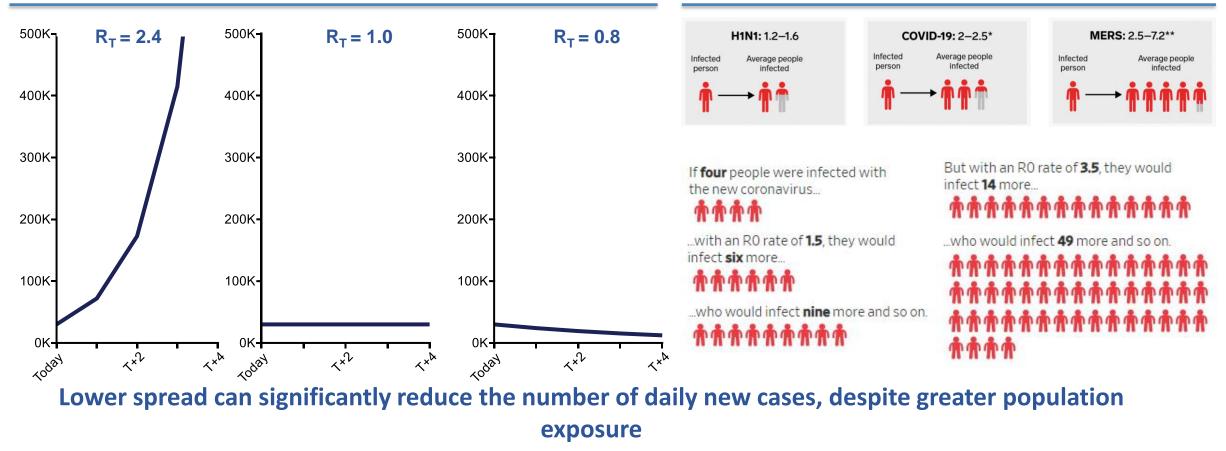
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Reduce R_T: Implement policies & procedures to reduce the rate of spread

Reducing R_T: Why It Matters

MA New Cases Under Different R_T



Visualizing R_T

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Reduce R_T

Less Expensive

More Expensive

Potential Policies to Reduce R_T

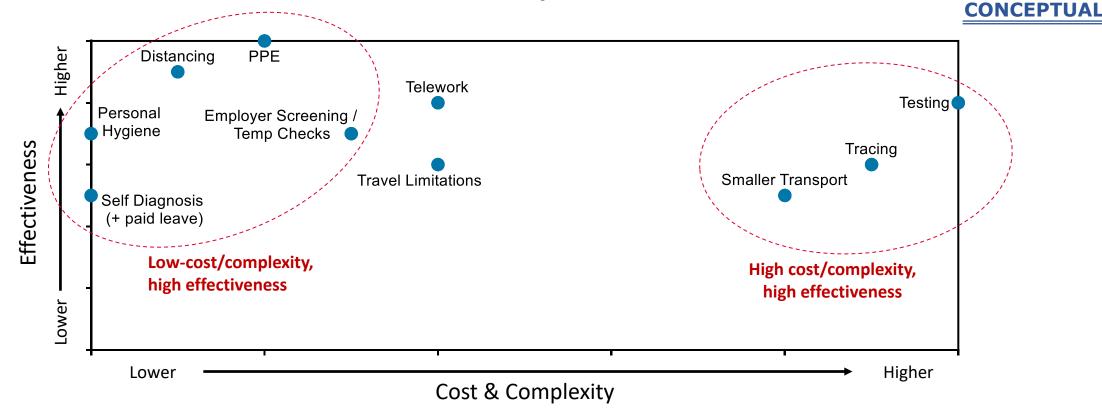
	PPE / Masks	Mandated mask & PPE use
	Personal Hygiene	Frequent hand washing or sanitizing. Avoid touching eyes, nose and mouth. Good respiratory hygiene
	Self-Diagnosis	Comprehensive check-list of symptoms each worker considers before leaving home
	Distancing / No Large Groups	Social distancing at work where possible. Staggered shifts and lunch times
A C	Workspace Cleaning	Frequent workplace deep cleaning. Hygiene zones with mandatory sanitization checkpoints in between
roup	Employer Screening	Temperature measurement and symptom screening upon entry
Ū	Re-designing Workspace	Re-modeling of workspace to ensure greater spacing between employees. Improved air filtration and ventilation. Touch-free handles and interfaces
	Telework	Encourage telework where possible
	Travel limitations	Discourage travel unless absolutely necessary. Before traveling, ensure virus levels low at home & destination
	Smaller Transport Methods	Limit use of mass transit when possible. Encourage carpooling or deploy corporate vans where hygiene easier
Group B	Tracing	Team of ~5,000 tracers in MA conducting manual interviews with positive cases and alerting and quarantining those who were in contact with a positive case
Ū	_ Testing	6-10 centralized testing centers in MA performing 100K tests a day

Large variety of possible strategies to help reduce R_T – should begin with most effective & lowest cost, but will likely need higher cost effective measures as well (testing, tracing)

Reduce R_T



Framework for Possible Workplace Norm Policies



Large variety of possible strategies to help reduce R_T – should begin with most effective & lowest cost, but will likely need higher cost effective measures as well (testing, tracing)

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Potential Policies to Reduce R_T

• Group A: Masks, Self-Diagnosis and Employer Screening

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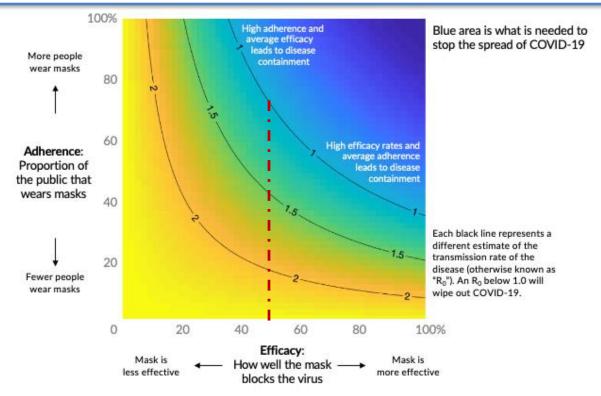
• Group B: Testing & Tracing

Reduce R_T

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Theoretical Effectiveness of Masks & PPE



Theoretical Mask Use Impact on R_T

Key Considerations

Reduce R_T

- Adherence: Higher adherence, even with less effective masks, can greatly reduce R_T. Consider making PPE mandatory
- Supply & Efficacy: Is there adequate supply of the necessary level of efficacy? (i.e., easy to supply cloth masks but lower efficacy)

Mean % Filtration Efficiency of Various Masks

Note: Data based on Bacteriophage MS2 (23 nm in diameter) - COVID-19 virus particles are ~125 nm in diameter

Scarf	100% Cotton Masks	Tea Towel	Surgical Masks	N95
49%	51%	72%	89%	95%+

Widespread use of masks, even lower quality cloth masks, can have a significant impact on R_T

Self-Diagnosis

Daily Symptom Checklist

Symptom	% of Cases w/ Symptom
Fever	64%
Sinus Pain	50%
Cough	46%
Altered sense of smell	44%
Expectoration	32%
Stuffy nose	25%
Chills	18%
Fatigue	18%
Sore throat	13%
Headache	13%
Difficulty breathing	11%
Joint or muscle pain	10%
Diarrhea	6%
Vomiting	3%

Potential Policy & Considerations

- Mandate employees / students certify (via smartphone app / website for example) they are not experiencing any of the listed symptoms
- Incentivize adherence with paid sick leave policies
- Provided adherence is high, self-certification could detect a significant amount of symptomatic cases, including mildly symptomatic cases
- Recent studies suggest true number of asymptomatic cases quite rare (2-6%), suggesting meticulous and accurate daily symptom surveying and self-reporting can be highly effective in lowering R_T

