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An Adaptive Risk-Based Strategy for Connecticut's Ongoing COVID-19 Response

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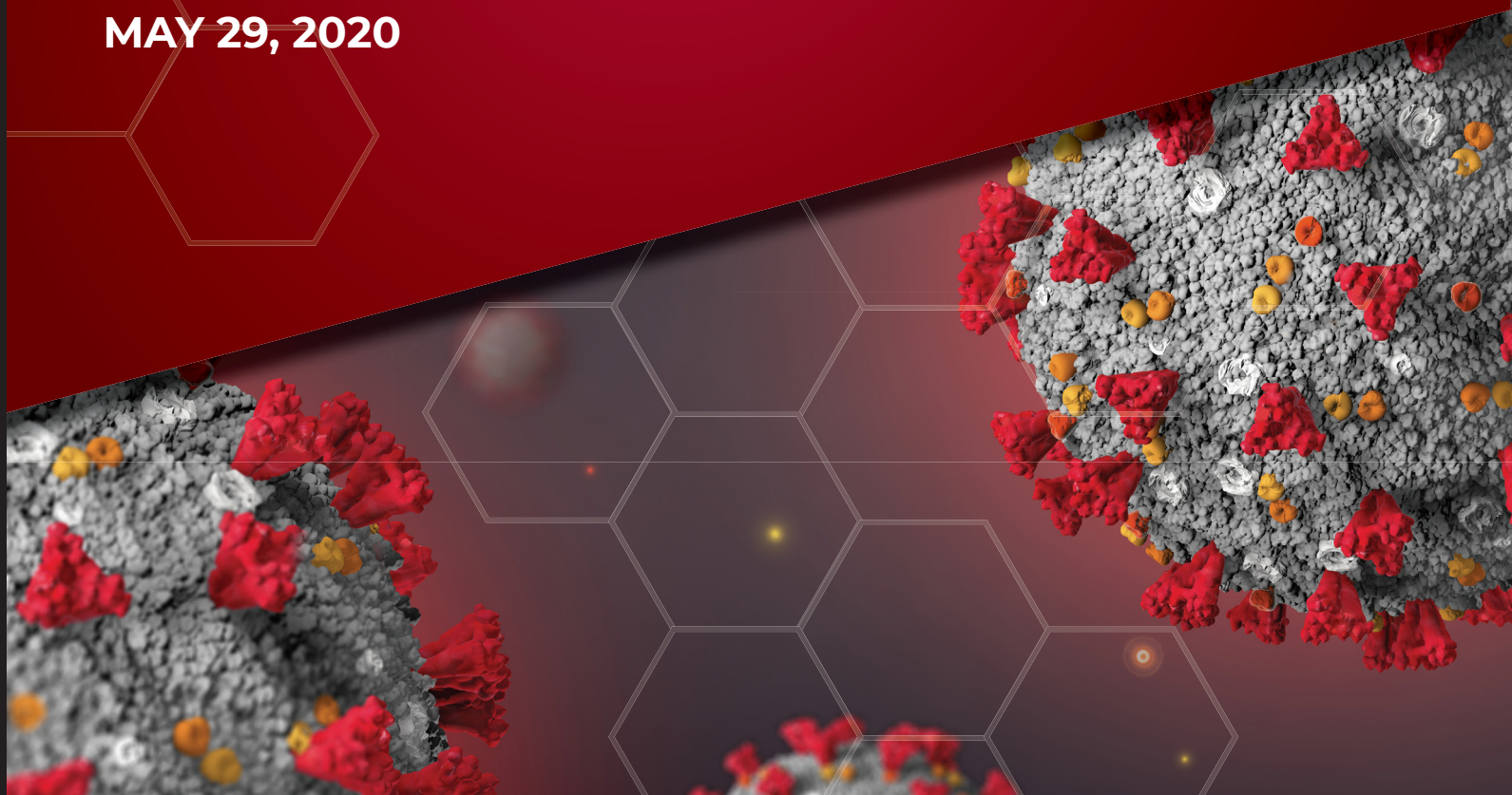

An Adaptive Risk-Based Strategy for Connecticut's Ongoing COVID-19 Response

Prepared by the
Connecticut Academy of Science and Engineering
for consideration by the
Office of Connecticut Governor Ned Lamont

May 29, 2020

Connecticut Academy Of Science And Engineering
An Adaptive Risk-Based Strategy For Connecticut's Ongoing COVID-19 Response

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Executive Summary

On March 11, 2020, the World Health Organization declared the spread of the novel coronavirus a pandemic. Immediately after, on March 13, the United States declared a national state of emergency, and states across the country soon followed with issuing broad stay-at-home orders and temporarily closing "non-essential" businesses. At the point of the initial spread of infections, containment is best sought through a strategy of identification, isolation and contact tracing. However, the novel coronavirus had spread stealthily to the point of broad community spread and major outbreaks. This necessitated the blunt mitigation approach of shutting down much of the economy. This greatly slowed the spread of COVID-19, and many states are currently below their initial peak levels of infection. Still, the U.S. has been hard-hit, with more than 1.5 million confirmed cases and about 95,000 deaths resulting from the disease. Compounding that adversity, the unprecedented mitigation efforts have resulted in the unintended consequence of severe economic impact with nearly 40 million people filing first-time unemployment claims in just nine weeks, and several major corporations declaring bankruptcy. In the U.S., this impact is particularly acute among service workers and many in minority and immigrant communities. They are doubly impacted by the disease and the economic hardships. While government aid can help buffer this, that is not a sustainable solution.

Hence, attention has recently turned to when and how to reopen the economy while continuing to protect public health. In some cases, state planning has taken place in partnership with neighboring states, such as Connecticut's participation in a coordinating group with six other states in the region. On April 13, Connecticut Governor Lamont announced the establishment of the Reopen Connecticut Advisory Group to address how best to reopen the economy while ensuring the safety of communities. With input from this group and other key stakeholders, the governor released the roadmap for reopening Connecticut on May 26.

With this backdrop, the Connecticut Academy of Science and Engineering (CASE) has concurrently taken the initiative to leverage its expertise in developing additional concepts for consideration in addressing the ongoing challenge of the COVID-19 pandemic. The decisions facing policy makers are inherently complex, posing difficult choices in balancing risks and benefits of various approaches to protecting public health. These choices involve highly interconnected systems where the direct and unintended outcomes are often uncertain. Probably most challenging is the dynamic nature of the epidemic with all that is still unknown about the disease. Roadmaps will need to be revised and updated over time. To this end, CASE has undertaken an initial look at the current challenge from a risk-based systems perspective. CASE convened a committee of experts across medicine, public health, engineering, science, and technology, with the committee members drawing on expertise from numerous colleagues in various fields to explore relevant issues and potential solutions.

The study itself was designed as more of a sprint rather than a traditional extensive study. It was deemed important to get and share early insights, even if they would need to be refined over time. The committee met initially on April 22 and completed its work a month later. The pace of new findings and articles from the global community kept reshaping or reinforcing initial conjectures. Work started with a review of what was known about COVID-19 and considered the numerous papers and reports on general reopening roadmaps and strategies. Work continued with analysis and modeling of Connecticut specific data and more focused consideration of targeted approaches for testing and mitigation. Many of the topics raised in this report merit further and deeper consideration as follow up efforts. CASE stands ready to assemble the broad expertise of its members, many of whom are also members of the National Academies of Sciences, Engineering, and

Medicine, in support of the state's particular needs.

It is hoped that the concepts and framework in this report will serve as a useful resource for the governor and leaders throughout Connecticut in both the public and private sectors. Even though this study was pursued specifically with Connecticut in mind, the principles described here are broadly applicable to other states.

The report is organized into sections that provide background about the current situation, offer general principles regarding an adaptive, risk-based approach to decision-making, testing and reopening of the economy. They build on each other but may be read separately as well. Section 2 provides a brief overview of what we currently know about COVID-19. It is by no means comprehensive and could quickly become outdated with the rapid pace of learning about the disease. Section 3 adds background regarding Connecticut's current situation and some of the particular challenges and opportunities ahead. In Section 4, we offer an adaptive, risk-balancing strategy for decision-making going forward, one that can provide the needed disease mitigation while avoiding the economic and health impacts of a prolonged shutdown. An integral part of any adaptive strategy is testing. Section 5 discusses a targeted approach to testing and mitigation that is more efficient and effective than scaling up to massive testing of everyone in the state as some studies have recommended. Section 6 puts these concepts together in offering a path forward to returning to work and continuing to protect the vulnerable. The concepts here are provided as general principles for consideration as policy makers and business leaders work together to provide detailed guidance for the various sectors of society. Section 7 addresses the urgency of working toward early outpatient treatments to minimize the severity of outcomes and reduce the load on hospital systems, and Section 8 presents the imperative to quickly and safely reopen the full healthcare system. The singular focus on COVID-19 has created increased risks through reduced care for other health conditions and could cause some atrophy of overall healthcare capacity. Lastly, Section 9 summarizes the key concepts and recommendations during this initial assessment.

On May 20, 2020, Connecticut initiated the first phase of reopening with limited relaxation of earlier mitigations. The seven-day moving average of new cases has declined to about half of the earlier peak but is declining slowly. COVID-19 is likely now endemic. The extent to which efforts to mitigate have blunted pandemic and local spread remains uncertain and whether alternative approaches would have been better adopted unknown; hindsight itself is biased and the disease continues to be very dynamic. The shutdowns have helped, but the toll has been massive.

We must pivot to a different approach to managing this disease, one that is more adaptive and targeted. Rather than prolonged and repeated universal shutdowns of "non-essential" businesses and activities, we can effectively deploy the tools of physical distancing, PPE, hand/face/surfaces hygiene, outdoor alternatives, antigen testing, contact tracing and teleworking and extended workhours to reopen in an adaptive fashion. We can do this in a way that continues to safeguard public health. We need to take full advantage of monitoring and modeling local conditions to fine-tune mitigations and continue protecting the vulnerable. This is a feedback control approach instead of an on/off switch. As we move forward together through these unchartered waters, these seven imperatives must guide a new strategy built on **COURAGE**:

Caution is warranted. We do not know how this disease will evolve and what future waves will look like. The possibility of exponential growth requires readiness for early action. As the current wave recedes, vigilance will be key to contain potential future outbreaks before they can spread broadly once again. Social cooperation in reasonable efforts to reduce viral spread (e.g., mask use, handwashing and physical distancing) is needed.

Open the full healthcare system. Our health systems have been nearly singularly focused on meeting the challenges of caring for COVID-19 patients. As a result, many people have deferred elective and even required care due to concerns for infection risks. They have waited to seek medical attention for their heart, cancer, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular illnesses, and other chronic diseases. This presents a significant health risk of a different type and must be addressed. We recommend a systematic SARS-CoV-2 antigen testing strategy for healthcare workers and for patients undergoing elective procedures. This screening combined with diligent PPE use and thorough sanitization of facilities will enable the safe restoration of our full-service healthcare systems.

Understanding comes from effective monitoring of the current situation. Antigen testing must be adequate, accessible, and accurate. The current levels of testing are not enough, but the levels needed are not massive. Connecticut is on a good path to reaching the weekly antigen testing volume required for effective response. Volume of testing will vary depending on the extent of the disease spread, and guidance regarding scaling that volume is provided in this report. Diagnostic testing to see if someone currently has the disease is actionable and should be widely available; antibody testing can provide useful insight regarding disease prevalence over time, but it is not actionable because we do not yet know that it correlates with immunity. Tracking the spread of the disease depends on both creative surveillance strategies and the capability to trace contacts of those who are infected. Automated privacy-preserving approaches for contact tracing when adopted broadly can augment but not replace traditional manual efforts.

Resources will be needed. They will be needed to scale up the state's testing and contact tracing capabilities. Public and private entities alike will need to keep investing in research for treatments, therapeutics and vaccines. Increased capacity of and coordination among our public health organizations and hospitals are critical to confront future risks of outbreaks.

Adaptation is key. We need to continue to learn and apply that learning. We will need to keep adjusting our response in a thoughtful and timely way. Here the key is to balance the benefits, costs, and risks appropriately. By using more targeted approaches to mitigations, one can achieve similar positive outcomes while minimizing the unintended negative consequences. Adaptation requires being able to anticipate trends correctly; however, past projections have varied so widely as to limit their utility for guiding mitigations and even future testing strategies. Along with the understanding gained from increased testing, useful Connecticut-tailored epidemiological models need to be developed and regularly updated with the latest information and data. Such models would also be invaluable in assessing the effectiveness of mitigation policies and guidelines.

Guard the vulnerable. It is unconscionable that so many have died in nursing homes, often alone. We must do better. A careful policy review is needed as to how many nursing patients could have been moved back home, to hotels, or to small pods of persons with highly limited mixing with others. There is much that can be learned and adopted from successful healthcare practices. The diligent use of PPE has enabled hospitals to significantly reduce spread among their staff and patients as compared to the population at large. Homeless shelters were spared the worst of the crisis when they decompressed their populations into empty hotels with individual rooms and bathrooms. We can keep our vulnerable safe while still affording them much needed contact with those that love them. We must take the time to understand true root causes and develop lasting solutions to protect the health of the most vulnerable groups in our state.

Education is essential. We need to equip the people of Connecticut with a practical understanding of risk and mitigation that enables them to adjust appropriately their everyday routines rather than being fearful of daily activities. For example, the concept of contact intensity, which includes duration of contact, number of contacts and physical separation distance, is much more useful than the current simplistic and rigid six-foot social distancing guidance. A clear differentiation of risks in different types of indoor and outdoor settings provides important insights on how best to conduct business and social activities without unduly compromising public health. Here too, models for disease transmission and analysis of various risks, particularly in indoor settings, can usefully guide policy makers. As decisions are made, communication of policies must be clear, consistent, and transparent without politicization. Without buy-in, even mandatory measures will fail. With buy-in, even simple guidance can be effective.

SECTION 1

Introduction

On January 21, the first confirmed case of the novel coronavirus in the U.S. was diagnosed in a Washington state resident who had traveled to Wuhan, Hubei Province, China. The first case of community spread was detected in California on February 26. On March 8, Connecticut recorded its first confirmed case. Now, two-and-a-half months later, over 90,000 people have died in the U.S. from COVID-19, including over 3,600 people in Connecticut.[1] The rapid and devastating spread of the disease necessitated state-wide mitigation measures of different types across the country; Connecticut enacted its own stay-at-home order effective March 23. While these mitigation strategies have been mostly effective at slowing down the spread of the disease, they have also exacted a great unintended toll on people's lives and livelihood.

In recent weeks, states have turned their attention to when and how to reopen their economies while continuing to protect public health. In many cases this has taken place in partnership with neighboring states, such as Connecticut's participation in a coordinating group with six other states in the region. On April 13, Governor Lamont announced the establishment of the Reopen Connecticut Advisory Group, co-chaired by Indra Nooyi and Albert Ko, to address how best to reopen the economy while ensuring the safety of communities. With input from this group and other key stakeholders, the governor released the roadmap for reopening Connecticut on May 26.[2]

With this backdrop, the Connecticut Academy of Science and Engineering (CASE) has concurrently taken the initiative to leverage its expertise in developing additional concepts for consideration in addressing the ongoing challenge of the COVID-19 pandemic. The decisions facing policy makers are inherently complex, posing difficult choices in balancing risks and benefits of various approaches to protecting public health. These choices involve highly interconnected systems where the direct and unintended outcomes are often uncertain. Probably most challenging is the dynamic nature of the epidemic with all that is still unknown about the disease. Roadmaps will need to be revised and updated over time. To this end, CASE has undertaken an initial look at the current challenge from a risk-based systems perspective. CASE convened a committee of experts across medicine, public health, engineering, science, and technology, with the committee members drawing on expertise from numerous colleagues in various fields to explore relevant issues and potential solutions.

The study itself was designed as more of a sprint rather than a traditional extensive study. It was deemed important to get and share early insights, even if they would need to be refined over time. The committee met virtually four separate times from April 22 to May 3 and continued with numerous ad hoc interactions. The pace of new findings and articles from the global community kept reshaping or reinforcing initial conjectures. Work started with a review of what was known about COVID-19 and considered the numerous papers and reports on general reopening roadmaps and strategies. Work continued with analysis and modeling of Connecticut specific data and more focused consideration of targeted approaches for testing and mitigation. Many of the topics raised in this report do, in fact, merit further and deeper consideration as follow up efforts. CASE stands ready to assemble the broad expertise of its members, many of whom are also members of the National Academies of Sciences, Engineering, and Medicine, in support of the state's particular needs.

It is hoped that the concepts and frameworks in this report will serve as a useful resource for the governor as well as for leaders throughout Connecticut in both the public and private sectors. Even though this study was pursued specifically with Connecticut in mind, the principles described here are broadly applicable to other states throughout the duration of this pandemic.

The report is organized into sections that provide background about the current situation, offer general principles regarding an adaptive, risk-based approach to decision making, testing, and reopening of the economy. Section 2 provides a brief overview of what we currently know about COVID-19 as a convenient resource. It is by no means comprehensive and could quickly become outdated with the rapid pace of learning about the disease. So we also have included a discussion of what we wish we knew about the disease and how the answers to these questions could affect what needs to be done. Section 3 adds background regarding Connecticut's current situation and some of the particular challenges and opportunities ahead. The binary approach of shutting down the economy for the public health benefit of containing a single disease was necessary in the beginning. But this approach comes at great cost and is clearly not sustainable.

In Section 4, we offer an adaptive, risk-based strategy for decision making going forward, one that can provide the needed disease mitigation while avoiding the economic and health impacts of prolonged shutdowns. An integral part of any adaptive strategy is testing. Section 5 discusses a targeted approach to testing and mitigation that is more efficient and effective than scaling up to massive testing of everyone in the state as some studies have recommended. Section 6 puts these concepts together in offering a path forward to returning to work and continuing to protect the vulnerable. The concepts here are provided as general principles for consideration as policy makers and business leaders work together to provide detailed guidance for the various sectors of society. The next two sections concern specific recommendations on two critical topics that to this point have been largely neglected. The first, covered in Section 7, is the urgency of working toward early outpatient treatments to minimize the severity of outcomes and reduce the load on hospital systems. While a vaccine is expected to be the best long-term solution, there is no guarantee of when or whether a successful vaccine will be broadly available. The second, discussed in Section 8, concerns the imperative to quickly and safely reopen the full healthcare system. The singular focus on COVID-19 has created increased risks through reduced care for other health conditions and could cause some atrophy of overall healthcare capacity. Lastly, Section 9 summarizes the key concepts and recommendations developed during this initial assessment.

SECTION 2

What We Know and Wish We Knew about COVID-19

The current COVID-19 pandemic is causing significant negative health and economic impacts on the world. An update to pandemic influenza guidance was published by the U.S. Centers for Disease Control and Prevention (CDC) in 2017, with little consequent political response or public health investment.[1] Publications in 2003-2005 predicted new coronaviruses could jump to humans and these continued to appear in 2015 and 2016.[2] In 2015, Bill Gates predicted a respiratory virus pandemic in a TED Talk and suggested ways to prepare in advance, but only one recommendation was actually pursued in advance of the current virus outbreak.[3] Several candidates for other coronaviruses ready to jump to humans in the future have already been identified suggesting this kind of problem may not be the once-in-a-lifetime event that everyone hopes it will be.[4] With this backdrop in mind, the chapter aims to cover the topics: What We Know and Wish We Knew about COVID-19.

What We Know

Coronaviruses

Overview

The appearance of coronaviruses, especially more dangerous ones, which infect domestic livestock or humans, has accelerated greatly in relatively recent times compared to previous history and more are likely to emerge. The two most recent previous pandemics, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), prior to COVID-19 resulted in a detailed scientific understanding of coronaviruses, but no vaccines or specific treatments were successfully developed all the way to achieving FDA approval.