Meticulous and accurate daily symptom surveying and self-reporting can be highly effective in lowering R_T

Reduce R_T

Employer Screening

Example Employer Screening Case Studies

- Wuhan, China all arriving employees must submit to at least four temperature checks daily
- Amazon using thermal cameras at its operations facilities to screen workers for fevers
- Some grocery stores are using non-contact forehead infrared thermometers to temperature test associates as they arrive for work
- Colorado governor announced temperature checks at workplaces will be part of reopening plan

Potential Considerations

- Not effective at reducing R_T on its own: only 64% of cases present with fever, and carriers are contagious in the period of time before fever manifests. Will need to be combined with other norms & screening measures
- Implementation could be challenging: will require additional PPE and thermometers that could be difficult to acquire
- Medical information will have to be safely stored: all temperatures taken should be treated as confidential medical information and stored as such

Temperature checks and other employer screening are useful tools when used in combination with other policies

Reduce R_T



Potential Policies to Reduce R_T

• <u>Group A</u>: Masks, Self-Diagnosis and Employer Screening

• Group B: Testing & Tracing

Testing & Tracing: Summary

- Testing and tracing can have a large impact on reducing R_T (up to ~2x more effective than selfisolating alone)
- In order to be effective, testing & tracing programs need to capture ~70% of contacts within 1-2 days. MA leading the way in the US on tracing (have already assembled a team of ~1000 tracers), but will likely need ~5-10x more tracers to accomplish this
- To accurately capture all cases & test contacts, will need ~100K tests/day. MA capacity slowly ramping (achieving ~10-15K / day currently). Need to rapidly explore avenues to performing ~100K tests / day, as ramping will likely take ~6-8 weeks post-contract

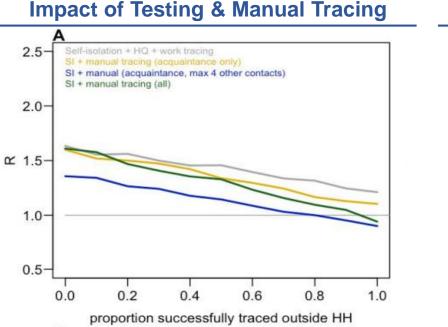


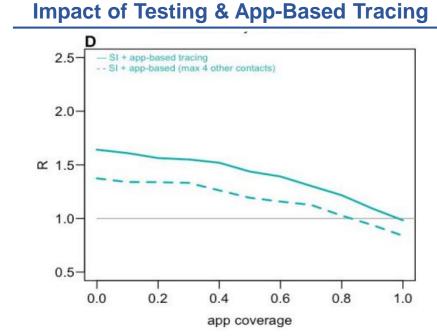
Although testing / tracing can have a significant impact on reducing R_T , that impact will be constrained by the time it takes to build up capacity, and the cost associated with large-scale efforts

Reduce R_T



Combined Testing & Tracing Program Effectiveness





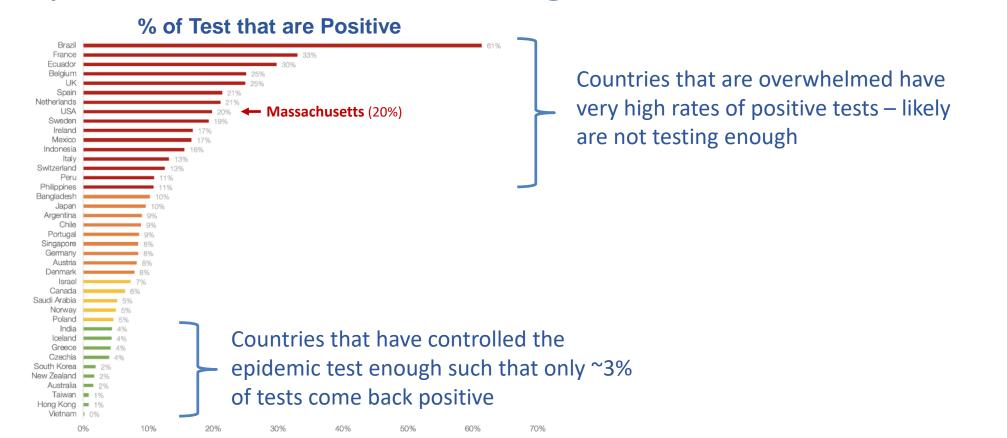
Study Conclusions

- Self-isolation of symptomatic cases alone: reduces R_T by 32%
- Household quarantine + selfisolation reduces R_T by 37%
- Self-isolation + app-based tracing reduced R_T by 44%
- Self-isolation + manual tracing of all known contacts reduces R_T by 57%
- Self-isolation + manual tracing of all contacts reduces R_T by 67%

Testing and tracing strategies can *more than double* the impact on R_T of self-isolation alone Three important factors to a testing & tracing strategy: (1) how many infected are ID'd and isolated, (2) how many contacts are traced and quarantined, and (3) how quickly each is done

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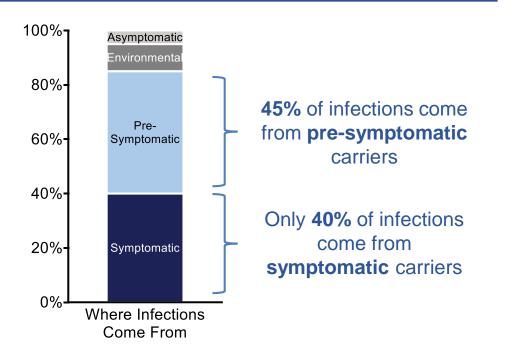
The Importance of Prolific Testing



The countries that have contained the pandemic only find ~1-3% positive cases during testing ~20% of MA cases come back positive – need to significantly increase level of testing

The Importance of Tracing

Estimated COVID-19 Transmission Sources



 If we only test and isolate people with symptoms, we can reduce R_T by 40% at most – this will not be effective enough on its own

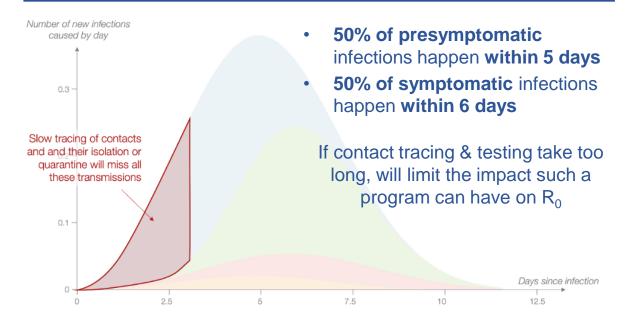
Reduce R_T

 If we also trace contacts and test them, possible to also catch the pre-symptomatics, reducing R_T by up to 85%

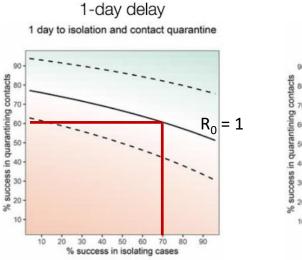
Recent research suggests ~45% of infections are caught from pre-symptomatic carriers If only test symptomatic individuals, can only reduce R_T by 40%. But a combined testing & tracing program that catches asymptomatic carriers can reduce R_T by up to 85%

The Importance of Speed

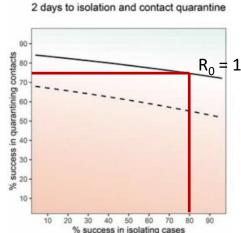
How Quickly Infections Happen



Testing & Tracing Speed v. Impact on R_T



If testing & tracing happens within 1 day, only need to successfully isolate **70% of cases & 60% of infected contacts to reduce R_T below 1**



2-day delay

But if takes 2 days to test & trace, will need to successfully isolate **80% of** cases & 75% of infected contacts to reduce R_T below 1

Speed is vital – the larger the delay between onset and successfully testing & tracing, the lower the impact on R_T. Need a program that can successfully test & trace 70-80% of contacts <u>within 2 days</u>

Testing: Who to Test

Possible Testing Plans

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MA Today	Bare Bones	Minimal	Moderate	Goal Expansive	Universal	
Population Tested	Those with strong symptoms, other causes ruled out in hot spots	Those with strong symptoms	Those with mild symptoms	Those with mild symptoms + contacts traced	Everyone every week	
# Tests Required / day in MA	~10K / day Current testing capacity	~20K / day ~1,500 positives @ 8% detection rate	~50K / day ~1,500 positives @ 3% detection rate	~100K / day ~1,500 positives @ 3% detection rate + 30 contacts/positive	~1M / day ∼7M residents ÷ 7 days a week	
Cost ¹	~\$6M / month	~\$12M / month	~\$30M / month	~\$60M / month	~\$600M / month	
% Pop. Tested						100%
Example Countries						

Need to prioritize who to test today and make testing as efficient as possible, while working to increase capacity to ~100K/day

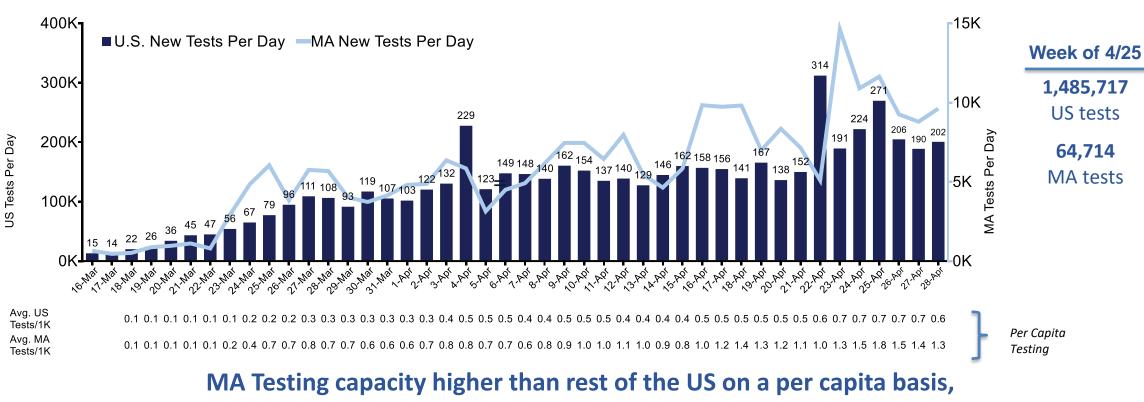
Source: Edmond J. Safra Center for Ethics at Harvard University: Roadmap to Pandemic Resilience, Worldometer, Tomas Pueyo 1: Assumes \$20 / test

Reduce R_T

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Current Testing Capacity



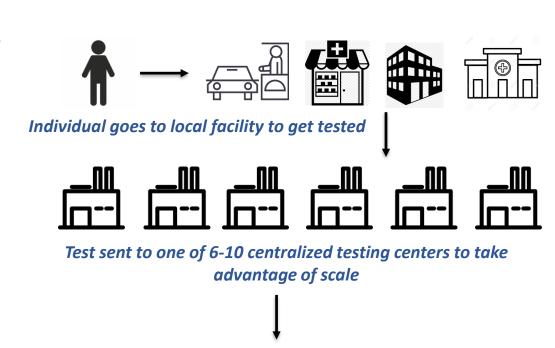


but both need to expand dramatically to reach goals of 30M national tests / week

Building the Necessary Testing Capability

Proposed Rapid Centralized Solution

- MA **contracts directly** with a large/multiple large diagnostics company(s) who can handle 100K+ tests/day
- Provider sets up 6-10 centralized testing centers to take advantage of scale and ramps up ability to perform 100K tests/day
- In addition to centralized facilities, **utilize current healthcare infrastructure** and local facilities (hospitals, urgent care clinics, pharmacies, etc.)
- Diagnostics companies require 6-8 weeks to ramp production – vital to set up contracts as soon as possible



Results delivered same-day or next-day

Given shortage of testing capacity, Massachusetts should <u>rapidly</u> explore avenues to secure capacity

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Testing: Timeline of Solutions

More expensive & difficult

Less expensive & easy

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Short-Term

- Centralized testing through a handful of large diagnostic companies
- 6-10 centralized testing centers
- Existing HC infrastructure used whenever possible

Production ramped to ~100K/day

Medium-Term

- Frequent saliva-based testing administered once a week
- 10 centralized testing centers continue to process tests, each able to process ~100K/day
- Production ramped to ~1M tests/day

Long-Term

- Universal at-home testing kits
- Saliva-based
- Cheap & easy to administer

Should work towards a more universal at-home testing program (infeasible today given technology and capacity constraints)

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Contact Tracing: Five Key Questions

1. Who Qualifies as a Contact?

Identifying who should be traced and their risk category

2. What Procedures Should Contacts Follow? Isolation and self-assessment based on risk level

3. How Many Contacts Do We Need to Trace? Extensive tracing of 70-90% of contacts needed to slow spread

4. How Many Investigators Do We Need? Thousands of investigators needed to trace 70-90% of contacts

5. How Do We Use Technology to Help?

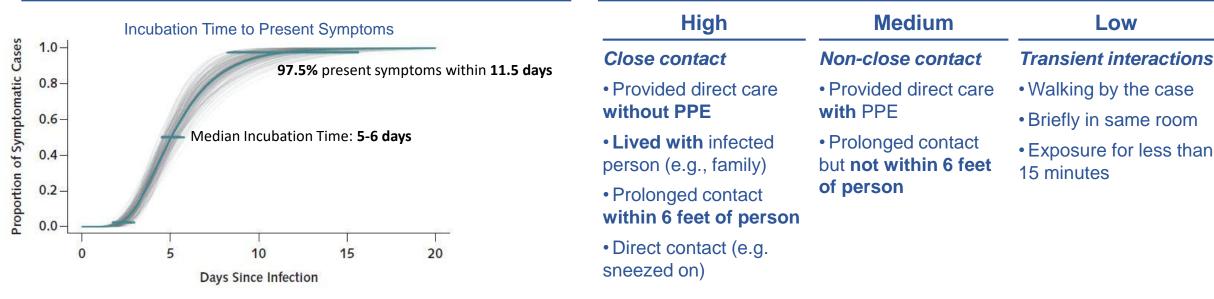
Digital tracing can increase efficacy considerably

Contact tracing necessary to slow spread and will require large manual and digital effort

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Who Qualifies as a Contact?

How Far Back to Trace



- Median incubation period is 5-6 days, full range up to 14 days Should trace & group contacts into high, medium, and low
- Need to track all contacts from previous two weeks

Should **trace & group contacts** into high, medium, and low risk buckets

Example Case Study: Canadian Classification System

Reduce R_T

H

Need to isolate and test family members, those in contact >15 minutes closer than 6 feet

Sources: Annals of Internal Medicine: "The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application", Stephen A. Lauer, MS, PhD; Kyra H. Grantz, BA; Qifang Bi, MHS; Forrest K. Jones, MPH; Qulu Zheng, MHS; Hannah R. Meredith, PhD; Andrew S. Azman, PhD; Nicholas G. Reich, PhD; Justin Lessler, PhD; Government of Canada: Public health management of cases and contacts associated with coronavirus disease 2019 (COVID-19)

What Procedures Should Contacts Follow?