Key Facts

Coronaviruses are a class of enveloped, positive strand RNA viruses that infect bats, as well as other mammals, including humans, and birds.[4] The viruses need an envelope to be viable and they are susceptible to inactivation by handwashing with soap and water as well as to sunlight. Of over 200 known coronaviruses, only seven have been discovered to affect humans. All can cause respiratory effects. Four of the viruses emerged to infect humans at points in times ranging from around 800 to 100 years ago. Two were classified as alpha coronaviruses (NL63, 229E) and two were beta coronaviruses (HKU1, OC43) based on their genetic sequences. These viruses typically are less pathogenic and cause mild respiratory symptoms. They are part of a group that includes other viruses that are characterized as causing the common cold. In the last 100 years, there has been a very dramatic increase in the number of coronaviruses that have been discovered to cause detrimental infections in domesticated livestock like cows and pigs and more recently in humans as well.[4]

In the last 20 years three beta coronaviruses have emerged that cause far more serious respiratory effects in humans including fatalities. The SARS-CoV virus that causes the disease SARS emerged in 2002 in Guang-

dong province in China. After causing 8000 known cases on multiple continents, it died out in the summer of 2004. MERS-CoV which causes MERS emerged in 2012 in Saudi Arabia and has resulted in dozens of cases annually on the Arabian Peninsula through 2019. Only one outbreak of MERS occurred elsewhere, due to the return home of an infected South Korean businessman. SARS-CoV-2 which causes COVID-19 was recognized on December 8, 2019, in Wuhan, China. In addition, a virus (SADS-CoV) emerged around 2017 to infect domestic pigs in China; that is worrisome because it can replicate in human cells in the laboratory.[4] Finally, researchers have shown that there are many coronaviruses circulating in bats that can grow in primary human airway cells cultured in a laboratory.[5] Thus, it is now believed that a number of these viruses, some related to the SARS class and some related to MERS class do not require a major or rare mutational event to emerge in the future to infect humans.[4]

The three most recently emerged human coronaviruses are usually more pathogenic than the earlier viruses and can lead to atypical pneumonia.[4] The mortality rate for SARS-CoV was estimated to be 9.6% while that for MERS-CoV is approximately 34%. The mortality rate for SARS-CoV-2 (CoVid-19) is currently less than both the previously mentioned viruses, but estimates are still evolving. The mortality rate for SARS-CoV-2 is likely higher than a typical circulating influenza which is estimated at well below 0.1% per infection. A reasonable estimate at present would be a 0.5-0.7% mortality rate. From 2003-2004, SARS-CoV caused 8 cases in the U.S. and 8,096 deaths worldwide. MERS-CoV through 2019 has caused two cases in the U.S. and 2,494 deaths worldwide. It mainly occurred in healthcare workers or other "super-spreader" events where uninfected people were in close proximity to an infected person. Outbreaks are contained mainly via patient isolation and "barrier" nursing in which personal protective equipment (PPE) and isolation effectively limit their spread. The currently circulating virus, SARS-CoV-2, the cause of COVID-19, is more contagious than the earlier viruses and thus is less forgiving of openings in barrier nursing controls and thus is harder to contain. Its negative impact both with respect to number of cases and deaths is still mounting and is vastly greater than for the previous two more pathogenic coronaviruses. There are currently no approved vaccines or drug therapies for the treatment of the SARS-CoV or MERS-CoV coronaviruses. For SARS-CoV, two vaccines were well tolerated and induced neutralizing antibodies in Phase 1 studies in healthy volunteers, but concerns were raised about safety due to immune enhancement (rather than immune protection). A MERS-CoV vaccine is still in development. The vaccine and drug development for SARS- CoV-2 (COVID-19) are discussed in more detail in a subsequent section.

SARS-CoV-2, the Cause of COVID-19

Overview

To summarize what is known about the SARS-CoV-2 virus itself, much has been learned about why it is so contagious, how it accomplishes its replication, and how it spreads both in the infected body and the population. The CDC has issued guidelines on how to prevent infection. These guidelines are likely to evolve as studies emerge. The genetic diversity and drift of this virus observed in circulating virus strains suggest significant variation, but there is no evidence that fundamental structural changes occur such that vaccines or drugs will not be generalizable for use in different strains. Antigen testing for infection depends upon RNA detection, while antibody testing assesses past infection. An antigen test in which saliva can be collected at home has received approval for use by the FDA. Testing is poised to take off to whatever level is ultimately determined to be needed.

Key Facts

As a result of the earlier outbreaks, the life cycle of the coronaviruses has been well studied and elucidated

which means much is known about how they infect human cells, replicate, and expand the amount of virus in the infection. Along with the Chinese report of the genetic map of the SARS-CoV-2 (in a mere two weeks of effort), information specific to SARS-CoV-2 has been obtained very rapidly.

Initial infection occurs when the virus enters the body and external protein spikes on the envelope of the virus attach to a receptor on the surface of a human cell which has the proper receptor on its surface. For MERS-CoV, the receptor is an enzyme called DPP4 but for SARS-CoV and SARS-CoV-2, the receptor is an enzyme called Angiotensin-converting enzyme 2 (ACE2).[4] ACE2 is a component of the renin-angiotensin system, a hormone system that regulates blood pressure and fluid balance among other functions. ACE2 also protects against severe acute lung failure.[6,7] ACE2 is expressed in the nose, in the lungs (mainly in type II alveolar cells), arterial and venous endothelial cells in most organs such as heart and kidney, enterocytes of the small intestines, and also cortical neurons and glia.[8] Once the virus attaches to ACE2, it enters the cell by two different mechanisms. Then the virus will begin using some of the host cells' own machinery to begin replicating and making more virus which is then released from the cell to infect other cells in the body or in someone who acquires the virus.

SARS-CoV-2 is perhaps five times more lethal and may be more contagious than non-pandemic influenza strains. The reason for its pathogenicity is the virus (spike) whose binding affinity (kD) for ACE2 of about 15 nM which is about 10-20 times stronger than for SARS-CoV.[9] The virus has an incubation period of up to 14 days and is just 2-3 days in many cases before onset of symptoms.[10] Studies suggest that the median incubation period is about 5.1 days and about 1% of people may have an incubation period longer than 14 days.[11] Further, 25-50% of the infected individuals have no or very mild symptoms. These features make SARS-CoV-2 a very insidious virus for its ability to spread undetected. For example, those who are asymptomatic may well be just as infectious and might infect others without even being aware they are a source.[10]

Therefore, it is important to wear masks, physically distance, and practice hand/face/surface hygiene in the face of ongoing transmission. One study found the peak viral load in throat swabs at the time of symptom onset and inferred that infectiousness peaked on or before symptom onset.[10] The basic reproduction number, (R_0), is the average number of new infections caused by each single case in an entirely susceptible population and is thus a quantification of infectiousness. R_0 estimated by the majority of studies for this virus ranges from 2.24 to 3.58, which is higher than that of SARS-CoV and most influenza strains.[12] If control measures are not employed promptly, the number of infected people increases exponentially in the early stages of a SARS-CoV-2 outbreak. As the probability of an infected person infecting uninfected persons drops with control measures, R_0 can drop below 1 and the epidemic can subside.

Studies of the genomics and gene variant drifts of the virus suggest that coronaviruses can tolerate significant differences in their structures and genomic makeup and still be infectious to humans. The coronavirus genome is highly prone to mutations that lead to genetic drift and some of these changes could potentially facilitate escape from immune recognition, though this is unclear at present.[4,13,14] The variability in the virus must be considered in the design of treatments and vaccines, guided by clinical trials in settings with diverse viral strains.

The virus is currently thought to spread mainly from person to person. COVID-19 may be spread by people who are not showing symptoms. The best way to prevent illness is to avoid being exposed to this virus. The CDC's May 2020 guidance for preventing infection is provided on the following page.[15]

CDC Guidelines for Preventing SARS-CoV-2 Infection

- Wash your hands often with soap and water for at least 20 seconds especially after you have been in a public place, or after blowing your nose, coughing, or sneezing.
- If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of your hands and rub them together until they feel dry.
- Avoid touching your eyes, nose and mouth with unwashed hands.
- Avoid close contact
- Avoid close contact with people who are sick, even inside your home. If possible, maintain six feet between the person who is sick and other household members.
- Put distance between yourself and other people outside of your home.
- Remember that some people without symptoms may be able to spread virus.
- Stay at least six feet (about two-arms' length) from other people.
- Do not gather in groups.
- Stay out of crowded places and avoid mass gatherings.
- Keeping distance from others is especially important for people who are at higher risk of getting very sick.
- Cover your mouth and nose with a cloth face cover when around others
- You could spread COVID-19 to others even if you do not feel sick.
- Everyone should wear a cloth face cover when they have to go out in public, for example to the grocery store or to pick up other necessities.
- Cloth face coverings should not be placed on young children under age 2, anyone who has trouble breathing, or is unconscious, incapacitated or otherwise unable to remove the mask without assistance.
- The cloth face cover is meant to protect other people in case you are infected.
- Do NOT use a facemask meant for a healthcare worker.
- Continue to keep about six feet between yourself and others. The cloth face cover is not a substitute for social distancing.

Cover coughs and sneezes

- If you are in a private setting and do not have on your cloth face covering, remember to always cover your mouth and nose with a tissue when you cough or sneeze or use the inside of your elbow.
- Throw used tissues in the trash.
- Immediately wash your hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.

Clean and disinfect

- Clean AND disinfect frequently touched surfaces daily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets and sinks.
- If surfaces are dirty, clean them. Use detergent or soap and water prior to disinfection.
- Then, use a household disinfectant. Most common EPA-registered household disinfectants will work.

Risk of transmission occurs:

- Between people who are in close contact with one another (within about six feet or two meters).
- Through respiratory droplets produced when an infected person coughs, sneezes or talks. These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. It is probable that smaller sized aerosols can also spread the virus.
- By people with symptoms, before they develop symptoms, or who never develop symptoms.
- By touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes. **However, this is not thought to be the main way the virus spreads**. Although the virus can survive for three days on plastic or steel and one day on cardboard, it is highly unlikely to be spread from products or packaging that are shipped over a period of days or weeks at ambient temperatures.

It seems probable that the guidance around distancing will continue to evolve as more is learned about transmissibility. A recent analysis of the data explains why the six-foot rule is an oversimplification and can be misleading as consideration of both exposure to virus and the duration are important.[16] The analysis showed the most significant infection events reported were indoors, with people closely-spaced, with lots of talking, singing or yelling. A separate contact tracing study makes the similar observation that the risk of a major infection event in an outdoor environment is low.[i] The guidance to maintain six feet of separation from others, while helpful and easy to remember, can make one too conservative outside and too comfortable inside. Walking past someone outdoors even within six feet poses negligible risk, but living in the same house with someone even while keeping more than six feet apart can pose risk of infection due to the extended duration of contact in an indoor environment.

It should not be surprising that there would be factors that increase the chances for infection based on demographics. Frontline health care workers are at increased risk of being exposed and infected, though PPE use can reduce risk substantially. Attesting to the effectiveness of PPE, at the latest update, only about 0.3% of Stanford's medicine workers without symptoms have tested positive for COVID-19 from the 11,000 of 14,000 employees that were voluntarily tested.[17] Nursing homes have seen high attack rates and death rates, reflecting crowding, entry of virus from outside the facilities, and high levels of chronic disease and age- or disease-related immunocompromise. Crowded working conditions such as seen in chicken and meatpacking plants favor transmission. Poverty, which can necessitate crowded home living and shared transportation such as for migrant workers are also likely contributors. Poverty also reduces the ability to shelter in place without the need to work outside the home. Thus, minority race and ethnic group status are risk factors, mediated by quality of nursing home, need for public transportation, need for ongoing work and income, and access to health care.

Herd Immunity

Herd immunity is a concept in both veterinary and human contexts of infectious threat.[18,19,20] Herd immunity means that the susceptible persons in the population are unlikely to acquire an infection because the level of background immunity in the rest is high enough to interrupt transmission cycles. R_0 as mentioned above is the average number of new infections caused by each single case in a susceptible population. For a communicable pathogen of a given infectiousness (R_0) and given route of transmission (respiratory, fecal-oral, sexual, blood-borne, mosquito-borne, etc.), the proportion of the animal or human population that must be immune for the R_0 to drop to under 1.0 due to lowered transmission probability is calculated. For influenza, the level of

i In one extensive contact tracing study of 7,324 cases in various regions in China outside of Hubei, only a single outbreak in an outdoor environment was reported. All the rest of the infections occurred in an indoor venue. Hua Qian, Te Miao, Li LIU, Xiaohong Zheng, Danting Luo, Yuguo Li, Indoor transmission of SARS-CoV-2, medRxiv preprint posted April 7, 2020.

herd immunity must approach 60-80%. As SARS-CoV-2 is more infectious than influenza, most transmission modelers believe that 70-90% of persons must be immune to achieve herd immunity.

Even if every person who had been infected was immune to reinfection, herd immunity is not being approached anywhere in the world, except perhaps local microenvironments.[18,19] For example, not even in the worst afflicted nursing homes where 40-70% of denizens were infected does viral coverage achieve the level where herd immunity would likely protect the remaining susceptible individuals in a second wave. Population surveys in New York, the most afflicted city in the world, suggest that only 10-20% of persons have been infected; given oversampling of at-risk persons, this may be an overall overestimate. Only 0.7% of 5,600 major league baseball employees tested positive for coronavirus antibodies.[21] In Spain, preliminary results from a study of blood samples from 70,000 participants suggests that only 5% of Spaniards had been infected with the coronavirus.[22] The figures varied significantly by geographical region with ranges from 14% to 2% of the population having developed antibodies after being exposed to SARS-CoV-2. Those who advocate for letting the virus be transmitted unchecked are poorly informed on the issue of herd immunity. Such a policy would result in immensely increased healthcare burden and mortality but would not achieve herd immunity before numerous waves of infection over many years.[18,19]

Hence, herd immunity is not a relevant concept for the COVID-19 pandemic since we do not have a safe, effective and available vaccine yet. Vaccination has proven to be the most reliable way to boost the percentage of the population that has developed immunity to a bacterial or viral infection.[18] As discussed in a later section, the timetable to an effective and safe vaccine is unpredictable. The sheer volume of independent efforts (over 100 vaccines now being developed) increases the odds for eventual success. Human SARS-CoV-2 immunology is complex, and markers and duration of effective immunity remain to be established. The level of antigen required to elicit a protective immune response has not yet been established for either a vaccine or an infection. For example, antibodies are elicited from severe cases of COVID-19 in hospitalized patients but it remains to be established if the virus levels in mild or asymptomatic cases produce the same level of immune response and protection. In fact, relatively low levels of antibodies have been observed in 10-20% of patients with symptomatic COVID-19 disease.[23] Whether viral mutation and evolution will result in genetically altered protein structures that disrupt immune recognition is not yet known.

The need for an annual influenza vaccine is an example of high viral mutation rates that alter a vaccine's ability to spawn protective immunity. Even if a vaccine judged to be effective and safe is developed in record time, a sufficient number of people, including those at relatively low risk for serious outcomes, would have to quickly agree to take it, a prospect which seems unlikely given past precedents. Finally, a single vaccine may not confer immunity in all populations; for example, the very young, very old, or immunocompromised populations may not develop complete immunity or need a higher dose in the inoculum.

Testing and Contact Tracing

The proper level of testing during the outbreak of COVID-19 is subject to debate, but there is a broad consensus that the level of testing in the U.S. has been too low. Several diagnostic tests for coronavirus infection have been developed. RT-PCR-based assays for the viral antigen (test for infection) and ELISA-based antibody assays (test for presumptive immunity) are now available; some tests provide results within 2-4 hours.[24,25] A test which enables at-home sample collection of saliva has recently received emergency use authorization by the FDA; this is an easier patient sample to obtain than a previously approved at-home test that used nasal/nasopharyngeal swabs.[26] The lack of sufficient protective equipment and testing supplies initially restricted the availability of tests but these situations continue to improve. The logistics of currently expanding antigen testing is being addressed to enable a safer return-to-work. Logical automatic paradigms which prioritize

sample testing and select where the sample will be analyzed based on information entered into electronic intake forms have been employed effectively, as for a health system responsible for more than half the population of the state of Utah.[25]

States are ramping up efforts and staffing to scale up contact tracing. At the start of the epidemic, most reporting of COVID-19 cases was by paper methods such as phone calls, fax or mail. A significant effort has been made to increase electronic tracking including dissemination of software that automatically reports COVID-19 cases after data entry.[27] Automatic applications (apps) such as Sara Alert™ are designed to facilitate tracking, track symptoms during quarantine, and tell people when they are safe to come out, and are being employed in states like Vermont and Washington; a city in Connecticut (Danbury) was an early adopter.[28] The state of Connecticut has also partnered with another self-reporting app, the 'How We Feel' app.

Tests for antibodies to determine whether a person has previously been infected and recovered were initially felt to be unreliable, but recently a test believed to have better accuracy has become available. While the test can tell whether a person has been previously been infected, it is currently uncertain whether a seropositivity predicts immunity to reinfection.

COVID-19: Focus on the Disease Caused by SARS-CoV-2

Overview

Measures to prevent the spread of virus and for individuals to protect themselves from infection have been developed by the CDC. The symptoms of the virus have also been described. The course of disease and how it causes the most damage in serious cases is becoming understood and supportive treatments are evolving. Remdesivir has received FDA approval for emergency use in this disease and seems to offer hope it will provide a treatment option. Unprecedented efforts are being applied to identify vaccines and treatments, such as passive antibodies and drugs, and to accelerate their development through rapid approval. However, historic timelines to develop these classes of therapies are usually measured in years, not months. It is hoped the high number of "shots on goal" and the significant levels of resources being applied will provide help in a 12- to 18-month timeline or possibly even faster. In the future, developing therapies with broad activity in advance to prepare for future viruses before they emerge would be hugely advantageous. Convalescent plasma therapy is looking promising so this may be an important interim treatment option, though trials to date are not definitive. The effectiveness of historic efforts to contain the pandemic and then reopen economies vary around the U.S. and the world. Divergent levels of success may help us learn key lessons about what works well and does not. People's behaviors and needs are clearly influencing public policy and must be factors under consideration when planning for future surges of infection.

Key Facts

Many persons infected with SARS-CoV-2 never develop symptoms. Symptoms of COVID-19 and CDC guidance on when to seek treatment are listed on the following page.[29] People with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness. Symptoms typically appear 2-14 days after exposure to the virus.

Children have similar symptoms to adults and generally have mild illness. Based on available evidence, children do not appear to be at higher risk for COVID-19 than adults. While some children and infants have been sick with COVID-19, adults make up most of the known cases to date. The symptoms of COVID-19 are similar in children and adults. However, children with confirmed COVID-19 have generally shown mild

People with these symptoms or combinations of symptoms may have COVID-19

- Cough
- Shortness of breath or difficulty breathing

Or at least two of these symptoms:

- Fever
- Chills
- Repeated shaking with chills
- Muscle pain
- Nausea, diarrhea
- New Rash
- Headache
- Sore throat
- New loss of taste or smell

This list is not all inclusive so a medical provider should be consulted for any other severe or concerning symptoms.

When to Seek Medical Attention

If you have any of these emergency warning signs* for COVID-19 get medical attention immediately:

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face

* This list is not all-inclusive. Please consult your medical provider for any other symptoms that are severe or concerning to you. **Call 911 if you have a medical emergency**. Notify the operator that you have, or think you might have, COVID-19. If possible, put on a cloth face covering before medical help arrives.

symptoms. Reported symptoms in children include cold-like symptoms, such as fever, runny nose and cough. Vomiting and diarrhea have also been reported. Some children are at higher risk for severe illness, notably a Kawasaki-like vasculitis coined PIMS-TS (Pediatric Inflammatory Multisystem Syndrome Temporarily Associated with SARS-CoV-2) by *The Lancet*, while the CDC calls it MIS-C (Multisystem Inflammatory Syndrome in Children). Whether genetic factors predispose some children to this rare complication is unknown, nor is it apparent why a tiny fraction of infected children get coronary arteritis. Life-threatening or lethal disease akin to Kawasaki Disease Shock Syndrome has been seen in children with SARS-CoV-2 infection. It is also not known whether children with underlying medical conditions and special healthcare needs are at considerably higher risk of COVID-19.

The understanding of the COVID-19 disease continues to evolve. The lungs are usually an initial and vulnerable target for SARS-CoV-2. In the minority of people who become the most seriously ill, the virus may attack nearly all the vital organs in the body including heart muscles, blood vessels, kidneys, intestines, nerves and brain.[30] The virus may damage some of the targets directly by its interaction with ACE2.[6,7] An over-zealous immune response (referred to as a cytokine storm) is believed to likely be responsible for the clinical deterioration of many patients.[31] An increased tendency for clotting in the blood, leading to strokes and other complications, also seems to be playing a role in adverse outcomes. There is a still-evolving picture how the virus may affect the body and in the case of most severe disease, result in a fatal outcome.[30] The wide range of organ targets may reflect the expression patterns for the ACE2 receptor.