	High Risk	Medium Risk	Low Risk		
Example	Family Member	Provided direct care while wearing PPE	Walked by on street		
Procedures	Quarantine at home for 14 days after exposure	 Self-monitor for symptoms such as fever or cough 	Follow actions recommended for entire		
	 Practice good hand hygiene and respiratory etiquette 	 Avoid close contact with individuals at higher risk for severe illness 	population		
	Self-monitor for symptoms such as fever or coughRecord temperature daily	 Follow actions recommended for entire population 			

Example Case Study: Canadian Guidelines

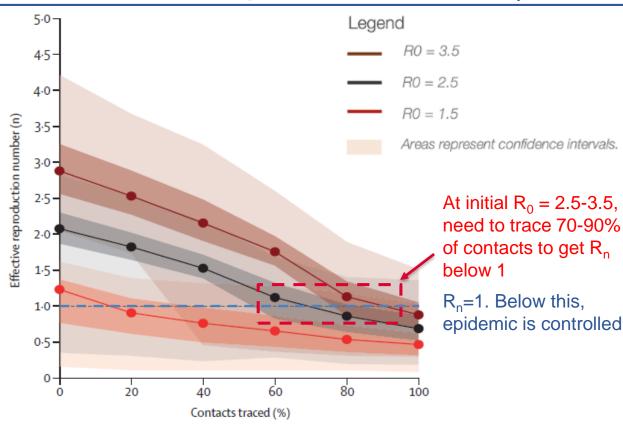
Need to determine policies & procedures for contacts to follow based on risk level. Should only high risk contacts be self quarantined, or should medium risk contacts be quarantined as well?

Reduce R_T

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How Many Contacts Do We Need to Trace?

Impact of Tracing on Reproduction Rate (R_T)



Key Considerations

Reduce R_T

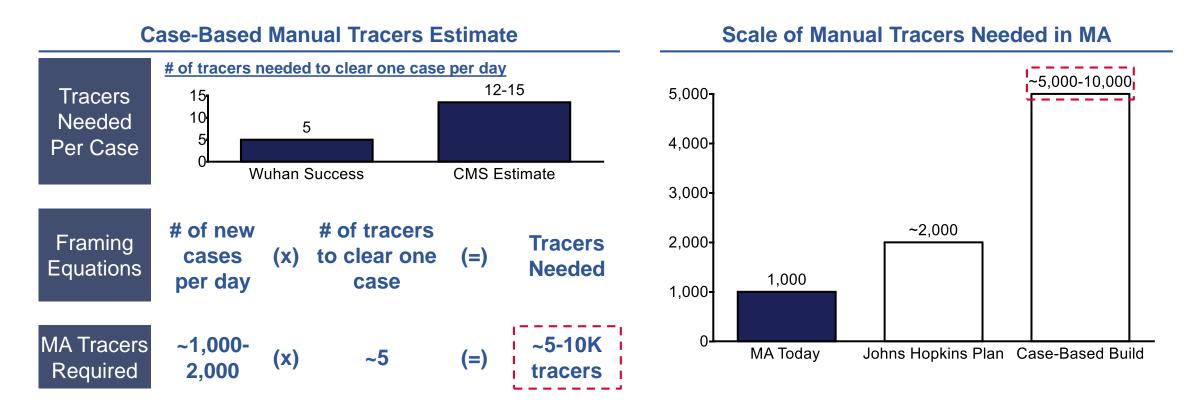
- Tracing required varies depending on basic reproduction number (R₀) of COVID-19 without remediating efforts
- If R₀ is 2.5, need to trace 70% of contacts to control epidemic – studies estimate 20 people per case
- If R₀ is 3.5, need to trace 90% of contacts to control epidemic – studies estimate 30 people per case
- Additional measures taken to help lower R_T will reduce burden on exactness in contact tracing

Will likely need to trace and isolate 20-30 closest contacts of each positive case as fast as possible

Sources: Tomas Pueyo, "Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts", Joel Hellewell, Sam Abbott, Amy Gimma, Nikos I Bosse, Christopher I Jarvis, Timothy W Russell, James D Munday, Adam J Kucharski, W John Edmunds, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Sebastian Funk, Rosalind M Eggo

T D

How Many Investigators Do We Need?



MA may need up to ~5-10K contact tracers

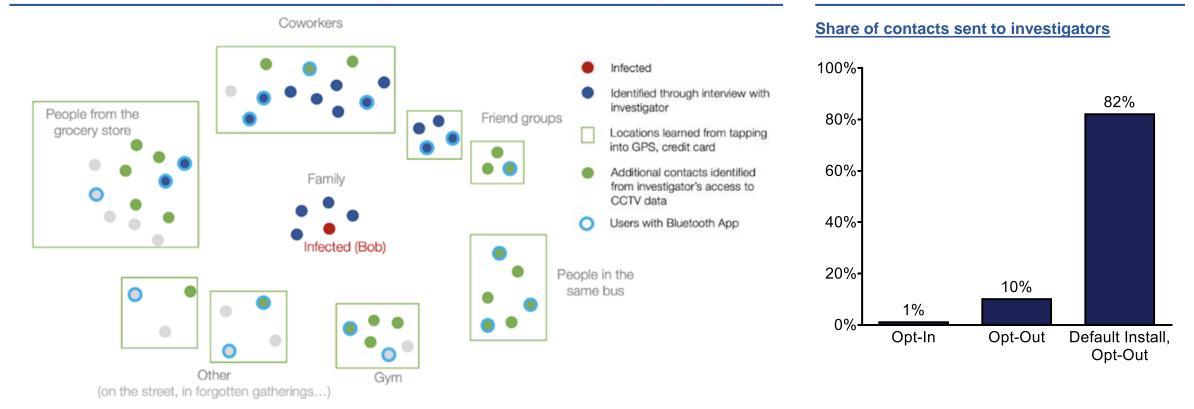
Reduce R_T

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How Do We Use Technology to Help?

Illustrative Contacts Identified through Manual Interview and Digital Tracing

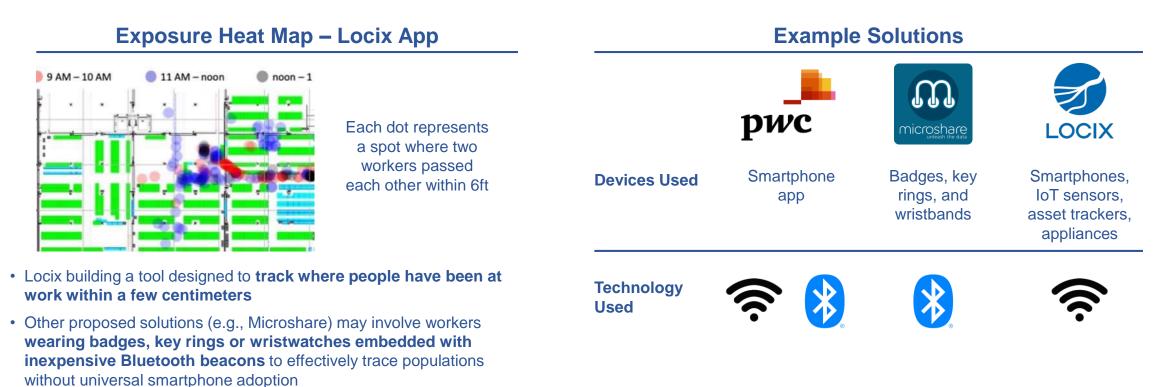
Opt-In vs. Opt-Out Bluetooth App



Will be difficult to identify 70-90% of contacts with manual tracing alone. Digital tracing can help manual tracers identify far more contacts, particularly with opt-out Bluetooth apps

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Workplace Digital Tracing: Example Case Study



Companies are building surveillance tools to monitor spread of coronavirus inside offices

Reduce R_T

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Legal Feasibility of New Workplace Norms

Key Legal Questions & Considerations

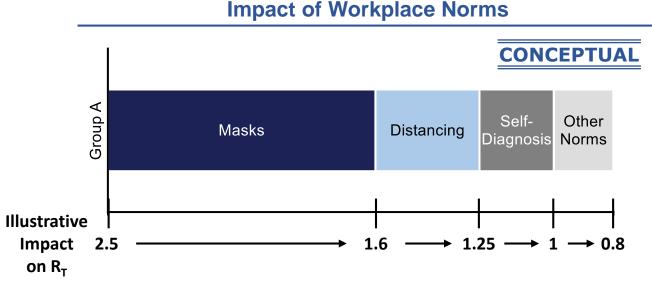
- How to make sure on-site temperature testing, symptom screening, and storing information are **compliant with HIPAA and the ADA**?
- Can compliance with health & safety guidelines be conditions of employment? How to deal with employees that refuse to comply?
- How to ensure a **non-discriminatory implementation** of policies and protocols?
- How to implement changes and protocols with a unionized workforce?
- How to deal with **potential negligence & lawsuit risk** related to new outbreaks and/or deaths?

Ropes & Gray Emerging Principles

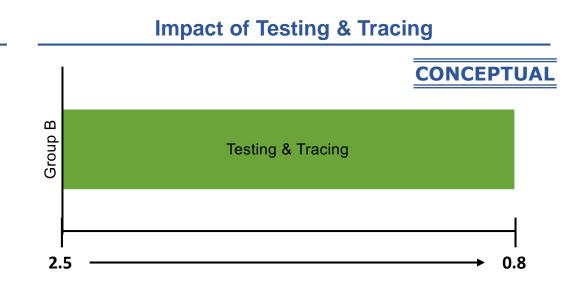
- Afford employees a safe working environment by adopting and enforcing scientifically-based work rules & providing appropriate supplies & support
- Align work rules & practices with guidelines from the cognizant federal, state, and local authorities
- Comply with federal, state, and local laws and regulations
- Respect the special requirements of **disability rights laws**, including as they apply to **comorbidity**
- Cooperate with state and local public health departments
- To the greatest extent possible, **keep private the health and social information** of individual employees

Several legal considerations to implementing new workplace norms. Key questions are (1) what the state should mandate, (2) consistent implementation, and (3) how to provide legal guidance for SMBs

Reducing R_T Summary Thought Model



- Workplace norms such as universal mask wearing, distancing and self-diagnosis can significantly reduce $R_{\rm T}$



 A robust testing & tracing program (~100K tests/day, 5-10K tracers + digital tracing) can have a similar impact on reducing R_T as workplace norms

Reduce R_T

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Contents

• Summary COVID-19 History & Economic Impact

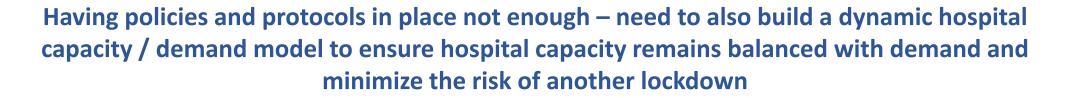
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- The Key Three Steps: *How* to Return to Work
- Timing: *When* to Return to Work

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When to Return to Work: Summary

- Building a dynamic hospital capacity / demand model based on current infection rate and system readiness for reopening critical to determining when to return to work
- MA currently managing hospital capacity well, with ICU beds only ~46% filled with COVID-19 patients
- However, **critical to not reopen too soon** a demand imbalance could lead to a second peak more severe than the first, as evidenced by St. Louis' re-opening during the 1918 Spanish Flu



Determining When to Reopen

Supply

- Availability of supply inputs: **beds**, **HC workers**
- Timeline & supply of therapeutic options
- System readiness for policies to reduce R_T (e.g., testing, tracing, PPE capacity)

Demand

- Current new case trajectory manageable / "curve flattening"
- Confidence in ability to track cases
- Model projecting anticipated hospital burden based on # ppl returning to work & projected spread

Case Studies

*1

China Return to Work

- Waited until new cases practically eradicated. Since then, new cases returned, but at much lower rates
- Firm workplace rules, rigorous testing, travel restrictions
- Comprehensive smartphone tracking



Spain Return to Work

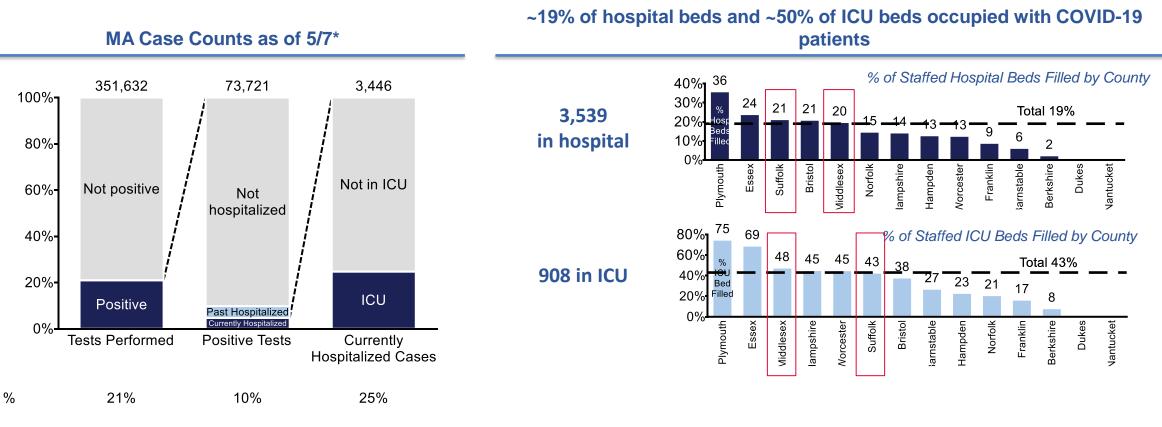
- Waited until new cases ~20% of peak
- Handed out 10M masks and 1M+ testing kits
- Allowing non-essential construction, manufacturing
 to return to work
- New cases since rose to ~80% peak levels, requiring immediate scale back – opened too soon

Need to model out supply and demand and reopen with a buffer on total capacity utilization



MA Hospitalization Rate & Capacity Data

RECALL



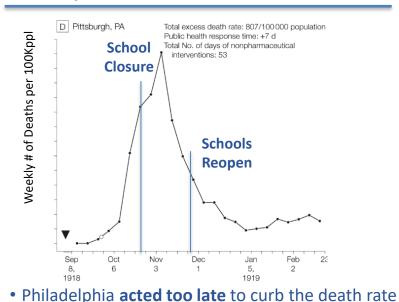
Approximately ~10% of positive cases in MA hospitalized ~19% of hospital beds and ~43% of ICU beds are currently filled by COVID-19 patients

*Hospitalization rate does not include patients previously hospitalized but since discharged, so likely higher than demonstrated by existing data Source: Mass.gov

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1918 Spanish Flu Precedent

Philadelphia - too late to shut, overwhelmed

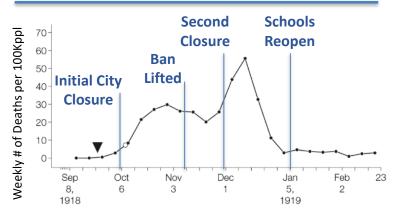


- after waiting until after a massive parade to

close the city, the virus overwhelmed hospitals

• But because initial rate so high, no second peak

St. Louis – reopened too early



 St. Louis acted early to curb the death rate – but opened too soon, causing a second spike much higher than the first