One of the major causes of deaths is acute respiratory distress syndrome (ARDS). After oxygen levels drop, X-rays and computed tomography scans typically show that patient lungs are riddled with opacities where spaces for air should be. Autopsies show their alveoli are filled with fluid, white blood cells, mucus, and the detritus of destroyed lung cells.[30] Thus patients have essentially suffocated and/or drowned. The widely publicized need for ventilators is complemented by an acute need for other equipment due to the many targets of the disease, including renal dialysis machines.[30]

Risk factors for a more serious disease course have been identified but the list is still evolving. Both older age and health co-morbidities are risk factors for severe clinical outcomes from COVID-19 infection. It appears that age per se is an independent risk factor. Over 80% of mortality has occurred in patients over 65-years-old. Immune senescence is likely an underlying reason for adverse outcome in those >65 and may limit the efficacy of a conventional vaccine. Other risk factors described by the CDC are serious heart disease and pulmonary hypertension, diabetes, severe obesity, chronic lung disease, moderate to severe asthma, kidney disease requiring dialysis, liver disease and immunocompromise. Emerging evidence suggests that death rates are higher than population percentages in some ethnicities including African American and Hispanic/Latinx. Whether this is due to more of the co-morbidity risk factor being present in this population or it is due to some other factors such as demographics, healthcare access, or genetics needs to be established. There is evidence that genetic variants such as DNA polymorphisms can make an individual more prone to infection by SARS-CoV-2. Why a minority of people, without any of the above risk factors including age, also succumb to the disease remains to be established.

Interventions to Treat or Prevent COVID-19

Currently there are no fully FDA-approved treatments for use in COVID-19 in the United States. However, numerous experimental treatments are being pursued. On May 1, 2020, the NIH's www.clinicaltrials.gov website showed approximately 991 global clinical trials versus 402 on April 23 for COVID-19 which illustrates the level of effort being applied to this pandemic. A detailed review of everything in trials is beyond the scope of this report. Approaches to treatment can be divided into two distinct areas: attempts to inhibit the virus and to ameliorate deleterious responses of the immune system that arise from the viral infection.

Many, general approaches to treatment that target the viral infection are being pursued in academic, industrial and government laboratories as well as in the clinical setting. These include the screening of approved drugs in an effort to repurpose then, screening available small molecule compound collections versus the virus or virus targets, targeted small molecule drug design versus the virus or human enzymes necessary to the virus, isolation and optimization of antibodies, anti-hypertensives, convalescent plasma therapy, and vaccine development.

Existing drugs that have seen considerable off-label use and evaluation in clinical trials include HIV protease

inhibitors, the antimalarials chloroquine/hydroxychloroquine with or without the antibacterial drug azithromycin, and the nucleoside analog remdesivir. The HIV protease inhibitors have failed to show efficacy to date. Chloroquine/hydroxychloroquine have received an emergency use designation from the FDA but are not recommended by the NIH for use in the treatment of COVID-19.[32] The positive effects of chloroquine or hydroxychloroquine alone has so far failed to be established and the NIH has recommended they not be used in combination with azithromycin due to the potential for a potentially serious cardiovascular side effect (an increase in the QT interval). One of the reasons for a mixed or an unclear effect of HCQ or CQ, at least in the hospitalized patients, is that the moderate or severe nature of the infection renders the condition no longer amenable to their anti-viral or anti-inflammatory effects. For example, HCQ's blood concentration in a human being is typically 1 micromolar at a daily dosage of 200-400 mg while the anti-SARS-Cov-2 effect in tissue culture has an IC50 of 4.5-17 micromolar effect.[33,34] It is possible that the HCQ dosage is not high enough to kill the virus in COVID-19 patients. Yet raising the dosage of HCQ would cause undesirable QTc prolongation risking serious heart rhythm disorder.

Remdesivir, a drug which underwent clinical trials versus the Ebola virus has been shown to inhibit SARS-CoV-2 virus replication in laboratory studies with infected cells and in animal disease models including a macaque model. The fact that it had the properties to be a repurposed drug and already had human clinical Phase 1 data showing safety, significantly shortened the timeline for development for use against SARS-CoV-2. It inhibits the virus's RNA polymerase enzyme in laboratory studies, and this is an enzyme critical for viral replication. The FDA has recently issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product remdesivir for treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in adults and children hospitalized with severe disease.[35] Severe disease is defined as patients with an oxygen saturation (SpO2) $\leq$94% on room air or requiring supplemental oxygen or requiring mechanical ventilation or requiring extracorporeal membrane oxygenation (ECMO). This use authorization is based on recent clinical data and experiences from compassionate use. Therapeutic treatment of rhesus macaques with remdesivir shortly before the peak of virus replication resulted in a significant clinical improvement, reduction in pulmonary infiltrates, and a reduction in pulmonary pathology. The conclusion of the study was the data support early remdesivir treatment initiation in COVID-19 patients to prevent progression to severe pneumonia.[36] Multiple clinical trials for remdesivir are ongoing including in some patients with less severe disease and details can be found on www.clinicaltrials.gov. Unfortunately, intravenous administration is needed, limiting its utility for out-patients or prophylaxis.

(See Section 7 for additional discussion of the potential efficacy of existing drugs.)

To realize FDA approval from drug discovery approaches for small molecules frequently takes years even if accelerated development scenarios are employed so they could not be a treatment in 2020. Efforts to develop compounds active versus both SARS-CoV-2 and also other coronaviruses would seem to have the most value. EIDD-2801 is an orally administered pro-drug which delivers a parent compound EID-1931 that is active against a broad range of coronaviruses, displays a high barrier to developing resistance, shows efficacy in animal models, and has started clinical trials in the U.K. and is soon to start in the U.S.[37,38] Among the advantages of an oral drug are that it could be used more easily in an outpatient setting and earlier in the course of the disease where an antiviral is expected to have greatest positive impact. Unfortunately, most drugs that enter Phase 1 trials never become an approved drug.

The isolation of antibodies from the plasma of recovered patients and also their optimization in order to stop viral infection is a process that has been employed with some success in other pandemics such as Ebola virus and have gone relatively rapidly.[39] Timelines to realize an antibody within a year or sooner have been proposed but other references suggest that if the optimization of isolated antibodies is needed to achieve the

desired profile, the process can frequently be slower.[39] It remains to be seen whether passive antibodies will neutralize SARS-CoV-2, nor do we know whether a combination of antibodies might be needed.[39] Crystal structures such as one showing the SARS-CoV-2 viral spike protein bound to ACE2 are being employed to accelerate new antibody development.[40]

Convalescent plasma therapy (CP) to clear the viral infection is being tried on patients in the clinical setting. This approach was used in the influenza epidemic in 1918. The plasma of recovered patients that should contain antibodies against the virus is transfused into infected patients who are having difficulty recovering from COVID-19 on their own. A clinical trial study in 10 severely ill patients concluded CP therapy was well tolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases.[41] Among the observations, clinical symptoms and related diagnostic criteria rapidly improved within three days.

The search for a vaccine which would confer immunity from infection of SARS-CoV-2 has become a massive worldwide effort. Multiple approaches to vaccines have been initiated and at least two are in clinical trials.[42,43,44] A mix of both new and traditional approaches is being pursued.[42,43] More than 100 separate research efforts are extant.[45] The sheer volume of approaches will increase the chances a safe vaccine capable of conferring immunity will be identified, though competition for resources may inhibit optimized progress. Public statements from some experts have suggested that vaccine might be available in late 2020, but this is improbable; a 12-18-month timespan is dependent on unprecedented success at every level.

The manufacturing of large quantities of some vaccine candidates is being considered to minimize delays to deployment, but this is feasible only for low-cost approaches. Typical timelines for vaccine development are four years or longer. Bill Gates in a 2015 TED Talk recommended at risk development of a new RNA vaccine technology/platform that could be deployed rapidly in response to new viruses that emerge. As a result of such an effort, an RNA vaccine candidate mRNA-1273 was the first to enter human trials.[42,43,44] Another vaccine which targets the viral spike, and which uses a yeast carrier, entered trials soon after as a result of efforts in China. Unfortunately, several factors suggest that the development of a SARS-CoV-2 vaccine may not be straightforward. The effectiveness of vaccination can be reduced in older populations or might require stronger dose inoculums than for younger people. Vaccine uptake by a skeptical population can be lower than optimal. Poorer nations may not gain early vaccine access. The coronavirus genome is prone to mutations and genetic drift so escape from immune recognition is a potential issue.[4]

To date, a vaccine against any coronavirus has not been advanced far enough to demonstrate efficacy in human trials or receive FDA approval. In the case of the earlier SARS-CoV outbreak, development of a vaccine was halted due to lack of funding after obtaining data in animal models and human Phase 1 clinical trials. Initial vaccine attempts against the earlier emerging SARS-CoV virus experienced an intolerable immunologic side effect (Th2 immune pathology) that was depended on the constituents so sometimes initial formulations require modification.[4] Development of a MERS vaccine is still in progress but it would not be likely to create immunity to SARS-CoV-2 in the current pandemic.

The second major approach to improving outcomes from COVID-19 is to address detrimental immune system responses. The cytokine storm is believed to play a significant role in causing a negative outcome for some seriously ill COVID-19 patients. A number of interventions, typically based on monoclonal antibodies (mAb) aimed at blunting or controlling the cytokine storm, have been proposed or are being pursued.[31]

Measures to Control the Pandemic

The lack of vaccines or effective treatments makes containment of virus spread and prevention of infection the only course of action to prevent the unnecessary deaths that would result if the healthcare system were overwhelmed. The personal mitigation strategies mentioned earlier of handwashing, social/physical distancing, sneeze/cough etiquette, and the wearing of masks are the best available protections from infectious spread. In concert, government controls, such as restricting travel and large gatherings, closing businesses and schools, and having everyone except for essential workers stay-at-home, have been employed across the country with varying success. These measures, together, have helped to flatten the infection curve enough in the U.S. to prevent overwhelming the healthcare system. The New York City metropolitan area may be an exception, particularly in selected hospitals such as Elmhurst in Queens. The areas around New York City have also significantly been affected due to the number of daily commuters who spread virus into their residential communities. This led to the proposal that plans for reopening should be developed on a logical regional basis rather than by criteria which are not relevant to the virus such as state borders.

China and South Korea, which had success in controlling the epidemic, opened up social restrictions only after new case numbers reached zero or near zero. While life in China is not completely back to normal, most of the country's businesses are now operating and there has yet to be a significant rebound in infection.[46] Other countries around the world are reopening or attempting to reopen under different paradigms so these will yield insights.

Like other challenges to public health and public welfare, as with the climate crisis and HIV/AIDS, responses to the COVID-19 pandemic in the U.S. have become politically polarized. Segments of the population that are ideologically opposed to government action tend to oppose public mandates that restrict mobility and commerce. But even among politically neutral segments of the population, attitudes about compliance with such restrictions vary with the perceived threat posed by COVID-19. Willingness to comply with mandatory or voluntary restrictions varies with perceptions of likelihood of becoming infected and expected severity of the infection, including chances of dying among older citizens and other at-risk groups.

What We Wish We Knew About COVID-19

Our understanding of COVID-19 will continue to evolve with many questions left to be answered as illustrated in the lists below. The answers to these questions could very well reshape how we need to respond to the current pandemic. It is precisely because of the dynamic and uncertain situation, that strategies for responding to the pandemic need to be adaptive. They need to change and adjust based on what is known both about the disease and the current local circumstances in the state.

Pressing Questions

- What are the best risk-informed strategies for reopening while balancing the health and economic needs of Connecticut?
- What is the best way to educate/train the public to sustain social distancing and the safest practices during reopening?
- Can high risk individuals protect themselves and still have high a quality of life before the virus is gone?
- What will be the impact on Connecticut and the surrounding region of many parts of the country reopening early as opposed to waiting for either the conditions described in the Federal guidelines or alternatively the zero-infection level used by some countries that have reopened successfully?
- What other practices from around the globe are effective?

Current Treatment Options For COVID-19

- What is the best way to reduce adverse outcomes using the therapies and treatment options available now?
  - If the early promise of convalescent plasma therapy continues what will be the best way to maximize the positive impact of this treatment on patients in Connecticut?
  - Will remdesivir's efficacy be significantly better with an early intervention as predicted by many experts, the macaque model data and based on precedents from other viruses?
  - Can this drug be impactful given cost/ IV administration / availability and how can its impact in Connecticut be maximized?
  - Is there an effective combination of agents available in the near term that reduces death rates from COVID19 more than remdesivir alone? More specifically can an antiviral such as remedesivir be used with one of the specific molecules designed to blunt detrimental immune system responses that are currently being evaluated in the clinical setting?
  - What else do we still not know about treatment and is there something else available now which can be added?

Containment

- How should testing for current infections be deployed and used for greatest impact?
  - What are optimal testing levels around the state?
- Will contact tracing be effective?
  - Compliance?
  - Best practices/incentives to maximize impact?
- How should testing for previous infections be deployed and used for greatest impact?
  - What will be the ramifications of this data?

Behaviors of the Populace

- What behaviors and reactions will be observed in the people of Connecticut and surrounding region as the COVID-19 outbreak proceeds?
  - How long will people adhere to mandatory or recommended restrictions in mobility, meetings with others, over extended periods of time?
  - How much would protective behavior change in different age groups and other segments of the population if and when mandates are being replaced with recommendations for voluntary self-restrictions of those behaviors?
  - What will be the behaviors arising from a significant percentage of the population facing long unemployment, an uncertain future, lower wages, and loss of health insurance?

The Virus, SARS-CoV-2

- Is the understanding of virus transmission and risk complete?
  - Is all of the guidance on protection optimal?
    - Is it clear and complete enough?
- Can the virus be eradicated?
- Will there be any seasonality to the virus incidence?
- What level of spread in the population would threaten containment?
- Will the circulating virus evolve over time to thwart immunity, require different treatments and or regular updates to vaccines?
- Why does the virus tend to spare or have less impact on some regions which would seem vulnerable?
  - Cultural, demographic, genetic or other factors?

Immunity
- Which antibodies confer immunity, if any?
- Are people who recovered from COVID-19 universally immune to reinfection?
- What is the duration of immunity?
- How does the virus interact with the immune system including differences in age and factors that cause more serious outcomes or alternatively preclude them?

Vaccines
- Which of the vaccine approaches will work best/be safe?
- When will one be ready?
- How long will a vaccine be effective?
- What level of vaccination can be achieved in population?
- Will vaccines create immunity in the old, young and immunocompromised?
    - If not, will population vaccination protect the at-risk populations?

Future Treatment Options
- Which of the approaches in clinical trials versus COVID-19 would be the best investment of the most resources?
    - Will they arrive in time to impact COVID-19?
        - Is prioritization necessary?
            - Prioritize drugs that work on a broad range of coronaviruses?

The Future
- What will be the short and long-term economic impact on Connecticut?
- Will the world have the vision and will to make investments that will minimize the health and economic impact of a future virus outbreak that seems probable?
- What should Connecticut do or require going forward?
- What behaviors and practices should become the new normal?

Summary

An impressive amount of information has been learned in a relatively short time period about SARS-CoV-2 and COVID-19 but many questions remain. Decisions will have to be made with imperfect information and likely without the benefit of having a perfect treatment or a vaccine. The balance of health and economy will likely require risk-based decision-making to best balance the needs of society in the United States and of Connecticut. This pandemic has come close to realizing the health and economic damage predicted by Bill Gates in his 2015 TED Talk and in narratives from the CDC around their 2017 revised pandemic influenza plan; given global economic damage, any preparation to minimize the impact of potential future outbreaks will be highly cost effective.

SECTION 3

The Connecticut Context

Connecticut sits in a region that has been hardest hit by the current pandemic. COVID-19 hit New York City harder than any single venue on Earth. As of May 22, 2020, the city's outbreak numbered 200,507 cases and 20,491 deaths. For the whole state of New York, there were 361,313 confirmed cases and 28,663 COVID-associated deaths. This represented 22.8% of the 1,584,800 cases and 30.3% of the 94,722 deaths in the U.S.[i] The top five states for coronavirus cases in the U.S. on a per capita basis include Connecticut and four neighboring states in the region: New York, New Jersey, Massachusetts and Rhode Island. With only 12.1% of the U.S. population, these five states collectively account for 41.4% of the cases and 52.6% of the deaths in the U.S.

Fairfield County in the state of Connecticut is about 15 miles from the Bronx. In March, the spread of SARS-CoV-2 into Connecticut from New York City was noted most acutely in Fairfield, proximate to Westchester County, New York. Into what context did the state of Connecticut receive this new virus? Why did Connecticut soon become the third-most afflicted state for COVID-19 mortality rates? By way of understanding better the geographic, social and circumstantial determinants of infection that led to this vulnerability, we may better mitigate and prevent COVID-19 devastation in the future.

Geographic and Socioeconomic Context

Nestled between New York City and Boston/Providence, Connecticut is linked by the convenient I-95 highway and frequent train service. Communicable diseases not uncommonly travel the trains and interstate highways from the densely populated cities to Connecticut. As one of the nation's smallest states, Connecticut ranks 48th in area (4845 sq. miles, ahead of Delaware and Rhode Island) and is among the most densely populated (741 persons per sq. mile) states, ranked 4th after New Jersey, Rhode Island and Massachusetts. Its 2018 population ranked 29th (3.57 million) among the 50 states. The population is 66.3% White, 16.5% Hispanic or Latinx, and 10.0% Black or African American, making it one of the most representative of all U.S. states in racial/ethnic distribution. Many immigrants reside in this immigrant-friendly state such that 22.1% of Connecticut residents speak a non-English language, and 6.8% are not U.S. citizens.[1]

Proximity to New York City contributes to Connecticut being one of the wealthier states by a variety of indicators. Fairfield County in the southwest of Connecticut is linked closely to the financial and corporate world in New York City. Fairfield ranks the 6th wealthiest among over 3,000 counties in the U.S., according to a 2019 analysis by SmartAsset, an online consumer financial magazine.[2] The U.S. Census Bureau publishes data on median household income by state based on the 2018 American Community Survey (ACS).[3] With a median household income of $76,348 ±921 (90% confidence interval (CI)), Connecticut ranks 5th, just behind Maryland, New Jersey, Hawaii and Massachusetts. At the same time, the report ranks Connecticut 2nd behind New York in the Gini index of income inequality; its poverty rate is about 10% which is half that of Mississippi with the nation's highest poverty rate.

In an effort to overcome some of these income disparities and attendant needs for lower income residents, Connecticut has a high tax rate, in part to provide adequate educational opportunities and a social safety net.

i Worldwide confirmed cases numbered 5,128,492 and deaths 335,063 on May 22, 2020, based on JHU database.

Kiplinger magazine cites 2019 data that Connecticut has the 9th-highest state and local gas taxes in the U.S.[4] Pension liabilities, toll-free roads, comparatively high state employee wages, and administrative inefficiencies have created a vicious cycle. High taxes contribute to flight of industry, business and high-income individuals for lower tax and lower wage states (the net population of Connecticut has been declining, -0.43% from 2017 to 2018, for example). The state government has been in serious fiscal difficulty for several years as a consequence.

Flexibility and rapid fiscal response by state government is constrained by finances and chronic inefficiencies. Furthermore, a weak-county, strong-town decentralized home rule system is enshrined in the Connecticut Constitution. Little governance is conducted at the level of Connecticut's eight counties; in fact, Connecticut counties exist largely as geographic names that define historically linked parts of the state. Rather, governance is the responsibility of its 169 "towns," a chaotic formulation that invites high cost due to a lack of economies of scale. The Connecticut State Library states, "…towns may contain incorporated cities or boroughs, as well as villages, post offices and railroad depots without a distinct government. For example: Mystic is a village located in both Groton and Stonington; Stafford Springs is a post office in the Town of Stafford; and Winsted is a city within the Town of Winchester. In other cases, the governments of once-incorporated cities and boroughs have subsequently been consolidated with the town they fall within."[5] Towns have few incentives to help each other or to cooperate in efficiencies, given the attitude of independence at a micro-level of governance, nor are there "smoothing" of economic inequalities across geographic jurisdictions. Rich towns provide a quality of schools and level of services that poor towns cannot afford.

A state riven with economic disparities and with a state government in financial extremis finds its local governments fractured into vanishing small units, poorly poised to fill in gaps that the state does not accommodate. Far more educational boards, fire and police jurisdictions, and local health boards exist than in counterpart states that have larger county-based or metro area-based governments, making coordination and cooperation that much more challenging.

Until COVID-19 led to a devastating pace of job loss, 94.5% of the Connecticut population had health coverage, with 52.4% on employee plans, 17.4% on Medicaid, 12.2% on Medicare, 11.7% on non-group plans, and 0.9% on military or VA plans. Per capita personal healthcare spending in the state of Connecticut was $9,859 in 2014. This is a 3.59% increase from the previous year ($9,517).[6] The County Health Rankings and Roadmap program of the Robert Wood Johnson Foundation highlights overall health rankings in health outcomes (Figure 3-1, next page) and health factors; in both elements, Windham and New Haven Counties rank lowest in the state.[7] Windham County has the highest prevalence of diabetes (10.3%) and of adult obesity (29.2%), with New Haven fairing little better. In 2009, the five poorest cities in the state were also four of five of its largest: Hartford (the state capital), New London, New Haven, Waterbury and Bridgeport. Stamford is the other larger city, while New London is smaller; Stamford is in Fairfield County. These five poorest cities are disproportionately populated by persons of color. For example, New Haven had 30% of the 2017 population is Latinx/Hispanic versus 15% in Connecticut as a whole, and the Black, Non-Hispanic population represented 32% versus 10% in Connecticut.[8] Its 2017 five-year-average household income was $39,191 versus $73,781 in Connecticut in that year. Connecticut's largest city is Bridgeport. All five cities are emblematic of extreme economic disparities.[9] Bridgeport has the second starkest wealth divide in the U.S.[10] Fully 23% of Bridgeport and 26% of New Haven residents live in poverty versus just 10% for Connecticut.

COVID-19 came into Connecticut when the state Department of Public Health was sorely underfunded; the towns of the state were uncoordinated; and the political and community response was slow to react. How did conditions affect who would be infected?

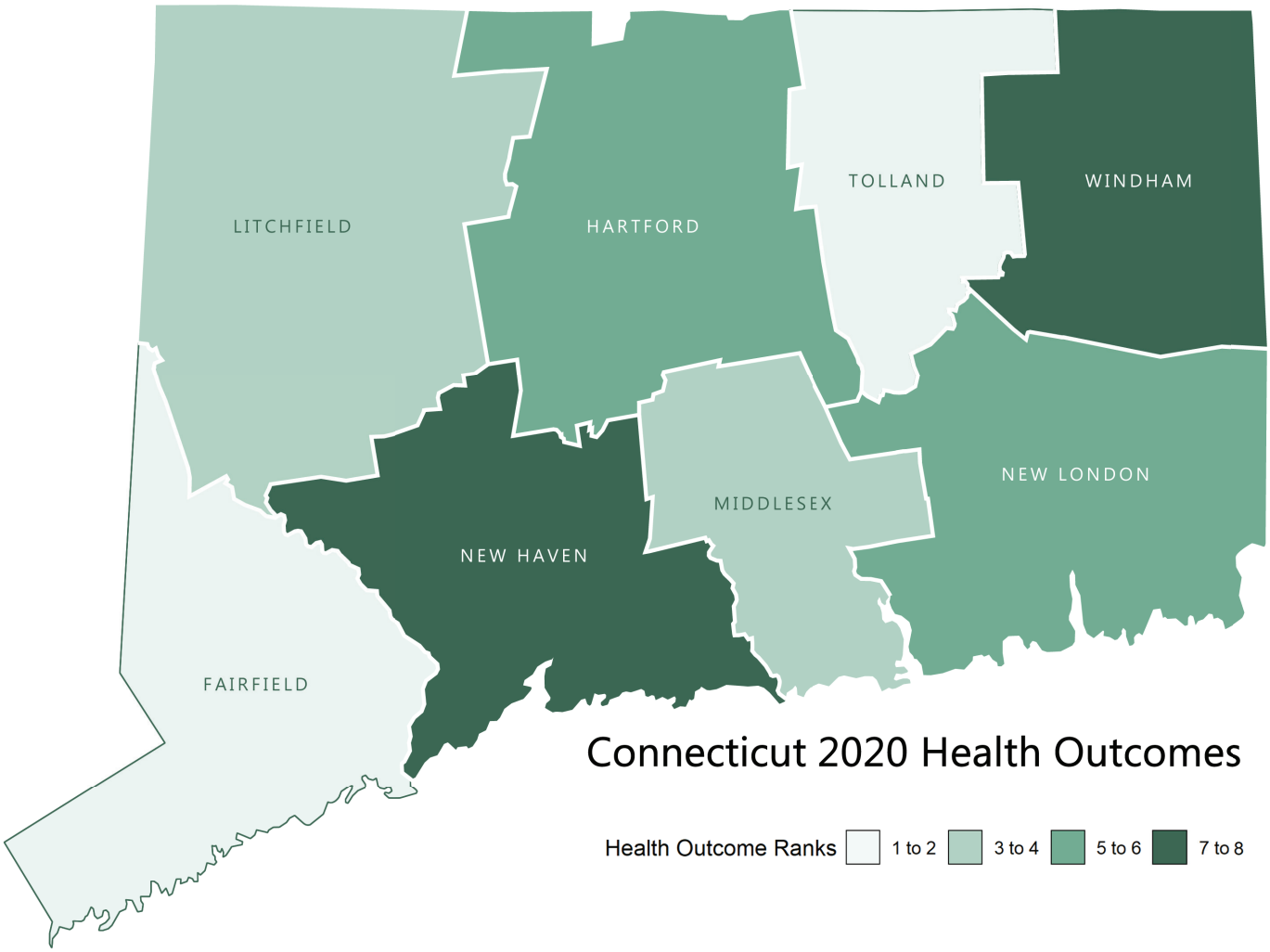


Figure 3-1. Connecticut 2020 Health Outcomes by county, as determined by the Robert Wood Johnson Foundation.

Vulnerable Populations

A fundamental principle of respiratory infectious disease epidemiology is that crowding increases risk of transmission. The poor, living in crowded tenements, were more likely to acquire tuberculosis, a fact known for centuries. Homeless shelters in New York City Armories in the late 1970s resulted in rapid spread of tuberculosis from active cases to men sharing their living space. Studies of viral and bacterial spread on airplanes correlates distance from the infected individual with risk of acquisition of the organism, with higher doses more likely to infect than lower doses.[11,12,13] SARS-CoV-2 is no different.

Early in the epidemic, we learned that the elderly were at far higher risk for COVID-19 complications and death. Aging is associated with declining immunocompetence, particularly over the age of 65 (hence, the recommendation is that persons are vaccinated against pneumococcus due to increasing risk at age 65.) Unlike the pandemic influenza of 1918-1919 that afflicted young and middle-aged adults disproportionately, or seasonal influenza in which the both the very young and the old are at higher risk, COVID-19 afflicts the immunocompromised elderly and younger persons who might be on immunosuppressive medications or suffering from diseases that compromise the vigor of the immune system. These may include cancer, autoimmune and collagen vascular diseases, immunosuppressive infections like HIV, and sickle cell disease. Finally,

those diseases that affect the lung put SARS-CoV-2-infected persons at risk of more severe COVID-19 lung disease. These include asthma, chronic obstructive pulmonary disease, smoking, cystic fibrosis and others.

Certain environments, then, were perfect storms for COVID-19. Nursing homes are communal living spaces that preferentially house the elderly and/or immunocompromised. Workers who rarely live in the nursing home come to work and return home daily. Activities of daily living, including personal hygiene may be adhered to fastidiously by elderly persons, or may be neglected due to physical or mental disabilities. Eating is typically communal. This served as a powerful incubator and multiplier of COVID-19 disease in Connecticut, as it did in the state of Washington early in the U.S. outbreak. As of May 13, Connecticut reported 1,927 COVID-19-associated deaths among nursing home residents (1,487 lab-confirmed and 440 COVID-probable).[14] This is more than 60% of the 3,125 deaths[15] reported in the state. Recent trends are showing much needed declines (see Figures 3-2 and 3-3 on the following page[16]). COVID-19 impact in nursing homes has been devastating across the U.S. with about one-third of all deaths in nursing homes and other long-term care facilities. The percentage in each state, however, varies dramatically from a low of none reported for some states to a high of 80% of all COVID-19 deaths in other states.[17] This situation deserves further study to identify effective mitigations and best practices and help states learn from each other in addressing this dire situation.

Poverty is associated with more crowded living. Persons of modest economic means may be more likely to be in "blue collar" jobs that did not permit working from home: custodial services, public transportation, nursing homes and assisted living, home health aide care, retail groceries, and hospital services like nurse aides and orderlies. Educational messages may not penetrate neighborhoods with lower educational attainment than in well-informed communities. Resources to purchase masks and hygiene products like hand sanitizers may be lacking and access to them may be limited.

Finally, vulnerability increases in other institutional settings. Jails and prisons are crowded settings with communal eating and exercise venues, and sometimes multi-prisoner jail or prison cells. Schools and universities have crowded classrooms, dormitories and cafeterias/eating halls. Many children and college students were on spring break when the Connecticut governor recommended stay-in-residence and closure of businesses and schools. This blunted transmission in the school setting. Cruise ships were crowded and many Connecticut travelers were infected. Whether travel on trains, buses and planes, or attendance at crowded events were responsible for many Connecticut infections is unknown, though a birthday party with 50 guests in Westport on March 5 is implicated in a number of early COVID-19 cases.[18] Homeless shelters were crowded and housed many vulnerable persons, and were decompressed suddenly and at high cost, by placing the homeless into safer hotel rooms.

In summary, proximity to New York was a fundamental contributor to the magnitude and timing of the Connecticut outbreak. Vulnerable populations – the elderly, especially in nursing homes, the immunocompromised, and persons of color and low economic means – were most likely to be affected and are overrepresented in deaths from COVID-19.

New York City and Westchester County Influence

Given the early outbreak in Fairfield County, adjacent to Westchester county, New York, and about 15 miles from the Bronx, one may look at the Connecticut epidemic as a wave. This wave spread north and east from its New York origin along the I-95 and I-91 interstate highway corridors, as well as the MetroNorth, Amtrak, New Haven-Hartford-Springfield (NHHS) Rail, and Shore Line East line.

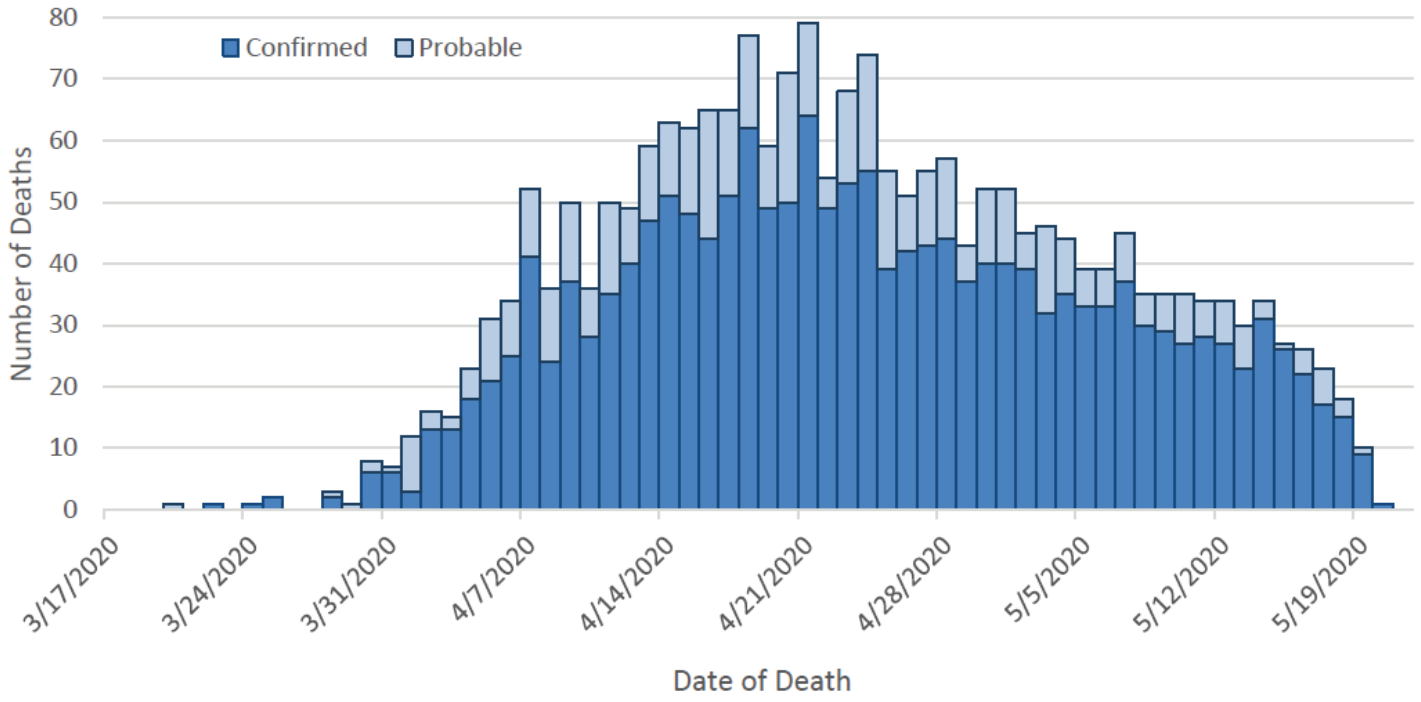


Figure 3-2. Number of COVID-19 associated deaths among nursing home residents by date of death.

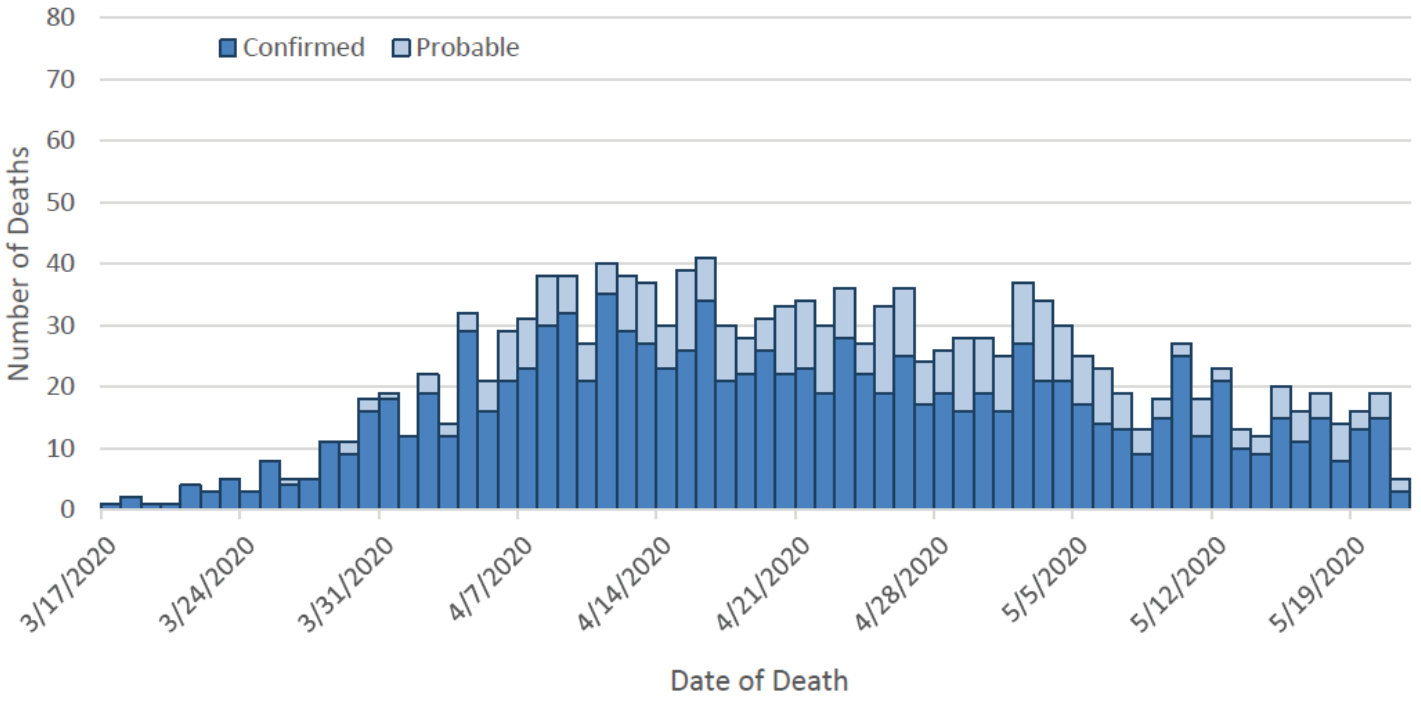


Figure 3-3. Number of COVID-19 associated deaths excluding nursing home residents by date of death.

Figure 3-4 on the following page displays the seven-day moving average of cases across the eight counties of Connecticut (Fairfield, Hartford, Litchfield, Middlesex, New Haven, Tolland, New London and Windham). Fairfield, New Haven and Hartford Counties account for 88.5% of the COVID-19 cases in the state.

More significantly, the cases were staggered in time like a wave across the state counties: Fairfield cases began on March 8, 2020; Litchfield on March 12, 2020; Hartford and New Haven on March 14, 2020; Middlesex on

March 18, 2020; Tolland and Windham on March 19, 2020; and New London on March 20, 2020. Infections then most likely propagated among the counties Hartford ↔ Litchfield, Hartford ↔ Middlesex, Hartford ↔ New Haven, Litchfield/Hartford ↔ Tolland, New Haven/Hartford ↔ New London and New London ↔ Windham, as can be seen from the correlation matrix of cases across the eight counties (Table 3-1). Windham and New London correlations are more diffused, indicating that the infections may be local or may have come from multiple counties.

Then, the natural question is how are the infections in Fairfield county (and possibly Hartford and New Haven Counties) related to the geographic proximity of Westchester and New York City.

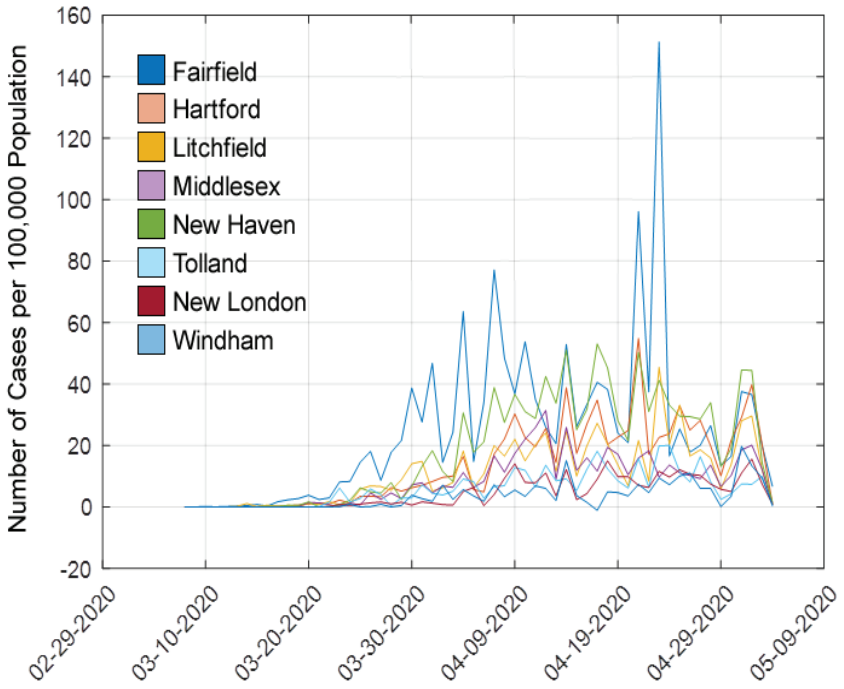


Figure 3-4. Daily cases in Connecticut counties. (Data from The New York Times, based on reports from state and local health agencies.)

County	Fairfield	Hartford	Litchfield	Middlesex	New Haven	Tolland	New London	Windham
Fairfield	1.00	0.583	0.758	0.466	0.664	0.605	0.478	0.489
Hartford		1.00	0.813	0.777	0.897	0.782	0.815	0.689
Litchfield			1.00	0.707	0.853	0.802	0.789	0.712
Middlesex				1.00	0.848	0.640	0.772	0.682
New Haven					1.00	0.805	0.824	0.689
Tolland						1.00	0.730	0.491
New London							1.00	0.722
Windham								1.00

Table 3-1. Correlation matrix of cases for Connecticut counties. (Only the upper triangular matrix is shown because it is symmetric.)

Cross-correlation is a measure of similarity between a time sequence, $f(k)$ and a delayed version of another sequence $g(k)$, say $g(k-L)$ as a function of the delay, L. A common application of cross-correlation function is the estimation of propagation delay between two similar temporal phenomena. The time lag, L_{max}, when the cross-correlation function achieves its maximum is the propagation delay. The value of the maximum cross-correlation describes the similarity of the two sequences at L_{max}. Indeed, the cross-correlation function is called a sliding dot product or inner product between the two time sequences, and L_{max} is the delay when the dot product is a maximum.