Denver - reopened with too little public guidance

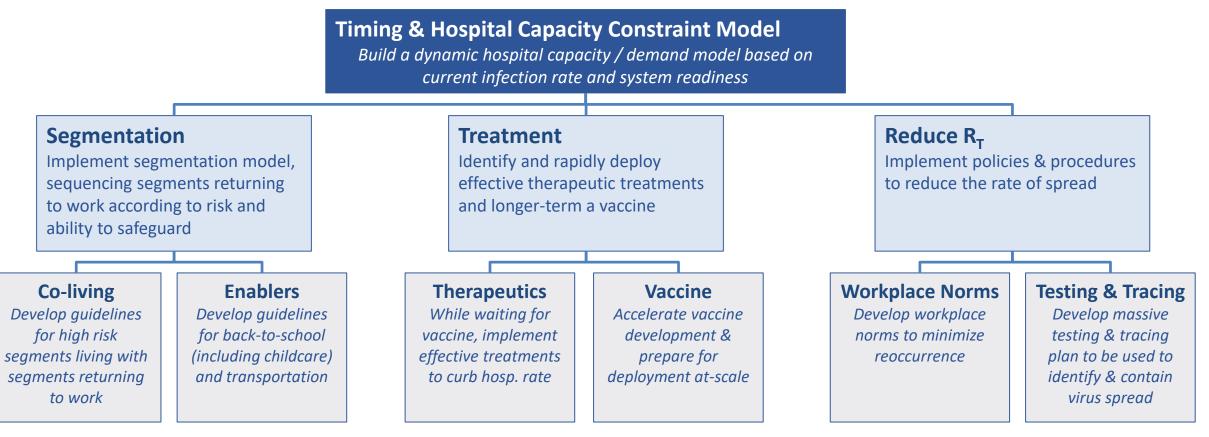


- Denver acted early to curb the death rate but opened with too little public guidance, causing a second spike with similar magnitude as first
 - After initial closure was lifted, the public thronged the streets by the thousands, and new cases rapidly spiked to rates higher than previous

City closures & social distancing highly effective if instituted early – but second waves are likely and can be worse than the first if proper measures not taken before re-opening

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The War on COVID-19



United we will win the war against COVID-19



Appendix

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Snibe Diagnostics

Sonic Healthcare

Thermo Fisher Scientific

Tianjin Beroni Biotechnology

VivaChek Biotech (Hangzhou)

Zhejiang Orient Gene Biotech

Zhengzhou Fortune Bioscience

Zhuhai Encode Medical Engineering

TIB Molbiol Syntheselabor

United Biomedical

Vela Diagnostics

Viracor EurofinsVision Medicals

Laboratory

YD Diagnostics

Zhongshan Bio-Tech

Zhuhai Livzon Diagnostics

Specialty Diagnostic (SDI) Laboratories

Stanford Health Care Clinical Virology Laboratory

University of North Carolina Medical Center

Yale New Haven Hospital Clinical Virology

SolGent

Testing Companies and Organizations, References

- 3D Medicines
- Abbott
- Aculabs, Inc.
- Anatolia Geneworks
- ARUP Laboratories
- A*STAR, Tan Tock Seng Hospital of Singapore
- Assure Tech
- Atila BioSystems
- AusDiagnostics
- Autobio Diagnostics
- Avellino Lab
- Bako Diagnostics
- Baptist Hospital Miami Pathology/Laboratory Medicine Lab
- Becton Dickinson
- Becton Dickinson, BioGx
- Beijing Decombio Biotechnology
- Beijing Diagreat Biotechnologies
- Beijing Kewei Clinical Diagnostic Reagent
- Beijing O&D Biotech
- Beroni Group
- BGI
- Biodesix
- BioMedomics
- BioMérieux
- BioMérieux/BioFire Defense
- Bioneer
- BioReference Laboratories
- Boston Children's Hospital Infectious Diseases
 Diagnostic Laboratory (IDDL)

Source: 360dx.com, CDC, FDA, company websites

- BTNX
- CellexCenters for Disease Control and Prevention
- Cepheid
- CerTest BioTec
- Chembio Diagnostics
- Children's Hospital of Philadelphia Infectious
- Disease Diagnostics Laboratory
- CirrusDx Laboratories
- Co-Diagnostics
- Core Technology
- Credo Diagnostics Biomedical
- DiaCarta
- Diagnostic Solutions Laboratory
- DiaSorin Molecular
- Diatherix Eurofins
- Diazyme Laboratories
- Eachy Biopharmaceuticals
 Euroimmun/PerkinElmer
- EuroImmun/Perkir
 Exact Sciences
- Exact Sciences
 Fosun Pharma USA
- Fosuri Priama OSA
 Fulgent Genetics/MedScan Laboratory
- Fulgent Genetics/MedScan Laborator
 Genetic Signatures
- Genetic Signat
- Genetron
- GenMark DiagnosticsGenomica/PharmMar Group
- GenoSensor
- Gnomegen

https://www.cepheid.com/en_US/systems/GeneXpert-Family-of-Systems/GeneXpert-Infinity

https://www.neumodx.com/wp-content/uploads/2019/03/NeuMoDx 288 Spec Sheet R2.pdf https://www.ibj.com/articles/roche-begins-shipping-emergency-approved-covid-19-tests-across-country

Gold Standard Diagnostics

https://www.medtechdive.com/news/over-90-of-1m-abbott-coronavirus-tests-sitting-idle-white-house-official/575794/

Guangzhou Wondfo Biotech

- Hackensack University Medical Center (HUMC) Molecular Pathology Laboratory
- Hangzhou AllTest Biotech
- Hangzhou Biotest Biotech
- Hangzhou Clongene Biotech
- Hangzhou Testsealabs Biotechnology
- Healgen Scientific
- Hologic`
- InBios International
- Innovita (Tangshan) Biological Technology
- Integrated DNA Technologies/Danaher
- Integrity Laboratories
- Ipsum Diagnostics
- Jiangsu Macro & Micro-Test Med-Tech
- JN Medsys
- Kogene Biotech
- KorvaLabs
- Laboratory Corporation of America
- LGC, Biosearch Technologies
- Lifeassay Diagnostics
- Luminex

https://investors.hologic.com/press-releases/press-release-details/2020/Hologics-Molecular-Test-for-the-Novel-Coronavirus-SARS-CoV-2-Receives-FDA-Emergency-Use-Authorization/default.aspx

https://www.thermofisher.com/us/en/home/clinical/clinical-genomics/pathogen-detection-solutions/coronavirus-2019-ncov/genetic-analysis/tagpath-rt-pcr-covid-19-kit.html (94 specimens in 3 hours)

https://www.bd.com/en-us/company/news-and-media/press-releases/bd-biogx-announce-fda-emergency-use-authorization-submissions-for-new-covid-19-diagnostics-for-use-in-us

- Maccura Biotechnology
 - Massachusetts General Hospital
 - Mayo Clinic Laboratories
 - Medical Systems Biotechnology
 - Mesa Biotech
 - Mount Sinai Labs
 - Nanjing Liming Bio-products
 - NanoResearch
 - Nantong Diagnos Biotechnology

- NeuMoDx Molecular
- Nirmidas Biotech
- Northwestern Medicine Diagnostic Molecular Laboratory
- Novacyt/Primerdesign
- NY State Department of Health (performed at Wadsworth Center and New York City Department
 Suzhou Kangheshun Medical Technology of Health and Mental Hygiene, Public Health Laboratories)
 Systaaq Diagnostic Products
 Telepoint Medical Services