In the context of COVID-19, the cross-correlation function helps answer questions, such as the following:

- When did the virus come from New York or Westchester to Connecticut? In this case, *g(k)* could be the daily infections in New York City or Westchester, and *f(k)* could be the daily infections in Fairfield, New Haven or Hartford, three of the major counties that accounted for 88.5% of infections in Connecticut.
- What is the time lag between the onset of the disease (e.g., positive detection for COVID-19) and recovery or death? In this case, *g(k)* is the daily infections in a county and *f(k)* is the daily recovered cases or deaths.
- For those requiring hospitalization, what is the time lag between the onset of the disease and admission? In this case, *g(k)* is the daily infections in a county and *f(k)* is the hospital admission data sequence.
- How long do patients stay in hospitals before recovery or death? In this case, *g(k)* is the daily hospital admission sequence in a county and *f(k)* is the corresponding hospital admission data.

Westchester experienced its first nine cases on March 4, 2020, while New York City had its first case on March 1, 2020. Correlation analysis of the three Connecticut counties with Westchester and New York City cases since then (Table 3-2) suggest large correlations between New York City and New Haven. Given this, it is possible that confined spaces in transportation (e.g., Metro North) were an important factor in the initial spread.[i]

County	New York City	Westchester	Fairfield	Hartford	New Haven
New York City	1.00	0.806	0.518	0.518	0.603
Westchester		1.00	0.375	0.380	0.425
Fairfield			1.00	0.618	0.694
Hartford				1.00	0.908
New Haven					1.00

Table 3-2. Correlation matrix of cases for selected Connecticut and New York counties. (Only the upper triangular matrix is shown because it is symmetric.)

When did the virus come from New York State or Westchester to Connecticut? To examine this issue, we computed the sample cross-correlation between New York City COVID-19 cases and the cases in the three Connecticut counties. Connecticut cases in Fairfield, Hartford and New Haven lagged New York City by 5, 5 and 6 days, respectively (see Figures 3-5, 3-6 & 3-7 on the following page). The peak in the cross-correlation function is flat with respect to cases in Westchester (not shown), and the cases in Fairfield, Hartford and New Haven lagged Westchester by 4, 14 and 12 days, respectively.

This implies that Connecticut residents were exposed by March 4, 2020. Given the lags in cases between New York state and Connecticut, we believe that some infections propagated to all three Connecticut counties from New York city/Westchester → Fairfield and New York City → Hartford and New Haven. It is important to note that this analysis does not factor in the impact of air travel which could also have seeded cases as a result of people returning from other states and countries.

i Correlations among the Connecticut counties are different in amplitude in the two tables only due to differences in time windows used for these two comparisons necessitated by the epidemic's earlier start in New York City.

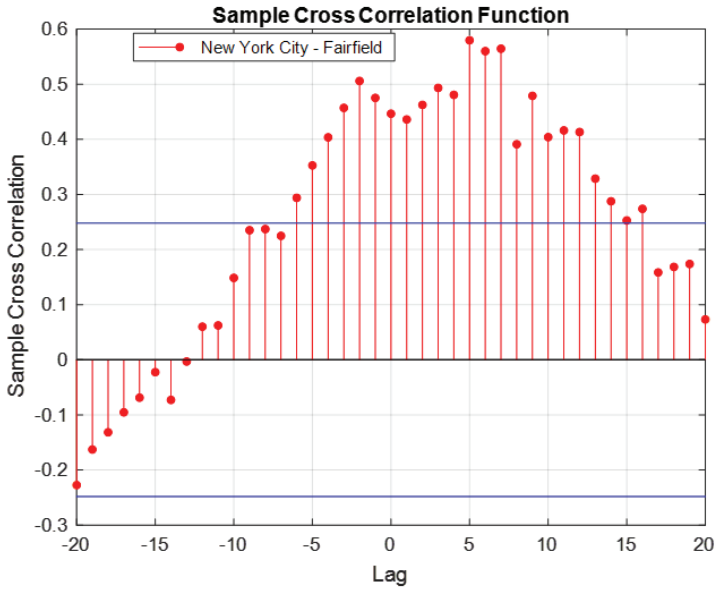


Figure 3-5.
New York City vesus Fairfield County

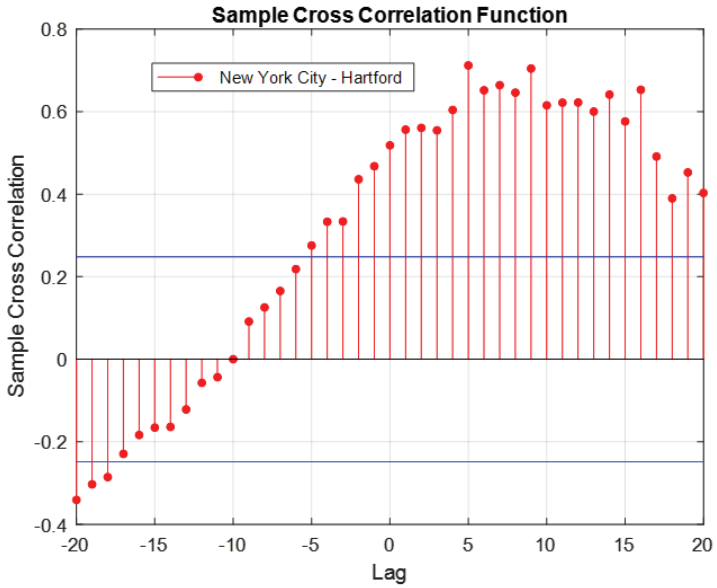


Figure 3-6.
New York City versus Hartford County

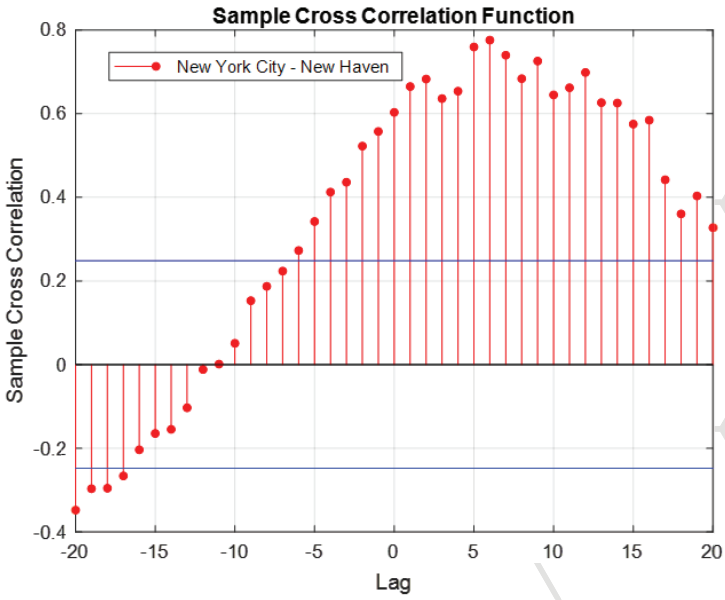


Figure 3-7.
New York City versus New Haven County

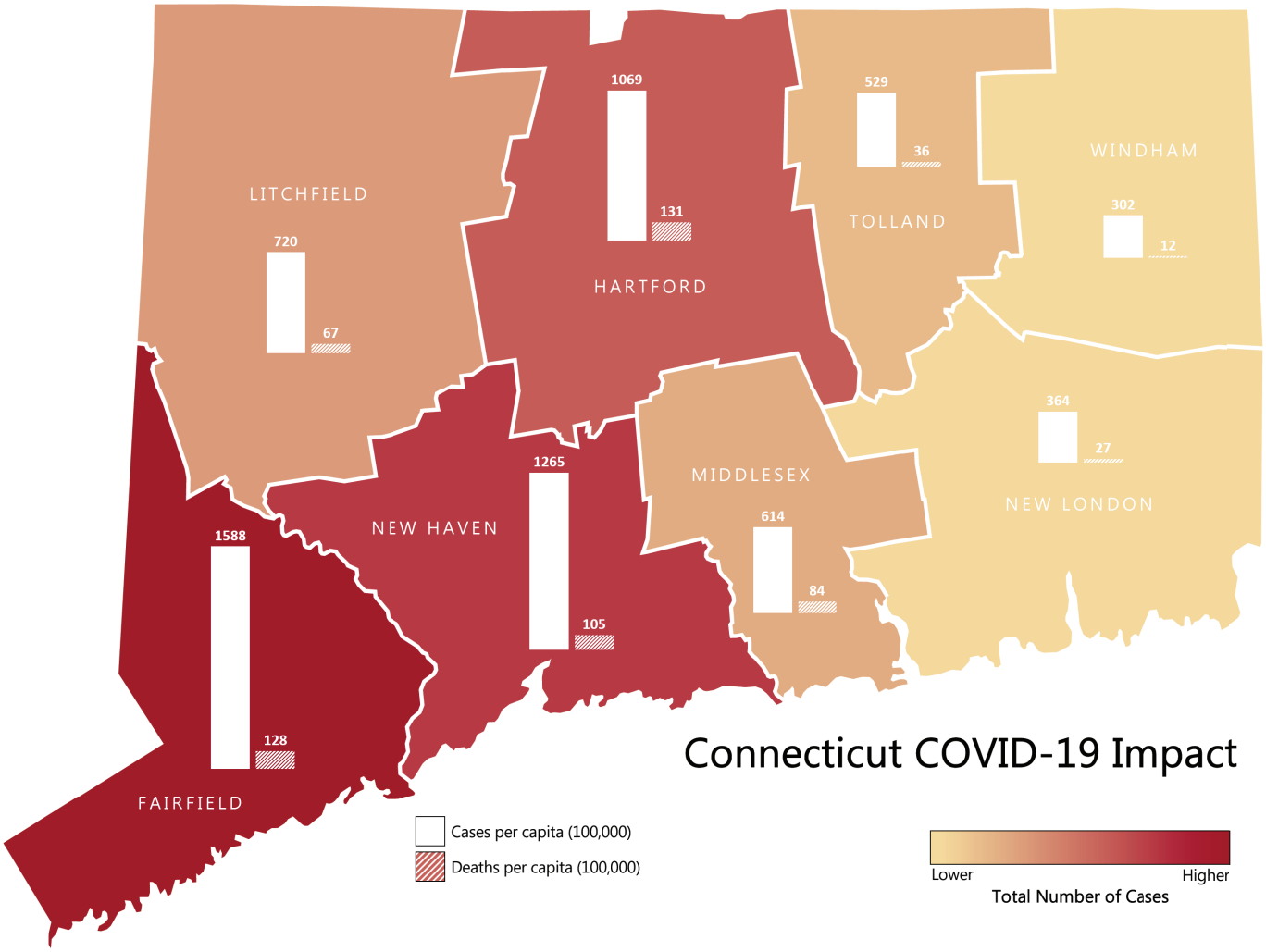


Figure 3-8. Connecticut COVID-19 impact, cases and deaths per capita by county, as of May 22, 2020.

At the present time, there remains a large variation in COVID-19 cases and deaths across the various counties in the state (see Figure 3-8). What is even more striking is the variation in case mortality rates among the counties (see Table 3-3). While some of the factors discussed above may have some bearing on these observed differences, there is no clear causal relationship observable at present. Further study is needed to correlate the potential contributing factors to learn how to improve Connecticut's ongoing response to the COVID-19 pandemic.

County	Deaths	Cases	Case Mortality Percentage
Middlesex	130	972	13.37%
Hartford	1,133	9,299	12.18%
Litchfield	121	1,303	9.29%
New Haven	874	10,663	8.20%
New London	73	903	8.08%
Fairfield	1,180	14,751	8.00%
Tolland	55	787	6.99%
Windham	14	336	4.17%
Total	**3,580**	**39,014**	**9.18%**

Table 3-3. Comparison of case mortality percentages among Connecticut counties as of May 22, 2020.

Health System Preparedness

Connecticut had more time to prepare for COVID-19 than did New York City and it fared better with lower infection and disease rates and greater capacity to cope once case rates rose. That said, it was still a huge struggle for Connecticut hospitals and health providers to address the pandemic. Surge capacity for hospital beds had to be accommodated at a rapid pace and at very high cost, converting ordinary rooms into negative-pressure rooms with environmental engineering work, using sports and other facilities for COVID-19 patients needing care, but not needing full scale hospitalization, or for non-COVID-19 patients.[19] Expanding intensive care unit (ICU) space into parts of the hospitals that were repurposed became essential for the burgeoning pool of needy patients. For example, the Yale New Haven Hospital used space in the top three floors of its Smilow Cancer Hospital for negative pressure COVID-19 ICU wards and nearby housing was arranged for physicians and nurses who had to extend their working hours.[20]

Similar arrangements were made at other hospitals in the state, including the heavily-afflicted Greenwich and Bridgeport Hospitals, to name just two. Historic highs were reached both for ICU census numbers, but also for number of persons being managed on ventilators at any given time. PPE was in very short supply and many hospitals received thousands of donated N95 masks sent from friends in China and elsewhere.

The context for this crisis was a backdrop of rising healthcare costs as Connecticut residents age, living longer with chronic illnesses. A failure to resolve social determinants of disease like homelessness, unemployment, drug addiction and mental health needs balloons the demands on the health system. A small number of persons with high social needs represent a disproportionate number of emergency room visits and hospital inpatient days. Such persons in the high income nations of Europe would receive more substantial outpatient assistance and social services than they do in Connecticut, reducing the costs and burdens for excess care in the health system. The costs of one night in an emergency department visit and hospital stay might pay for three months of rent for a homeless person, for example.

Connecticut has experienced a major prescription opioid epidemic that has cost millions of dollars in excess hospital, clinic, emergency medical technician, police and corrections, and mental health/substance use services costs. An increase in needle use for heroin-fentanyl injection has been documented with attendant hepatitis C virus infections and HIV and hepatitis B virus risks. Only Appalachia outranks New England for the magnitude of the opioid epidemic in rural America.

Connecticut's capacity to cope with these challenges is better than many states, less than others. Assets include highly functioning Federally-qualified community health centers (FQHC), excellent Veterans Health Administration hospitals and clinics, highly capacitated hospitals, clinics and healthcare practice services in the non-profit and for-profit sectors, and a small state with close proximity to services for nearly all residents. The table on the following page (Table 3-4) suggests Connecticut's status in a variety of indicators compared to four states, the two with the closest population sizes to Connecticut but differing in many other characteristics (Utah and Oklahoma), and two that share many characteristics with Connecticut and are adjacent (Rhode Island and Massachusetts).

State and its Estimated 2020 Population [21]	Number of Hospitals [i,22]	Hospital Beds per 1,000 Population [23]	Staffed Beds [i,22]	Staffed Beds Calculated from AHD [i,22]	Total Discharges [i,22]	Patient Days [i,22]	Gross Patient Revenue (billions) [i,22]
Connecticut (CT) Pop. 3.58 million	34	2.0	8,798	2.5	368,120	1,742,965	$40.20
Oklahoma (OK) Pop. 3.92 million	90	2.8	10,289	2.6	406,719	1,895,322	$48.11
Utah (UT) Pop. 3.05 million	35	1.8	4,621	1.5	205,860	814,305	$19.50
Rhode Island (RI) Pop. 1.06 million	11	2.1	2,440	2.3	108,782	503,639	$10.46
Massachusetts (MA) Pop. 6.83 million	73	2.3	15,192	2.2	743,119	3,618,061	$71.41

Table 3-4. Comparison of hospital resources among Connecticut and four other states.

To cope with the COVID-19 pandemic, Connecticut had comparable hospital resources to nearby states and to those with comparable populations (Utah's population has many fewer smokers and alcohol consumers and is healthier than most state populations, on the whole). Of course, the Connecticut epidemic was worse than any of the comparator states, suggesting greater strain on the system for Connecticut.

Obesity has proven a serious risk factor for mortality from COVID-19. Obese patients are more likely to have more stressed immune systems, have respiratory compromise, require ventilator-support, and more likely to die if they need ventilator support. Adult obesity rates in Connecticut are comparatively favorable to other states, though rates still quite high by the standards of other high-income nations.[24] The Robert Wood Johnson Foundation's State of Childhood Obesity project estimates Adult Obesity Rates as follows for the five states compared above (state ranking): Connecticut 27.4% (44th), Oklahoma 34.8% (10th), Utah 27.8% (40th), Rhode Island 27.7% (41th), and Massachusetts 25.7% (47th).[25]

In summary, the Connecticut health system was reasonably well capacitated to cope with COVID-19. Better planning for surge capacity for beds, ICU facilities with negative pressure ventilation, adequate numbers of ventilators, and especially adequate PPE, including mechanisms to sterilize and reuse gowns and masks, would have saved money in the long run, given the need for emergency and rushed capacitation and the human capital spent in securing needed supplies and facilities.

Public Health Response

The CASE committee acknowledges that this is an ongoing story and the post-hoc assessment awaits data and evaluation. Hence, our comments are more impressions than reliable data-based assessments. The Connecticut Department of Public Health (DPH)[26] is recognized as a better-than-average state health department whose capacitation has suffered with substantial funding limitations that have accompanied the state's fiscal challenges. Its epidemiologists and other key staff responded quickly to the emerging threat, including establishing a surveillance tracking system for the novel disease,[27] contact tracing in Fairfield county and expanding COVID-19 antigen testing for suspected cases. However, staff became overwhelmed quickly and contact tracing was abandoned.

i Non-federal, short-term, acute care hospitals (hospital beds/1,000 population calculated to compare with KFF data).

A team from the Yale School of Public Health (YSPH) formed a volunteer workforce in collaboration with the state DPH and the New Haven Department of Health to stand up contact tracing in New Haven. The long-standing Emerging Infections Program, a partnership of the YSPH, state DPH, and the Centers for Disease Control and Prevention (CDC), took the organizational and technical lead.[28] This 200 person workforce of public health (YSPH), nursing students (Yale School of Nursing), medical students (Yale School of Medicine), and staff and faculty (mostly YSPH) was impressive, but must be contrasted with the 1,000 paid contact tracers mobilized in nearby Massachusetts and another 1,000 hired in NYC. That only a fraction of the state could benefit from contact tracing and that it depended on a quickly trained volunteer workforce is inspiring and concerning at the same time.

The Connecticut DPH has served as a resource of epidemic control at many levels beyond its limited contact tracing capacities, however. Facilitation of expanded testing capacity has been helpful to many towns and cities. Education towards risk reduction has extended throughout the state, aided by public and social media. Addressing misinformation has been a continuous effort. Advising the Office of the Governor, the Department of Correction, and a myriad of state and local entities has taken immense effort, pivoting staff from usual duties. Finally, there have been non-profit and community-based organizations that have partnered with governmental agencies, universities and schools, businesses, hospitals, social service agencies, and advocacy organizations to assist persons with food insecurity, housing insecurity, needs for healthcare including mental health and substance use services, and a host of other tasks. The history of this response is still being made and has yet to be written.

Summary

Proximity to New York City and Westchester County, New York; strong transportation connectivity to the Tri-State region (including New Jersey) via auto, train and proximate high-volume international airports; and strong commuter ties all fueled the Connecticut epidemic. A high degree of vulnerability of elderly, immunocompromised, and socially vulnerable persons is noted and many such persons populate the cities and towns of Connecticut. A wave-like spread occurred from the southwest of the state to its northeast along transportation corridors. The Connecticut health system was reasonably capacitated to cope with the pandemic, but at very high cost given a lack of pandemic preparedness. Lessons learned can help the state respond earlier and with better planned preparedness and capacity for future waves of the novel coronavirus. This will help with other emerging threats, such as pandemic influenza or climate-change associated insect-borne outbreaks or emerging zoonoses.[29]

SECTION 4

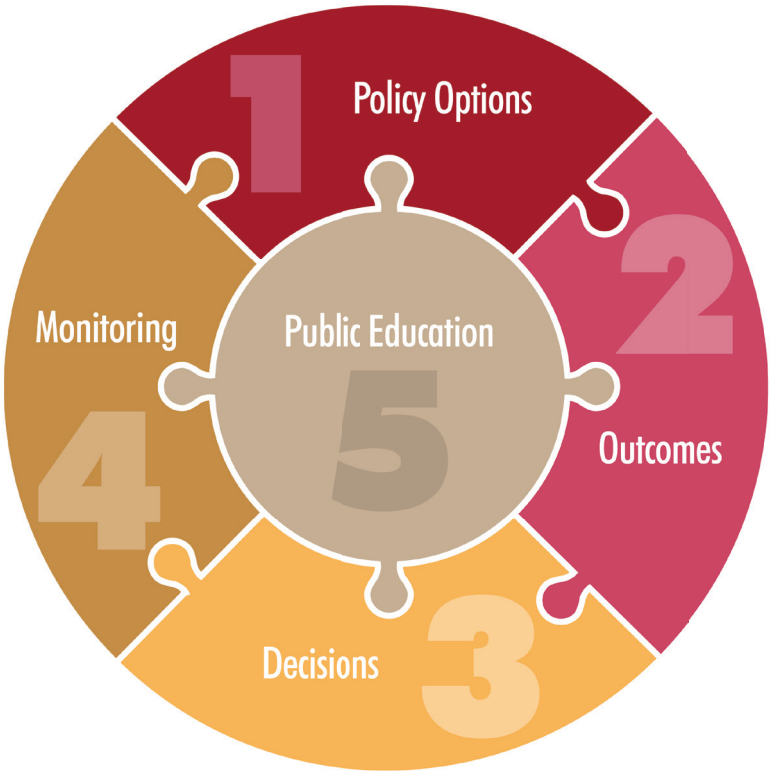
A Dynamic Risk-Balancing Strategy

Public welfare has many facets and policies designed to protect the lives of Connecticut residents, but sometimes come at a cost to their economic livelihood and to that of companies in the state. Now more than ever policy makers need to face difficult tradeoffs as they guide the state out of the COVID-19 crisis. These choices are not binary options between heath and economics as they are often simplistically portrayed. There are significant health **and** economic impacts on **each** side of these decisions. It is important that these tradeoffs are made transparently and wisely. Public and corporate decision makers need to provide intellectual leadership in planning and implementing the transition that will gradually open nonessential businesses, childcare facilities, schools, universities and public transportation, while at that same time seeking the input of stakeholders, from medical/epidemiological experts to corporations, unions and other stakeholder groups and the general public.