Rutgers University Clinical Genomics Laboratory

Orig3n

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- Ortho Clinical Diagnostics
- Osang Healthcare

Quest Diagnostics

Rendu Biotechnology

Sentinel Diagnostics

ScienCell Research Laboratories

Shanghai Fosun Long March Medical

Shenzhen Landwind Medical

Science/Shanghai Fosun Pharmaceutical

- PathoFinder
- PCL
- PerkinElmerPhamatech

Promedical

Qiagen

Quidel

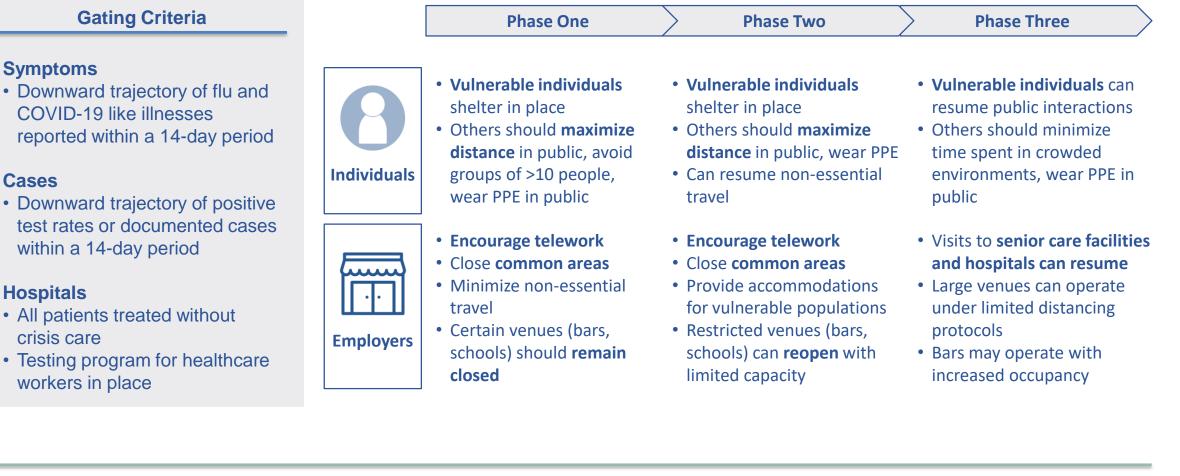
Roche

SD Biosensor

Seegene

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White House Return to Work Framework



BACKUP



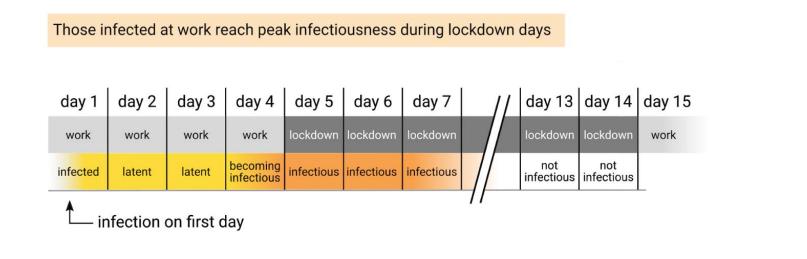
Intermittent Work Phasing Option

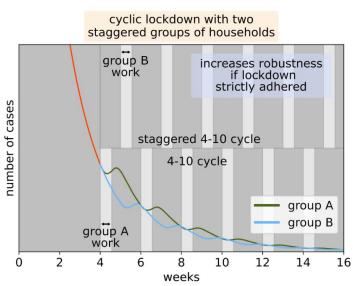


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To reduce risk of second wave, could begin by phasing groups in cycles of 4 work days and 10 lockdown days

Potential Impact





Could explore alterative back-to-work phasing to help reduce healthcare burden while allowing groups to return part-time earlier, potentially before system fully ready

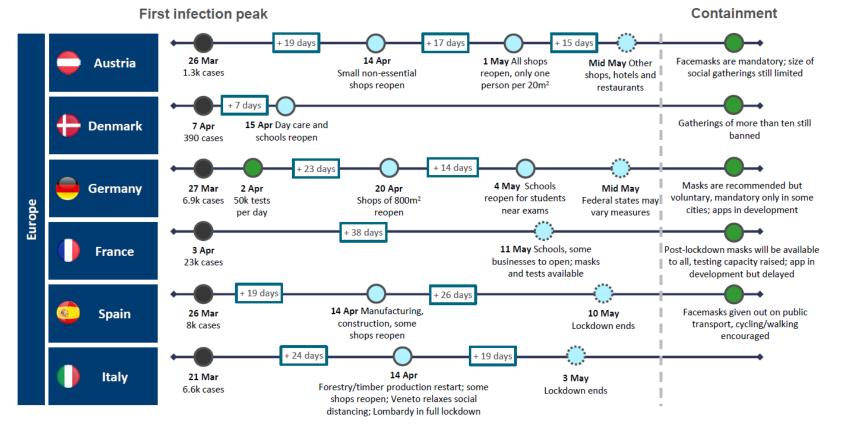
Source: Prof. Uri Alon, Prof. Ron Milo, Prof. Nadav Davidovich, Prof. Amos Zahavi, Dr. Hagit Ulanovsky; Intermittent Work: A feasible strategy for a return to economic activity that can prevent a second wave of COVID-19; Weizman Institute of Science

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European Timelines



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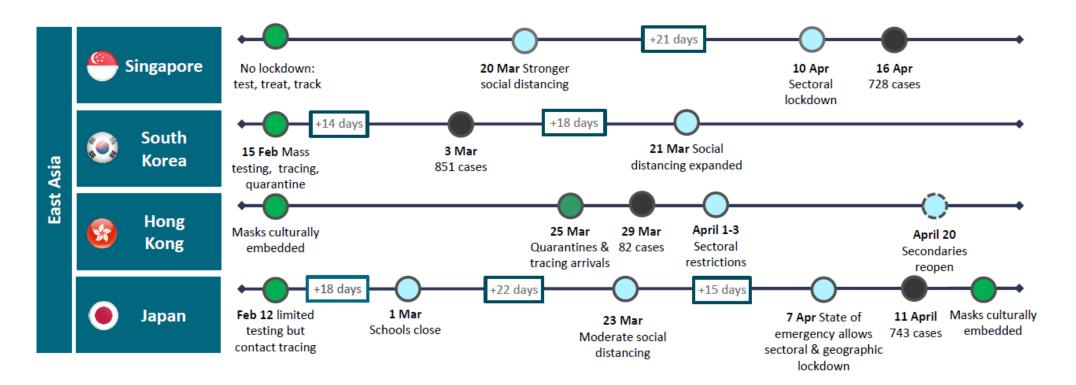
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European countries are starting to ease, but containment strategies appear limited, risking acceleration of the virus. This may mean a return to lockdown

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East Asia Timelines



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East Asia countries are strongly emphasizing containment (masks, testing and tracing), which has enabled most countries to avoid full lockdowns and keep infection spikes below western peers

Testing: How to Test

Case Study: Drive-Thru Testing

- South Korea has set up drive-through testing centers. Tests take 10 minutes and results texted to you the next day. Able to test ~10ppl/hour
- At this point, **all 50 U.S. states** have also adopted drive-through testing centers. However, currently can take **up to a week to get results**

Other Potential Testing Locations



Drive-Thru



Pharmacy





BACKUP

At Work

Hospital / Urgent Care Center

Should utilize current healthcare infrastructure to make testing **widely available** and **easy to access**

Goal is to make testing easy and quick, in order to test & track as many individuals as possible within the first 2 days of exposure