In this section we propose a conceptual framework that will allow policy makers to consider the risks and benefits of a full range of strategies going forward; to consider and integrate the effects of these strategies on multiple outcomes that matter to the well-being of the state and its citizens; and to implement an initial strategy. The strategy is inherently adaptive as new information about the impact of existing strategies on the spread of the disease as well as on the citizens and companies become available. Likewise, new treatments or vaccines coming online would modify the assessment of risks and benefits of strategy options.

Decision Framework

Our framework, depicted here, requires policy makers to be clear about the following key elements:



1. **Policy options**, which are the "inputs" to the dynamic planning and implementation system to be put in place; these are controlled by the policy maker.

2. These policy options have **outcomes** for infection rates, healthcare delivery and thus mortality rates, for the economy, and a host of other things. These outcomes are the "outputs" of our system and are provided by experts and models. They are known only probabilistically given large uncertainty about key variables, some of which will be resolved over time with experience and feedback.

3. **Decisions** about *when* to introduce *which* policy options and when to increase or decrease the relaxation

of existing restrictions on movement and commerce, which require acknowledgement of the **goals** of the policy and agreement on the relative importance of different goals. Implicit or explicit goals determine the output dimensions on which policy options get evaluated. The importance of different goals will differ between stakeholders, a difference in values due to different circumstances and impacts that needs to be resolved, and may change over time, as some risks recede and other goals gain in importance.

4. The outcomes of policy decisions need to be **monitored** and the results of such monitoring as well as external changes in the world (e.g., new treatment options or vaccinations coming online) need to be **fed back** into the system. Policy decisions needs to be revisited and updated at regular intervals or after significant changes in information.

5. Finally, policy makers and their expert advisors have to complement their decision-making function with a **public education** function, providing their citizens and companies with state-of-the-art information about best practices that will minimize the risk of infection for themselves and others while allowing a gradual and targeted return to normal operations. They need to monitor public misconceptions and look out for and correct willful or accidental dissemination of misinformation, some of it potentially motivated by misguided attempts to politicize responses to COVID-19. They also need to consider limits to the public capacity and willingness to embrace change and to shape the trajectory of policy options in ways that minimize reversals in direction.

Next we elaborate on these five key elements.

1. What is the full range of policy options at our disposal?

Most policy levers (e.g., the opening of schools or businesses) are not binary, but can be broken down into actions that differ more continuously in their risks and benefits.

The reopening of nonessential companies in Connecticut can be broken down in the following ways: a) the ability to work from home for most workers; b) the criticality of the firm/industrial sector to the state economy in terms of percentage of its contribution to the state GDP or to public welfare, in the eyes of the public; c) the employment it provides (as a critical determinant of public welfare as well as tax collection). This would allow basic government actions (opening, closure, ban) to a much more nuanced categories of economic activities (information, finance, retail, hospitality industry) and workers (home/not home) and predict, using modeling, the impact of these actions on the state GDP, employment and budget.

The Connecticut workforce can be further segmented by demographics to estimate its susceptibility to COVID-19. This includes such workforce characteristics as age and comorbidity and would enable analysis of government actions as they may apply to various demographic segments of the workforce. Assessment of the population's susceptibility to COVID-19 by modeling allows to plan and manage functionality and capacity of the healthcare system.

Application of government actions can be made more nuanced by demanding certain controls on the part of business management. Reopening of non-essential business activities can be done while requiring PPE, social distancing, employee screening, self-diagnosis, closure/ban on large public transportation units, and certain types of travel restrictions.

It is worthwhile to consider timing for the government strategies/actions. Timing considerations apply to reopening of economic activities gradually. This would allow one to test real (not modeled/predicted) impact

on the infection rate and durability of the healthcare system.

It is may also be worthwhile to enact government strategies with geographical considerations. Business concentration and sizes, demographics of the population, local controls, availability and capacity of the healthcare system, public transportation infrastructure are not distributed uniformly in Connecticut. Optimization of government strategies both in terms of their timing and regional characteristics may offer distinct benefits. While this may imply important political considerations and discussions, benefits of this course of action may be decisive. This, as mentioned, can be analyzed with the help of modeling.

The set of considerations listed above generates a very complex set of policy options for the government. There are, however, useful guides available for how to reduce this complexity to manageable levels, as in the Comprehensive "Funnel Framework" Diagram on page 20 of the Massachusetts High Technology Council Report COVID-19 Back-to-Work Planning Briefing.[1] State and local government and industry leaders may want to group interventions into a small number of incremental discrete stages, as described in several existing reports, and then need to decide on the right combination of relaxations and protective mandates for each phase.

2. What are the outcomes of the policy options generated above that need to be considered?

The Johns Hopkins report Public Health Principles for a Phased Reopening During COVID-19: Guidance for Governors[2] focuses on the increased risks of transmission of the virus as current restrictions on mobility and commerce are relaxed, which will negatively impact health care delivery capacity and mortality rates. But many other outcomes matter as well, including many on which a prolonged shut-down of commerce, education, entertainment, civic life and mobility has severely negative consequences: unemployment rates, personal and corporate bankruptcies, state income, state GDP, but also the physical health (aside from COVID-19 infections), mental health, and educational advance of its citizens. We will discuss the need for tradeoffs between these dimensions in the next subsection, but in order to make informed tradeoffs, the effect of a manageable set of possible policy options on these outcomes will need to be known.

Providing an assessment of these medical, epidemiological, economic, social and psychological outcomes for a given set of policies is not easy, given that there is large uncertainty about key variables that will influence these outcomes. Fortunately, the input of domain experts and evaluation tools (like the RAND Corporation's The Health and Economic Impacts of COVID-19 Interventions: State Policy Evaluation Tool,[3] rudimentary at present, but expandable in nuance and scope) can provide public and private sector decision makers with the needed information. Such tools conduct simulations that evaluate the outcomes of any given policy intervention under a broad range of possible futures that make different assumptions about the kinds of things we do not know at the present time (see Section 2 of this report), including the behavior of the SARS-CoV-2 virus, the future availability of treatments and vaccines, the degree to which citizens (in different age groups, or other demographics, like political ideology) will continue to comply with mandated restrictions, wear mandated or recommended protective equipment or keep safe social distancing, their willingness to trade off privacy concerns with health and public health concerns (e.g., by signing up for tracking apps), and the uptake of reopened services (like hair salons, restaurants or schools).

Instead of evaluating policy options for the full set of possible ways of what the world might look like and act like in a week, month or year, we can also examine a smaller number of such futures that give us an idea about the extent by which the outcomes of policies may differ as a function of those uncertainties. Scenario-based approaches do that, selecting for example a best-case scenario, a worst-case scenario, and a few other scenarios in between. As more information about the behavior of the virus, the behavior of citizens, and

the availability of treatments or vaccines becomes available, it is useful to think whether there are metrics (e.g., the trajectory of the rate of new infections and some other critical values) that would signal whether we are transitioning from one scenario to another one. After the outcomes of different policy approaches (e.g., proceeding more cautiously with gradual and graduated openings versus proceeding more rapidly) have been evaluated, using either the full uncertainty space or a subset of scenarios, this information can be put to use. Comprehensive ways of doing that include the Robust Decision-Making framework developed by RAND,[4] which uses this information to improve on the set of considered policy options. Simpler and more intuitive ways of using this information are described next.

3. How do we then decide between the different possible ways in which we can relax existing restrictions on movement and commerce, in which order and at what speed?

Such decisions require us to make tradeoffs between different goals (e.g., 'protecting lives' versus 'protecting livelihoods;' reducing morbidity and mortality from COVID-19 versus from the reduction in elective medical procedures). The relative importance of these different goals needs to be examined and acknowledged. It should be recognized that a) there will be disagreement and conflict about these tradeoffs between stakeholders, due to different circumstances and risk exposures that need to be resolved by consultative processes and negotiations, and b) that these tradeoffs may change over time, as some risks recede (e.g., the COVID-19 infection rate) and other goals (e.g., keeping citizens employed, educated and entertained) can gain in importance.

In order to decide on the first set of actions to take or whether to move on to the next phase of relaxations, policy makers need to be clear about their goals, define what would constitute successful achievement of that goal, and use the information about the outcomes of different policy options provided by the simulations described in Step 2 above to evaluate which policy or policies will most likely get them to achieve their goals. Because goals that matter (e.g., saving lives versus saving livelihoods) are often in opposition, one needs to be clear about the tradeoff one is willing to make, as there is no policy that can achieve both goals at high levels, at least initially. The same information about the likely outcomes of different policies under different future states of the world that serves as a guide to the benefits of a given policy thus also serves as a guide to its risks, and policy makers can deal with unavoidable yet potentially painful and toxic tradeoffs by looking for policy options that reduce unemployment and the threat of a looming recession of unprecedented magnitude while trying to keep the number of new infections below some critical value. Summarizing such information in dashboards that can be dynamically updated can be very useful.

4. Effective monitoring of the outcomes of policy decisions that have been made and implemented over time is crucial, as is the use of such feedback information to dynamically adjust the policy.

Policy makers will want to know when it is okay to move to the next phase, or whether and how likely they need to go back to a more restrictive phase. Here empirically based models and adequate testing that provide a clear picture of the conditions at a state level will be extremely valuable. Additionally, information that provides early warning of potential emerging hot spots is absolutely critical as the best defense for arresting the spread of a new cluster is early detection and mitigation. To the extent possible, metrics, milestones and timelines should be established to keep priorities clearly in view and to ensure the discipline of follow through and continued attention to important but not currently urgent matters. The effective use of integrated dashboards with current information about policy impacts and consequences is a simple but effective way to do so.

5. Decision-making is not the only responsibility of policy makers. They also need to communicate available knowledge and clearly explain the rationale for policy decisions to the public.

Without buy-in, even mandatory measures will fail. With buy-in, even simple guidance can be effective. Policy makers need to manage citizens' and other stakeholders' expectations, letting people know that we are in this process for the long run, using appropriate metaphors (e.g., dealing with COVID-19 is like a protracted war and not like a passing hurricane).

The word clouds in Figure 4-1 below show a graphical representation of the most commonly used words in a) the governor's press releases, b) transcripts of press conferences, and c) headlines in Connecticut media. We leave it as an exercise for the reader to decide what key messages were intended and whether they were heard.

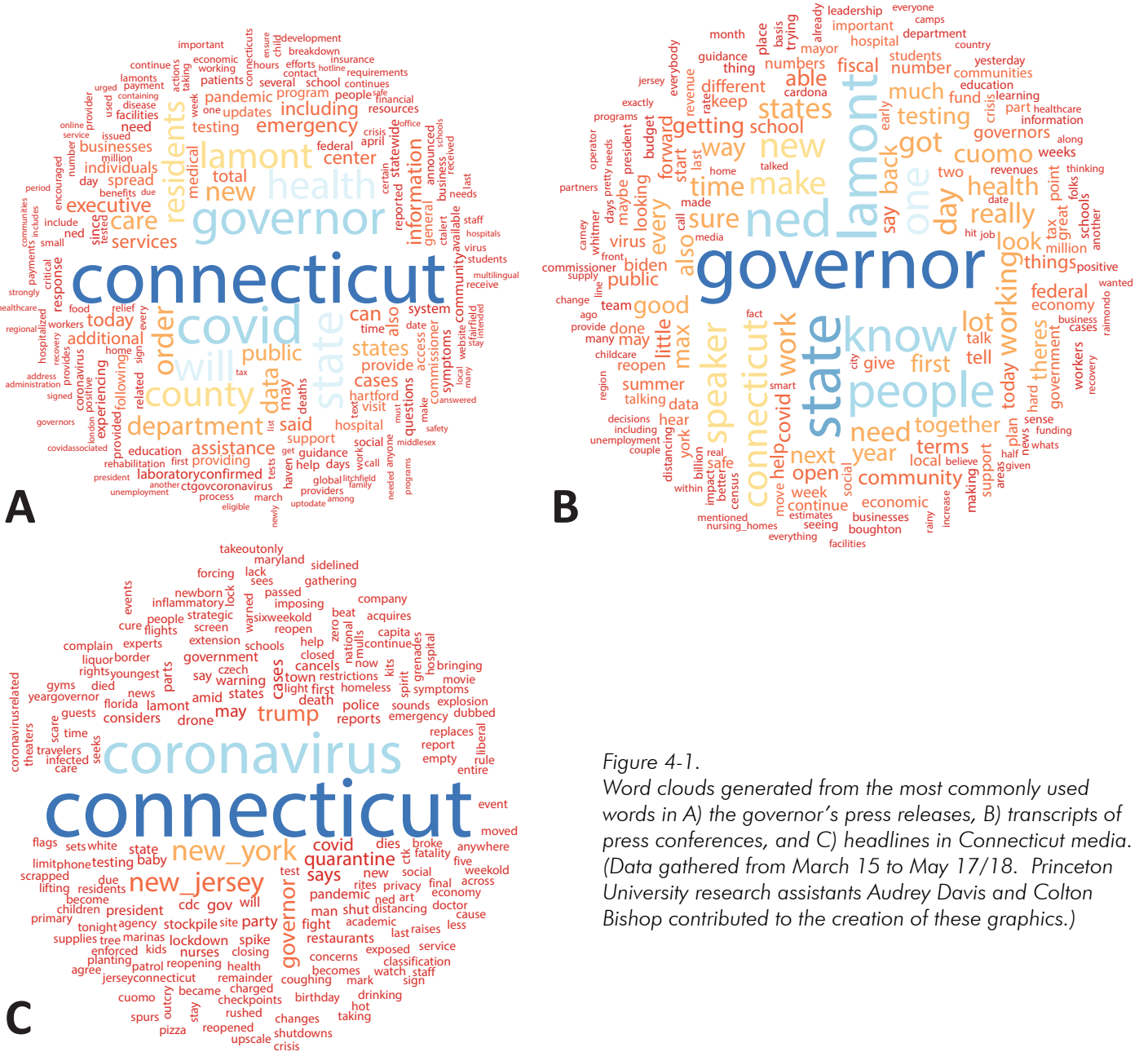


Figure 4-1.
Word clouds generated from the most commonly used words in A) the governor's press releases, B) transcripts of press conferences, and C) headlines in Connecticut media. (Data gathered from March 15 to May 17/18. Princeton University research assistants Audrey Davis and Colton Bishop contributed to the creation of these graphics.)

Leadership involves motivating people to contribute to the public good, to suffer short-term pain to protect themselves and their communities and their state for longer-term gain. People differ objectively in their risk exposure to the virus, but also in their subjective and not always accurate perceptions of those risks. Some feel safer than they should and endanger themselves and others by failing to take mandated or recommended precautions. Others may lack the confidence to return to normal working or living conditions even when such behavior has become safer again. Perceived transparency in decision-making and serious (rather than proforma) stakeholder consultation builds public trust, a necessary if not sufficient condition for cooperation and compliance. And perceived competence as well as empathy builds confidence and reduces fear.

Beyond Binary Thinking

It would be great if a simple model could point the way forward. Unfortunately, the deep uncertainty about the current pandemic makes this impossible. And yet, decisions cannot wait. They have to be made with limited time and information. When much is unknown and the stakes are high, extreme actions (such as shutting down all but essential activities and commerce) that focus on achieving a single pressing goal may be the most obvious choice and generate broad public buy-in. However, as more information becomes available and the full costs of extreme actions on dimensions other than the reduction in loss of life due to COVID-19 become apparent, policies to manage the disease have to become more nuanced and need to consider a broader set of goals and feedback in an adaptive fashion.

Toward that end, we offer these recommendations:

- **Expand how we think about risk** (with or without models). Risk exists on multiple issues, and policies that reduce the risk of virus infections increase the risk of economic ruin or the risk of dying of other causes. Even on a single issue, risk is not binary (present or absent) but exists on a continuum, and attempts to reduce a specific risk to zero come at the cost of increasing other risks. Finally, risk has dimensions of likelihood of occurrence, severity of impact, and individual and collective perception. It is the perception of risk, rather than the actual risk, that motivates and sustains protective behavior, even if those perceptions are driven by factors that differ from statistical analyses and do not always agree with expert evaluations. Thus, understanding public perceptions of risk is especially important as one seeks to change behavior.

- **Pivot from the current characterization of goods and services as essential versus non-essential and seek to find ways to make all of them safer.** Much of what is deemed non-essential significantly impacts people's lives and livelihoods if closed for extended periods. Other than the obvious essential services, such as food, medical, fire and police, many others are often debated and vary in judged importance from state to state. Instead of engaging in such debates, policies should focus on ways of reducing the risk of virus transmissions for both "essential" and "non-essential" businesses.

- **Be adaptive with a keen sense of the current conditions and trends.** As the initial wave of infections has shown, different states and even portions of states can show very different patterns. Similarly, risk reduction techniques that are appropriate at the very beginning, such as contact tracing, are almost intractable when the epidemic is widely endemic. A state-wide massive shutdown that is appropriate at the beginning when little is known needs to be replaced with more adaptive and targeted approaches that can have the same effectiveness but with much less harm on society on other dimensions. This is enabled by expanded testing coupled with a state specific epidemiological model that includes the interactions with neighboring states in the region.

- **Develop a cautious, gradual, transparent, and disciplined process that uses iterative feedback to ensure the sustainability of relaxations and long-term success.** Take a systems approach to identify key metrics and track these regularly with an integrated dashboard that shows current status, trends, and projections for future progress. Use this in communication so that the rationale for actions are explainable and engender buy-in. This should include both virus risk mitigation as well as metrics of recovery of the economy. Perform analytical stress tests of critical elements of the system, such as healthcare capacity and rapid response readiness for containing new outbreaks. For major strategic decisions, implement a process that allows for stakeholder consultation and a consideration of tradeoffs between a full range of costs and benefits.

SECTION 5

Targeted Approach to Testing, Contact Tracing and Mitigation

Societal Reinforcement Learning in Action

With COVID-19 we are operating in a novel, highly uncertain and dynamic decision-making world. We are learning, assessing the situation to the best of our ability and making decisions; indeed, we are operating in a world of "societal reinforcement learning in action." Just like in games, we make errors, learn from them, and we adapt. Unlike games, errors here have enormous loss of life consequences and that is why risk-informed decision-making is essential.

A data-driven, risk-informed approach to decision-making in environments, such as the COVID-19 pandemic, requires robust, adaptive and resilient decision-making[i] based on reliable data. Data, analytics and context-driven decision support based on that data helps us in assessing what we know (e.g., detecting anomalies), what happened (assessing the situation), why it happened ("root cause analysis"), forecast what could happen ("preview the evolution of the situation"), proactively recommend explorative and exploitative actions to mitigate the situation, and visualize and convey the risk associated with the decisions in an easily understandable way to policy makers. Thus, situation aware-

Testing levels recommended to lift stay-at-home order in Connecticut are hither and thither. For example, the Rockefeller Foundation supported report from Harvard University's Safra Center for Ethics recommends 5 million tests per day for the U.S. and as many as 20 million tests per day by late July. That translates to about 50,000 test per day for reopening Connecticut and 200,000 tests per day by late July. Harvard's Global Health Institute recommends 10,000 more COVID-19 tests than the current 2,800 tests per day. That translates to about 12,800 tests per day and approximately 90,000 tests per week. Yale's Howard Forman recommends testing at least 100,000 individuals per week. New York is planning to scale up to 40,000 tests per day. Proportionally to state populations (19,453,561 for New York versus 3,567,287 for Connecticut), this corresponds to about 7,500 tests/day (52,500 tests per week) for Connecticut. The comprehensive testing method at 7,500 test per day will take about 16 months to test each individual once, let alone testing of individuals twice a week.