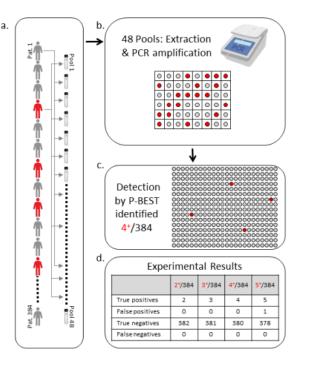




Making Testing More Efficient: Test Pooling Case Study BACKUP

Stanford's Test Pooling

- In early testing, Stanford **pooled samples into groups of 9-10** and tested the group
- Of the 292 groups pooled, only two came back positive – further analysis showed that one person in each group was positive
- Concluded **pooling can make mass testing far more efficient**, but only works when **prevalence is low**



Recent COVID-19 Sample Pooling Study

- A recent study showed pooling samples in groups up to 48 samples/group preserved accuracy (all positives identified, with no false negatives)
- Group recommends pooling methods for asymptomatic carriers (e.g., in expected low prevalence groups) – can make such testing far more efficient

Research still emerging, but may be possible to pool samples in groups of 10-50, significantly increasing testing efficiency (able to run 100K pooled tests in the same time as 10K individual tests)

What Tests to Use: Viral Testing Overview

BACKUP

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Key Con	Testing Companies & Capacity									
How it works: Viral genetic information extracted using swab and amplified in a machine using PCR What it detects: If you currently have COVID-19 Average cost: TBD		 Abbott Molecular BD BioGX Cepheid DiaSorin Molecular 		d	 LabCorp NeuMoDx PerkinElmer			 Full List in Appendix Quidel Corporation Roche Molecular Systems Thermo Fisher Scientific 		
Pros	Cons			ample	High Th	roughn	ut Mach	ince / D	roducte	
 Detects current infection High throughput 	 Slow results Requires many swabs, limited reagents 	Company	Abbott	BD / BioGX	Cepheid		NeuMoDx		Thermo Fisher	
Inexpensive	 High throughput machines require trained technicians 	Machine / r Product	m2000	BDMax	GeneXper Infinity		288 Molecular	COBAS 8800	TaqPath	Lab Developed Tests
 Can collect at home 		Daily Capacity	470	360	>2,000	1,150	864	4,128	>1,500	>200

0 0

Ideal for combination testing and tracing program because of ability to detect infection in real time

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What Tests to Use: Antibody Testing Overview

Key Cor	Testing Companies & Accuracy							
How it works: Samples blood, test device detects antibodies created by body to fight virus What it detects: If you previously had COVID-19 Average cost: TBD		Companie	 Abbott BioMedomics In Bioperfectus Technologies Cellex Decombio 		is • Innovita		 Full List in Appendix VivaChek Biotech Wondfo Biotech SD Biosensor Biolidics Limited Biomedomics Epitope Diagnostics 	
Pros	Cons							
Can identify previous	 Antibodies slow to develop 	Sample Test Specificity						
infections	 Unclear how protected 	Company Bi	oMedomics	Bioperfectus	Dec	comBio	DeepBlue	Innovita
Takes seconds to test	those with antibodies are	Specificity	87%	95%	(90%	84%	96%
Doesn't require swabs	 Program based on 		Premier	Sure	UCP	VivaChek	Wondfo	Epitope
Can detect previous	antibody testing could	Company					vvonuro	<u> </u>
asymptomatic cases	encourage ppl to catch	Specificity	97%	100%	98%	95%	99%	90%
	virusFalse positives			alidation for fir t be accurate	st kits wi	thout data va	lidation. The a	bove data is
Ideal for identify	ing percentage of popula	tion that h	as been i	nfected, b	out les	s ideal foi	r testing/t	racing

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What Tests to Use: Saliva v. Nasal Testing

Nasal or Throat Swabs

- Currently most broadly administered test
- Recommended by the CDC
- **Invasive** (involves a long Q-tip-like swab stuck up the nose or into the back of the throat)
- Can take **1-5 hours** to run the test
- Requires a trained professional to administer
- Can have a false-negative rate of ~30%+

Saliva Tests

- Recently received FDA emergency use authorization
- Minimally invasive (simply spit into vial)
- Can be **reliably self-administered**
- Requires less PPE and personnel to administer
- Not enough information to determine accuracy, but recent studies estimate ~90% to ~95% as effective as nasal or throat swabs

Other Emerging Options

BACKUP

- DNA test that can deliver results in 40 minutes using CRISPR
- Take-home test FDA recently authorized the first take-home kit; receive kit with doctor approval and mail back

Should keep track of emerging testing technologies and focus on options that make the testing process as easy and quick as possible while retaining accuracy

Dedicated to Growth... Committed to Action

Range of Digital Tracing Options

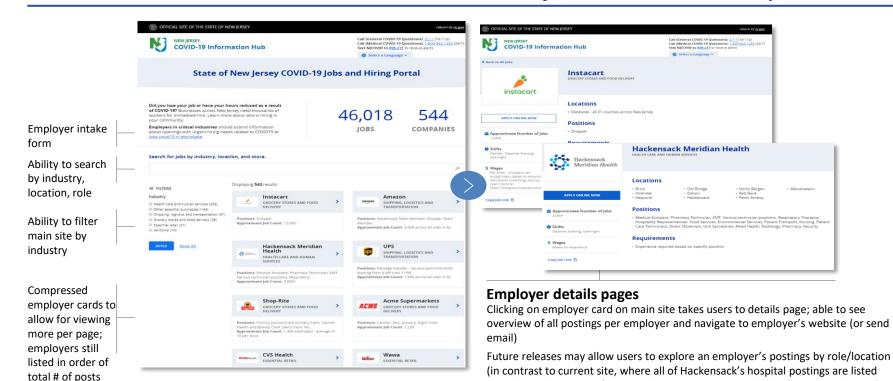
			Centralized			
		Google and Facebook	Europe	South Korea	China	
Description	Policy	Alerts users if they've been in contact with a positive case	App that uses central servers to alert contacts of positive cases	Government publishes detailed reports about confirmed cases	Traced residents who left Wuh involuntary quarantine	
	Technology Used	iPhone and Android devices, Bluetooth	Bluetooth, central servers, cell phone data	Cellphone data, credit-card transactions, security footage	Phone and location data, travel history, drones, security footage	
Date Deployed		In development	In development by consortium of institutions & companies	Traced residents in February, gave access to local officials March 4th	Lockdown of Wuhan January 23 rd , traced residents soon after	
Success		NA	N/A	Average of 30 cases a day	0 reported new cases	
Opt-In/Voluntary?		✓	1	X	×	
Information Disclosed	Age and gen	der 🗶	✓	\checkmark	√	
	Travel history	y 🗶	\checkmark	1	\checkmark	
	Address & lo	cation 🗶	✓	\checkmark	\checkmark	
	Contacted pe	ersons 🗶	X	\checkmark	\checkmark	

Digital tracing can be highly effective, but privacy concerns a key issue

BACKUP



Reimagining Support Services: Workforce Redeployment BACKUP



New Jersey State Platform Example

How it works

Job posting platform, featuring postings by employers whose labor needs are spiking due to COVID-19, hosted by NJ Economic Development Authority

No matching service, **purely 'bulletin board' style**.

Outcomes so far

Job posts: 540+ employers posted 46,000+ jobs on the site as of 2 April

Visitors and clicks: Site had ~340K unique visits in its first 10 days, with ~20K aggregate clicks on "Apply Now" buttons

New Jersey has set up a 'bulletin-board' style platform to help match unemployed with new labor needs

together, without specific wage data, # postings per role, locations per role, etc.)