There are a number of rules-of-thumb for computing the number of tests needed per day.[1] Since the infection period is roughly two weeks, predict the mean and standard deviation of the number of daily cases over a two-week period. Then, a rough rule of thumb for the number of tests per day is: $N=(n_c+3\sigma_c)*c_s$ where n_c is the expected number daily cases, σ_c is the standard deviation of the daily cases, and c_s is the number of close contacts per case with social distancing. With two cases on average per 100,000 population (that is about 71.3 cases per day for Connecticut), $\sigma_c=30$, and $c_s=10$, this is about 1,630 tests per day. The state's projected 6,000 tests per day is more than adequate for this level of caseload, including testing asymptomatic individuals who may have been missed and later identified by way of infected individuals, testing individuals in hotspots, and randomized serological testing for prevalence estimation. The World Health Organization has said that a positive case rate of 10% reflects adequate testing. Connecticut is already within reach of this guideline. Should the number of cases increase significantly, then the number of tests would also need to increase as noted in the equation above.

i Agile Recommendations via context-dependent, risk-aware decision support systems (DSS) for different event types. If the events are anticipated, the DSS suggests pre-planned and robust courses of action; for unfolding events, DSS adapts plans from currently known action sets; and for unforeseen situations, the DSS continually plans, executes, monitors, assesses and re-plans, possibly with new action sets. A plan specifies *who does what, when, where, how, with what and why.*

ness (SA) to control the spread of the disease and mitigation is essential.

Why Comprehensive and Frequent Testing is Intractable

Testing is the means to achieve SA. Unless cheap, superfast (<5 minutes), super-reliable (>0.999) at home self-testing is available, comprehensive testing of people is intractable and also not required for effective coverage (see the box on the previous page).[1,2,3]

Connecticut's daily test results, including the seven-day moving average trendline of the percentage of tests that are positive, are presented in Figure 5-1 below. In tracking the spread of COVID-19, it is important to have adequate and consistent testing. As the number of tests are ramping up, it can be difficult to tell whether new infections are actually increasing or simply appear to be so because of the increased testing. When infection rates are generally low, a low positivity percentage is one indicator of adequate testing.

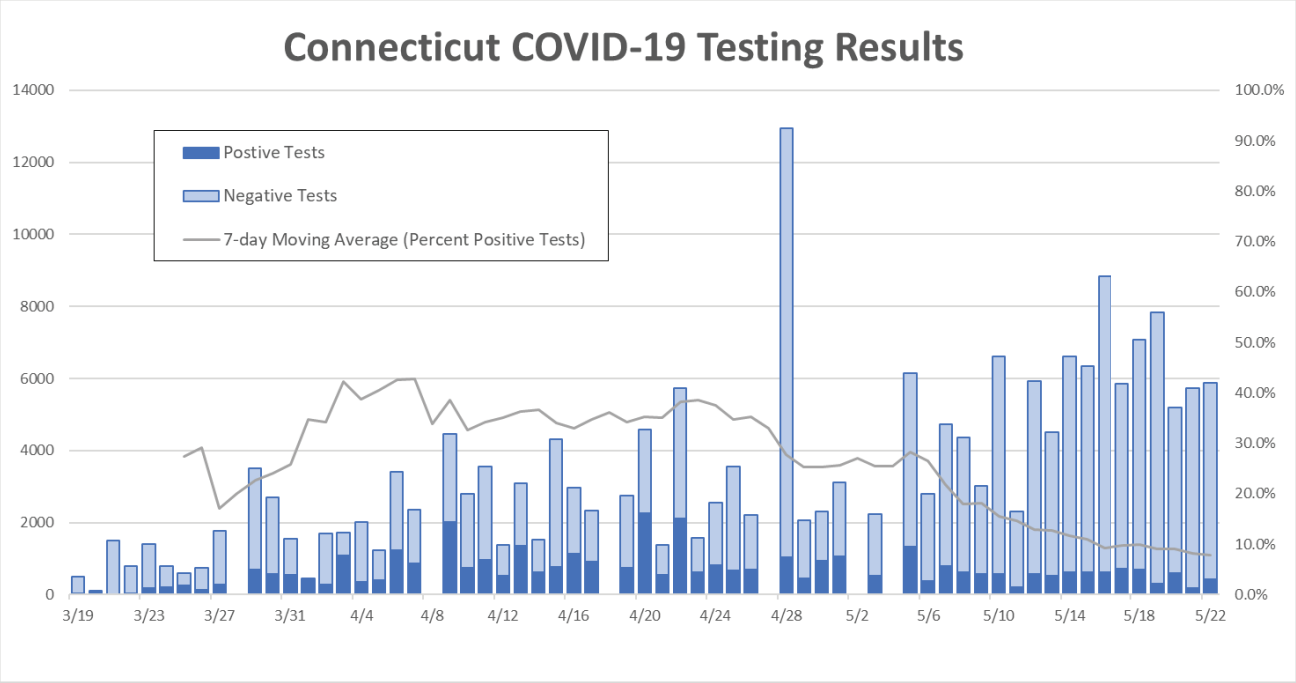


Figure 5-1. Connecticut COVID-19 testing results, as of May 22, 2020.

Then How to Test to Ensure Workplace Safety with High Confidence

The estimates discussed regarding the amount of testing pertains to recommended minimums for the state that scale based on the current extent of the outbreak. When one includes specialized needs for certain workplaces or the healthcare system as discussed in Sections 6 and 8, more testing could be required. A key practical idea for efficiently meeting such increased requirements is to detect and stamp out smaller outbreaks before they get big via sequential and randomized group (pool) testing. Group testing was introduced in 1943 to test large groups of U.S. military personnel for syphilis prior to deployment.[4] A number of extensions to this method ensued over the years, including the case when tests are unreliable.[5] The group testing method requires one to detect COVID-19 RNA in a mixture of samples; recent work has demonstrated that it is possible to do so using the RT-PCR test.[6,7] As shown in Figure 5-2 on the following page, if the disease prevalence is low, the gains can be as high as a factor of 5-6 (effectively, one can reach the same effect as conducting 36,000 tests per day if one has 6,000 tests per day capability).

However, if the prevalence is high (i.e., if a large portion of the population is infected), the gains from group testing are modest (about 15%).[8] To gain even better efficiencies, we recommend adaptive stratified random sampling[i] based on test outcomes, questionnaire responses, observed cases, cell phone data,[ii] demographics, occupation, recent distancing experience and health status of individuals that would prioritize limited test resources to maximize the information gained from testing (i.e., minimize the uncertainty (entropy) about the disease evolution) to enhance situational awareness. Procedures should be used to guarantee consistency across federal guidelines, state regulations and workplace practices on testing as much as possible.[iii]

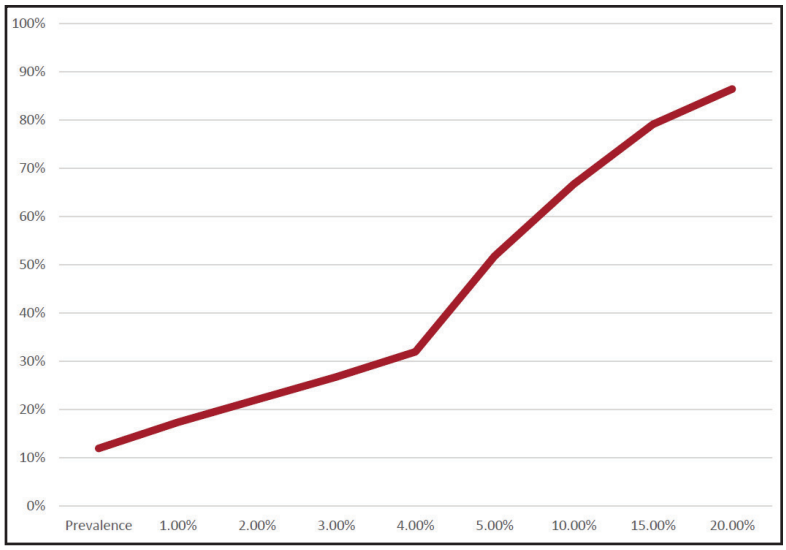


Figure 5-2. Percent required test resources via generalized binary search (group size=16) compared to comprehensive (100%)

What Types of Testing

Diagnostic testing seeks to build confidence in people so that they can feel safe to reemerge into the economy, as well as to control the spread of the disease. A positive diagnostic test initiates the trace-isolate/quarantine event sequence. Serological (antibody) testing provides insights into prevalence and identifies donor candidates for convalescent plasma therapies. Indeed, a seropositivity is (nearly) a go home-free card to enter society. Sewage testing for COVID-19 virus can pinpoint hot spots of virus activity in office and apartment buildings.[9]

The diagnostic testing process should be decentralized at point-of-care (hospitals, urgent care clinics, general practitioner's offices, retail clinics, pharmacies), drive-through locations and work places with around 500 or more employees. Results should be provided as rapidly as possible since early action is an important factor in effectively managing this disease at both the individual and community level. We recommend that diagnostic testing should be prioritized according to CDC guidelines.[10] Serological testing should be randomized to conserve testing resources and to provide ongoing surveillance information regarding disease prevalence.

Privacy-Preserving Contact Tracing Apps

Apple and Google have teamed together to develop a privacy-preserving, Bluetooth-based,[iv] hack-resistant smart phone API to develop contact-tracing applications based on measurements of the closeness and duration of contact between people. It works on both Android and iOS operating systems and uses a decentralized protocol termed Decentralized Privacy-Preserving Proximity Tracing (DP3T).[11] The contact tracing applications built on the Apple-Google API can provide facilities for opting in to share their phone number to tracing personnel to aid in contact tracing, but it is not part of the system architecture. These applications can augment

i In stratified random sampling, one divides the patient population into relevant subgroups and then, using a computer-generated list of random numbers, draws a sample from each subgroup. Cluster sampling, in which one divides the population into clusters, and selects a subset of the clusters randomly, may be more appropriate for serological (antibody) testing.

ii Cell phone data, via privacy preserving Google-Apple Application Programming Interface (API)-based apps, can aid individuals in avoiding risky individuals, locations and events. It also helps in identifying high-risk venues for proactive testing.

iii Formal methods use mathematical proof as a complement to manual methods and offer guarantees of consistency.

iv Named after the 10th-century king Harald "Bluetooth" Gormsson, famous in Scandinavia for uniting the Danes.

the services provided by the tracing and public health personnel in the following three ways:

- Make the interview process of an infected COVID-19 patient faster by automatically pre-filling the contact interview form. The patients should be informed of the potential risks of sharing the data by the interviewer.

- If an individual tests positive for COVID-19, the application can alert recent contacts to call a doctor, get tested, or self-isolate. The app should consider a number of indicators, such as the duration of contact, proximity of contact, number of contacts, time of contact in relation to symptom onset, location of contact (household versus non-household), age-band of sources and recipient, and severity of symptoms in determining the individual's infection risk.[12]

- Health authorities can use the app to alert people on emerging hotspots and people who may have recently visited places that are categorized later as contaminated. The app will allow health authorities to infer an infection affinity graph of people, and this can aid in allocating testing resources and in relaxing social distance guidelines.

Research shows that an adoption rate of 60-70% is needed to relax social distancing[i] and this depends on the reliability of Bluetooth technology in providing the distance, which, in turn, manifests as false positives and false negatives. Bluetooth's received signal strength indications (RSSI) depends on environmental conditions (e.g., crowd versus free space, walls, proximity to several phones, orientation of the phone) and multiple RSSI over time may need to be fused to get a better estimate of the distance and duration of interactions.

Further research is needed on the issue of false positives and negatives and the associated unintended consequences. Before adopting any automated contact tracing technology, one must also consider and ensure adequate protections for privacy, equality and fairness.[13] A well-planned pilot deployment could help address these concerns ahead of time. This topic of automated contact tracing is one area where the state could benefit from a thorough analysis by CASE.

How Many to Sample for Prevalence Estimation [14]

Randomly sampling the state population for antibody testing and in work places for diagnostic testing is essential. Let P be the true proportion of infected individuals in a population of N, and p the sample estimate of P (e.g., number infected/N). Suppose the required margin of error in the estimated proportion is d. Then, if we are willing to take a small risk α that the actual estimation error is larger than d, i.e., Probability $(|p - P| \geq d) \leq \alpha$, a good first approximation of the sample size for large N is $n_\infty = t^2 p(1-p)/d^2$. Here t is the abscissa of the normal curve that cuts off an area α at the tails (t determines the risk that we are willing to take that our sample estimate will exceed the desired margin of error, d; typical values of t are 2 or 3). For example, if $p=0.1$ and $d=0.01$ (10% error in the estimation of prevalence, p) and $t=2$, the number of samples $n=3600$. For a relatively small group (when N is a few hundred or a few thousand as in a work place), the formula for the sample size should include the finite population correction $n = N\, n_\infty/(N + n_\infty - 1)$.[ii,15] When

i If transparency around privacy is lacking, the adoption rate will plummet below 20% (with Singapore as example). Privacy means that the Department of Public Health personnel get an affinity graph of infected (potential or actual) people, while maintaining privacy (by using the so-called Cuckoo filtering technique one only learns his/her own risk score).

ii When prevalence P is very small (e.g., when the risk is very small), a simple adjustment that adds α–dependent corrections to measurements provides better estimates.

tests are unreliable with sensitivity, TPR[i] and specificity[ii] TNR, the sample estimate, p should be corrected[iii] as $p_c=(p+\text{TPR}-1)/(\text{TPR}+\text{TNR}-1)=(p-\text{FPR})/(\text{TPR}-\text{FPR})$.

Who to Test

Testing should at the least include periodic testing of healthcare and other at risk individuals, essential workers (public transportation, food stores, utility), all who show symptoms,[iv] group screening of asymptomatic individuals at work or major gatherings, and randomized testing of the public for surveillance. As the testing capacity ramps up, testing should correspondingly be expanded to include work places (e.g., retail stores, financial and insurance companies, technology companies, farms, sports facilities, ferries). At steady state, monitoring via a randomized testing protocol will ensure confidence in state population.

When and Where to Test

The information should have high value in the sense of minimizing the uncertainty in the awareness of the situation and maximizing the expected quality of policy decisions. We recommend information-theoretic (e.g., mutual information[v]) and "wrapper-based what-if" analysis approaches using the risk-informed decision framework as the basis for information seeking decisions of how often and where one should test. For example, how much uncertainty is reduced in the forecasted indicators over a time horizon, such as the infection rates, hospitalizations, ICU beds, ventilators, deaths, and impact on economic output, could inform such decisions. In this vein, privacy preserving contact tracing applications, such as those based on Google and Apple developers' API, may provide valuable information. It is critical that the apps adhere to the recommended privacy standards, and this should be ensured by analyzing the privacy posture of any apps that the state might recommend. In addition, Bluetooth is not very reliable in terms of estimating distance and some work needs to be done in terms of modeling the impact of these errors on the quality of data collected (see the section on privacy-preserving contact tracing).

Diagnostic Testing Protocol

We assume that every location practices preventive measures: social distance measures, deep cleaning every shift and every office zone, PPE (masks, gloves, disinfectant stations), checklists, temperature monitoring, and a buddy system among employees to prevent risky behaviors.

Once a location (a town or a work place) or a group of people (e.g., in a nursing home, hospital, a manufacturing firm, public transportation, retail/food store, financial or insurance company, utility, technology company, farm, sports facility, a ferry) is selected for diagnostic testing, the following protocol is recommended:

- Clinically screen as many potential positive patients as possible before administering the test. All patients

i Sensitivity is variously referred to as true positive rate (TPR), (1-false negative (miss) rate, (1-FNR)) or 1- type II error (1-β), detection probability (P_D), hit rate (h), recall (R) in the engineering, psychology and machine learning communities.
ii Specificity is variously referred to as true negative rate (TNR), (1-false positive rate, (1-FPR)], or 1- type I error (1-α) and selectivity.
iii Evidently, observed or estimated p = P TPR + (1-P) (1-TNR). This is the same formula given in https://jamanetwork.com/channels/health-forum/fullarticle/2765693 using a non-standard notation.
iv This is relevant in late fall to distinguish between influenza and COVID-19. It may be obvious now and test resources may be saved.
v Mutual information (information gain) measures how much more is known (entropy before sampling and expected entropy after sampling) about a situation with testing.

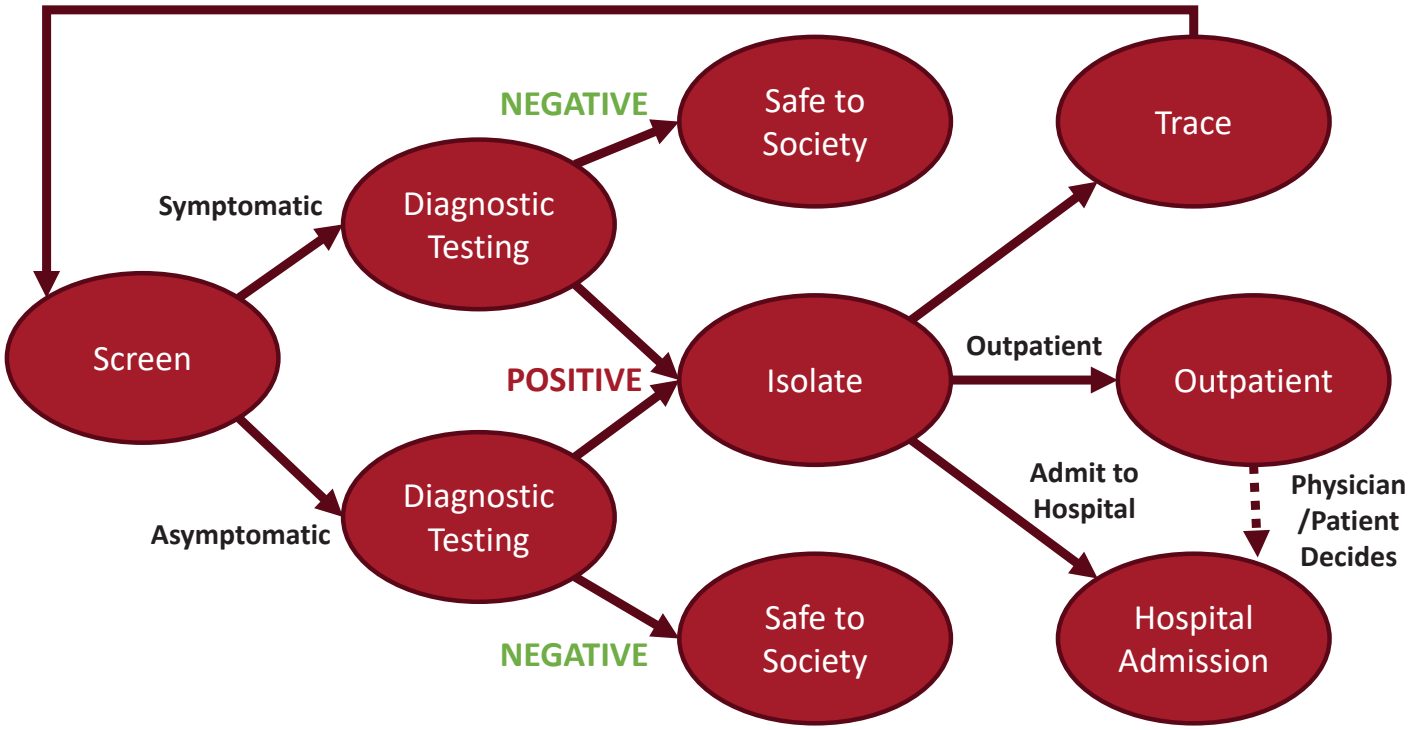


Figure 5-3. Diagnostic testing protocol.

with COVID-19 symptoms[i,16] or having recent contact with positive COVID-19 patients[ii] are deemed symptomatic. The rest are categorized as asymptomatic.

- Conduct diagnostic (RT-PCR) testing using saliva or nasal swabs for individuals with COVID-19 symptoms.[iii,17] Test asymptomatic individuals using sequential (outcome-dependent) group testing at the location. If an asymptomatic patient is positive, follow the isolate-trace-screen process as in Figure 5-3 above (tracing is elaborated below). If the test outcome of a group of asymptotic individuals (bulk sample) is negative, the group is deemed safe.[iv,18] On the other hand, if it is positive, divide the batch sample in half (hence the name binary search) and test again. Continue this process until positive asymptomatic individuals are identified.

- Categorize isolated patients into outpatients or those requiring hospitalization.

- Monitor outpatients for temperature and O_2 levels.[v] Admit patients to hospitals at the recommendation of a physician or patient. Self-monitoring or remote monitoring are potential options for outpatients.

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i Cough and shortness of breath or difficulty breathing or at least two of these symptoms: fever, chills, repeated shaking with chills, muscle pain, headache, sore throat, new loss of taste or smell.

ii Close contact is defined as: a) being within approximately six feet (two meters) of a COVID-19 case; close contact can occur while caring for, living with, visiting, or sharing a healthcare waiting area or room with a COVID-19 case – or – b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on).

iii Saliva testing requires less resources, personal protective equipment, and personnel than nasopharyngeal swabbing. There are also proposals for breathalyzer testing.

iv There are methods to deal with unreliable test outcomes that allow successful identification of the defective Items or allow their identification with some confidence.

v Statistics from New York state show that 66% of hospitalizations are patients that are quarantained. Providing O_2 monitors to these patients at a modest cost or for free and frequent monitoring of these patients via contact tracing personnel can substantially reduce the death rates.

- **Contact Tracing:** For every positive case, trace their contacts. This requires a cadre of tracers. The number of tracers required depends on the number of contacts, number of cases per 100,000 at which the state opens, the state population, testing delay (in number of days), time to interview a positive case, and the time to communicate with contacts of the positive case. Applications that monitor these statistics will aid in matching the tracing personnel to the case demands. In addition, privacy-preserving contact tracing applications may provide relevant information to the tracers and improve their productivity. It also helps in proactively targeting testing locations and in accurately counting recovered patients. App-assisted contact tracing may work like a "helpful" call center as follows:

  - One option (Option A) is for human tracer to set the initial thresholds on duration of contact, proximity of contact, number of contacts, time of contact in relation to symptom onset, location of contact (household versus non-household), age-band of sources and recipient, and severity of symptoms to weed out numbers from the app. A more practical and desirable option (Option B) is for the tracer's supervisor to set the thresholds at the beginning of each day or week.

New York is estimating 30 tracers per 100,000 population and is recommending opening the counties at two positive cases per day per hundred thousand population. This corresponds to approximately 5,836 tracing personnel for New York and corresponds to about two positive cases and their contacts per tracer over a 30-day period. Massachusetts is hiring 1,000 tracers to identify pockets of infection and trace contacts of infected patients to control the spread of COVID-19. This corresponds to approximately 14.5 tracers per 100,000 population and at two positive cases per day per hundred thousand population, this corresponds to about four cases and their contacts per tracer over a 30-day period. Translating this to Connecticut population, the required number of tracers range from 516 to 1,070. We believe that 710 tracers should be adequate to cover the state of Connecticut (3 cases and their contacts per tracer over a 30-day period). This number can be adjusted as the data on testing delays, time to interview a positive case, the time to communicate with contacts of the positive case and the productivity gains accrued by the contact tracing applications becomes available and is assessed via models.

  - During the interview process:
    - Tracer should assure the patient that the data will not be shared for any purpose other than contact tracing and the wellbeing of the state's population. Tracer should ask the patient whether he/she wants to share proximity events and whether this may include time stamps and GPS coordinates.
    - The contact tracing application would have pre-filled major parts of the contact interview form. Tracer gets additional contacts, if any, by interviewing the patient. This may include contacts not in the phone.
    - For those in the contact tracing app, asks questions about people that satisfy the app thresholds. Need to have a mechanism to transmit information to the tracer on people that may have already contacted the health department based on the app. For those not yet contacting the health department, individuals to be contacted should automatically be in the queue to be contacted by the current tracer or in the common queue of a pool of tracers.
    - For option A, tracer can decide to set new thresholds or leave them where they are.

  - For option B, supervisor can review the false and missed infections rates for the past day or week and set new thresholds for the following day or week.

Serological Testing Protocol

To estimate prevalence of the disease, augment diagnostic testing by periodically conducting stratified and randomized antibody testing of asymptomatic patients.[i] If an asymptomatic individual has antibodies, it helps in determining prevalence and the individual is a candidate as a donor for convalescent plasma.

Cost of Testing

CVS Health is offering diagnostic tests free-of-charge. Quest charges $129 for an anti-body test.[19] Medicare cost schedule for different types of diagnostic tests range from around $35 to $100, depending on the test.[20] Assuming roughly 3,000 of the 6,000 tests per day are not covered by insurance, cost of testing is expected to be (3000*129*365)=$141.25 million per year. This may be further reduced by negotiating bulk testing contracts.

Supply Chain Management

Solve supply chain issues via agile sourcing and cooperation with regional and federal partners. Unreliable supply chain issues can be partially alleviated using diversified (preferably national) sourcing, inventory buffers and blockchain and location intelligence to ensure integrity in sourcing.

Mitigation

Risk prevention (avoidance) and risk reduction (containment) are two ways to reduce risk. Risk avoidance seeks to minimize vulnerabilities, which can pose a threat. In the context of a targeted approach to mitigating COVID-19 risk, risk prevention involves keeping people with health conditions that make them susceptible to COVID-19 at home. This applies to nursing home residents and possibly designating individuals with comorbidities as temporarily disabled until the COVID-19 risk is mitigated. Another way of avoiding risk is to provide the ability to work from home for those that can do it (e.g., software professionals, graphic artists, professors and consultants). Indeed, the state and private employers should consider remote working as a long-term strategy to reduce costs and pollution. Since the minority and low-income populations are disproportionally affected by COVID-19, the state should have a process and a policy for coordinating and aiding non-governmental organizations and volunteers to disinfect low-income buildings, provide masks, disinfectants and soaps, and educate on the benefits of social distancing. Risk reduction deals with minimizing risk consequences or likelihood of occurrence. This includes instituting temporary segmental systems in business sectors. Segmentation could be by time (time shifts, alternate days, staggered schedules such as three days in and four days off), space (zones with separate entrance and exit), priority (e.g., manufacturing versus software engineering). Businesses should be encouraged to maintain functional redundancy across time shifts and zones to mitigate risk. Additional risk mitigation strategies include deep cleaning of work spaces every day and after every contact with a customer, mandatory use of personal protective equipment (masks, gloves), easily accessible disinfectant stations, physical separation of employees (social distancing), monitoring employee temperatures at the beginning of each day, checklists, frequent reminders during the day (no shaking hands and encouraging employees that have COVID-19 symptoms to go home or stay home), encouraging buddy system among employees to ensure that the guidelines are followed. Facilities could also explore the utility of installing far-UVC lighting to kill the virus.[21] Finally, since the risk of transmission is much greater indoors,

i Stratified random sampling divides the population into homogeneous groups called strata (plural for stratum). Grouping can be done by age, gender, comorbidity, socioeconomic status, race, educational background, county, geographic intensity of the disease, etc.

it is important for buildings to maintain good air circulation with appropriate filtration and an adequate mix of fresh air.[22]

Clinical Trials

We recommend that the state's hospitals should actively participate in clinical trials for therapeutic drugs and vaccines. This has the beneficial effects of making Connecticut a leader in COVID-19 treatment, gaining knowledge of how trials are proceeding, and educating the public on the best therapies and vaccines.

SECTION 6

Returning to Work and Protecting the Vulnerable

The objective of this section is to provide a set of evidence-based recommendations for returning to work and protecting the vulnerable in the state of Connecticut. These recommendations span dramatic increases in testing; implementation of patient tracking and contact tracing; monitoring of local COVID-19 infection rates and trends; ensuring availability of sufficient supplies of masks and hand sanitizers; and enforcement of preventative measures such as wearing masks and social distancing.

The United States and Connecticut are facing momentous decisions relating to how and when the nation and the state should reopen our workplaces and social fabric. Arguably, this situation is significantly aggravated by the lack of a proactive public health response to the emergence and growth of the coronavirus epidemic at its origin in our country with timely and adequate communication and execution of policy about social limitations, testing and contact tracing. Consequently, at this time the United States finds itself with a declining but still high daily infection rate, with no more than 4% of our population having been tested, and with no robust approach for contact tracing available. Therefore, it's clear to us that learning from the experiences of other, more successful, nations is extremely valuable as we proceed to open our society and workplaces.

A superb example of an appropriate, proactive and committed public health response to containing the spread of the coronavirus...hence positioning the nation to a relative orderly and successful opening is Taiwan, one of the most at-risk areas outside of mainland China due to its close proximity, ties and transportation links.[1] Taiwan health authorities acted very quickly in addressing the coronavirus epidemic and implemented 124 action items that were informed by experiences gained during the 2003 severe acute respiratory syndrome (SARS) outbreak. Within days of the COVID-19 outbreak in Wuhan, Taiwan closed its border and very closely monitored people returning from mainland China, stopped cruise ships from docking at its ports, and deployed new punishments to individuals breaking home quarantine instructions. Everybody who tested positive was followed very closely by a participatory self-surveillance mobile app and by human monitors who would track these people; checking in with them on a twice-a-day basis. Should these individuals leave their homes with their phone, this status would be detected, and a reminder of their isolation responsibilities would be transmitted. These approaches really made a huge difference to Taiwan's successful COVID-19 containment.

A second example of an exemplary public health coronavirus response early on in the pandemic was Singapore.[2] Singapore had several advantages that made it very effective: one major land border with Malaysia, tight control on people entering by air, a world-class health system which was hardened from lessons learned in combatting SARS and strong government investment, and a system of rules and policing that can benefit a government response. But in the last two months, the number of confirmed coronavirus cases has spiked from under 500 to over 30,000 as of May 22. So what went wrong? The answer appears to lie in overlooked clusters of cases among migrant workers living in cramped dormitories, 12 beds per room, commuting back and forth in crowded pickup trucks to work. This example illustrates the social gradient, societal inequities, non-clinical factors, and social determinants of health (SDOH) that are critical to factor into decisions about returning to the workplace.

The rate of individuals with positive reverse transcription-polymerase chain reaction (RT-PCR) test results in the United States and for Connecticut provides an indication of adequacy of testing. As of May 22, 2020, the United States reported a positive test rate of 11.9% (1,592,656 out of 13,419,058 total tests) and Connecticut reported a 19.6% positive test rate (39,640 out of 202,328 total tests).[3] This data implies that Connecticut is neither conducting sufficient testing nor testing a lot of people with mild or no symptoms, but only picking up more severe cases. If Connecticut were to do extensive population testing to properly establish our state's situation, then we would likely see the PCR-**positive rate to be much lower**. Without this data, it becomes very difficult to discern the actual state of the pandemic in Connecticut. Commendably, the state has ramped up testing recently with an average number of 34,000 tests per week and an average positivity rate of 10.7% during the first three weeks of May.[3] The World Health Organization's current recommended benchmark for reopening is a positivity rate of 5% or below.[4] Testing of much of the population will also have to be repeated at regular intervals until and when the new case growth rate approaches or becomes nearly zero. Rapidly moving to such an extremely high level of testing is essential as we approach the challenges of opening our workplace without achieving a near zero increase in case numbers.

China, South Korea and Taiwan have had measurable success in controlling the epidemic; **these countries opened up only when new case numbers reached near zero**. The United States and Connecticut, having started testing and monitoring somewhat late, are currently demonstrating a reduction in daily new cases; however, they are not yet near such a level.

Background

Published literature in 2020 was reviewed from the MEDLINE library database and manual searches. Select studies that address pragmatic and clearly defined steps for reopening workplaces are summarized. The American Enterprise Institute (AEI) provides a roadmap and measurable milestones for the United States to reopen through federal government leadership in collaboration with states and public-health and health care partners.[5] AEI recommends leveraging technology to aggregate and analyze data in real time for case identification and containment, contact tracing, population immunity tracking, and adequate medical supplies, as well as expanded investment in pharmaceutical research, development, and deployment of effective diagnostics, therapies and vaccines. AEI outlines the four phases of 1) slow the spread, 2) state-by-state reopening, 3) establish immune protection and lift physical distancing, and 4) rebuild our readiness for the next pandemic, and also provides the triggers to go from one phase to the next. Johns Hopkins University (JHU) uses AEI's report as a basis to build upon for their reopening guidance to state governors.[6] JHU proposes four principles for action to reopen when: "1) the number of new cases has declined for at least 14 days; 2) rapid diagnostic testing capacity is sufficient to test, at a minimum, all people with COVID-19 symptoms, including mild cases, as well as close contacts and those in essential roles; 3) the healthcare system is able to safely care for all patients, including providing appropriate personal protective equipment for healthcare workers; and 4) there is sufficient public health capacity to conduct contact tracing for all new cases and their close contacts."

Harvard University proposes massively scaling up of testing, contact tracing, social isolation (coined TTSI) and quarantine starting with 5 million tests per day by early June and 20 million tests per day by late July, which would enable reaching 2%-6% of the population daily.[7] Harvard University further proposes a four-phased approach of 1) stabilizing essential sectors (40-55% of the workforce), 2) expanding essential workers (70%), 3) ending collective stay-at-home (80%), and 4) full pandemic resilience (100%). The Rockefeller Foundation recommends robust testing, tracing, and coordination starting with significant growth in testing from 1 to 3 to 30 million tests per week over the next six months, launching a COVID Community Healthcare Corps to administer tests and contact tracing, and creation of a national system to track COVID-19 status.[8] The IBM

Institute for Business Value presents a COVID-19 Action Guide for Executives containing seven imperatives for emerging stronger to a different new normal.[9] These imperatives for beyond the great lockdown include mid-term and longer-term guidance to: 1) empower a remote workforce, 2) engage customers virtually, 3) remote access to everything, 4) accelerate agility and efficiency, 5) protect against new cybersecurity risks, 6) reduce operational costs and enhance supply chain continuity, and 7) support health providers and government services. In a second report, the IBM IBV shares several guiding principles for returning to the workplace in waves and a set of readiness checklists. IBM is offering free tools through The Weather Channel app, weather.com, and an online dashboard to help citizens stay informed and track reported COVID-19 cases down to the county level in the United States using information available from the World Health Organization and multiple national, state, and local governments.[10,11]

Insights emerging from China can provide additional reopening guidance for the United States. Attention must be paid to employee mental health and well-being when returning to work post-pandemic as evidenced by a survey of 673 employees after returning to work showed a high rate (10.8%) of post-traumatic stress syndrome (PTSD), anxiety (3.8%), stress (1.5%) and insomnia (2.3%) with no statistically significant difference between workers/technicians and executives/managers.[12] Epidemiological models showed that maintaining physical distancing measures helped to delay and reduce infection peak when staggering return to work; however, the effects are influenced by school children.[13] Model predictions of Wuhan following lockdown and quarantine on the pandemic's timeline and the impact of the potential of a second outbreak after return-to-work in the city are described by Roda et al.[14] The combination of targeted serosurveillance to determine an individual's transmissibility potential with direct pathogen testing is suggested as a possible approach for determining readiness for that individual to return to work.[15]

An Ideal Approach to Opening

An ideal way to get back to business is to **minimize the potential for reinfection and surge and to open the state in a controlled way by preventing the threat of opening too soon, experiencing surge, and needing to retreat or close again in a cyclic fashion**. The goal is to contain the spread of the coronavirus to a sufficiently low enough level that is acceptable to society. Ideally, Connecticut should not reopen until new case numbers approach the low levels achieved by China or South Korea. China reported no new local infections on March 18.[16] To do otherwise may potentially lead to facing a number of unfortunate open-and-close cycles. This condition would be highly disruptive and seriously impact the health and economic wellbeing of Connecticut residents.

The challenge with relaxing restrictions is that officials will not have a reliable sign of the consequences for at least two weeks, the upper end of the incubation period of the virus. Experts suggest no new infections for at least fourteen consecutive days will indicate an outbreak to be considered over.

Worldwide data suggests to us that it would be unwise to open our society up too soon. Specifically, the United States and Connecticut are significantly behind Western Europe in terms of the epidemic curve.[17] The data as of May 22, 2020 indicates th the United States has 30.7% (1,601,000 / 5,211,000) of the global total cases. New daily cases have come down from recent peaks but are still declining slowly in the U.S. overall and are around 50% below their prior peak in Connecticut. Consequently, we agree with many national experts who believe **it's not prudent to open our workplaces too quickly as doing so could result in more problems**. **China went to zero growth before opening up**. It's a huge risk to ignore other countries experiences when there are many examples teaching us that **by opening the workplace too soon, we actually delay the ultimate return to normalcy and may potentially cause much more economic**

distress as well as deaths. As famed virologist David Ho pointed out, "I think everybody would like to get back to business, but the easiest way to get back to business is not to go through this in cycles. It is just to contain it to a low level, and society, collectively, should debate what level that should be. Do we need to go as low as China or South Korea? Or can we do something at a low level but still do a lot of testing and contact tracing, as well as social distancing?"[18]

A Pragmatic Approach with Some Risk

Factors involved in a return-to-work decision are likely to include the items provided in the list below. Institutions will need to implement customized procedures for their worksites prior to any return of employees to workplaces. All workplaces whether office buildings, universities, hospitals, retail stores, restaurants and bars, factories, schools, services providers such as hair and nail salons and barber shops, private gyms and clubs, and others will have unique issues which must be addressed. We have made suggestions for some of the factors that should assist employers and associates in providing an appropriate level of safety confidence. In such situations, teleworking and work-from-home options should be continued or until an effective vaccine is found. If employers are determined that they can assure their employees of a sanitized, safe work environment, then the workplace should be opened slowly, with great caution and reserve, and with substantive measurement.

Factors

- Monitoring state and local COVID-19 infection rates and trends, including those of neighboring states to Connecticut (New York, Massachusetts and Rhode Island).
    - **Testing needs to be expanded dramatically in Connecticut, New York, Massachusetts and Rhode Island, especially since many Connecticut employers have associates living in these nearby states**. This action is essential if we are to see a full return to the workplace. Where possible, such testing could be done by the large employers at the workplace. Connecticut should take stock of all its labs, including academic labs, suitable to process the tests. A program to significantly increase skilled testers, tests, personal protective equipment (PPE), reagents etc. should be undertaken immediately.
- Gathering employee symptoms regularly.
- Staggering and phased approach for essential sectors, essential workers, and then others.
    - Recommendations for the approach for a staggered return to work are provided in the next section.
- Incorporating company policies as they relate to different sites and job roles.
- Including employee vulnerability, given individual health and comorbidities. The subject of vulnerabilities is covered in the next section.
- Understanding state and local regulations, including those of neighboring states to Connecticut (New York, Massachusetts and Rhode Island).
- Communicating in response to employees' questions in a scalable and comprehensive way.
- Implementing policies for suspected cases.
- Implementing and enforcing policies for admittance to facilities and conduct on premises.
    - Provide sufficient supplies of masks, hand sanitizer, and disinfectant wipes.
    - Before entrance is granted to the workplace, use of hand sanitizer, temperature scan, close daily monitoring and proof of evidence of no symptoms according to CDC guidelines, and formal sign-in.
        - All organizations should **establish control and health management procedures** governing employee entry and exit from the workplace as well as guidelines for opening and closing specific workspaces. These procedures should be consistent with state guidelines and be in place before the workplace is initially reopened...**with a clear understanding about responsibility and**

authority.
  - Wear mask at all times.
  - Social distancing of at least six feet.
    - Initially limit in-person meetings at all levels (preferably continue with web meetings or conference calls).
    - Daily monitoring of virus results, then reevaluate procedures.
    - Deploy directional arrows for one-way entrances, corridors and stairwells, as needed to maintain social distancing.
    - Re-layout of open office space to maintain social distancing.
    - Marked positions for staggered queueing and seating at entrances, lobbies, tables, offices, conference and assembly rooms, lounge areas, labs and cafeterias.
    - Addition of plexi-glass separators as needed to maintain social distancing
  - Frequent handwashing.
  - No handshaking or physical contact.
  - Practice hygienic sneezing, coughing and disposal of used tissues.
- Increased building air ventilation.
- Frequent building cleaning and sanitizing.
  - Areas include kitchens, bathrooms, cafeterias and breakrooms, conference rooms, and most importantly doors and door handles.
  - Frequent personal office and workspace cleaning.
  - Thorough cleaning with disinfecting wipes first thing in the morning (regardless of what the cleaning service does overnight), of keyboards, mice, monitors, desktops and telephones.
- Offer pre-package food offerings in cafeterias (no buffet style self-service).
- Evaluate feasibility of contact tracing.

Recommendations for a Staggered Return to Work Approach

A phased, staggered approach for returning to work and protecting the vulnerable is depicted in Figure 6-1.

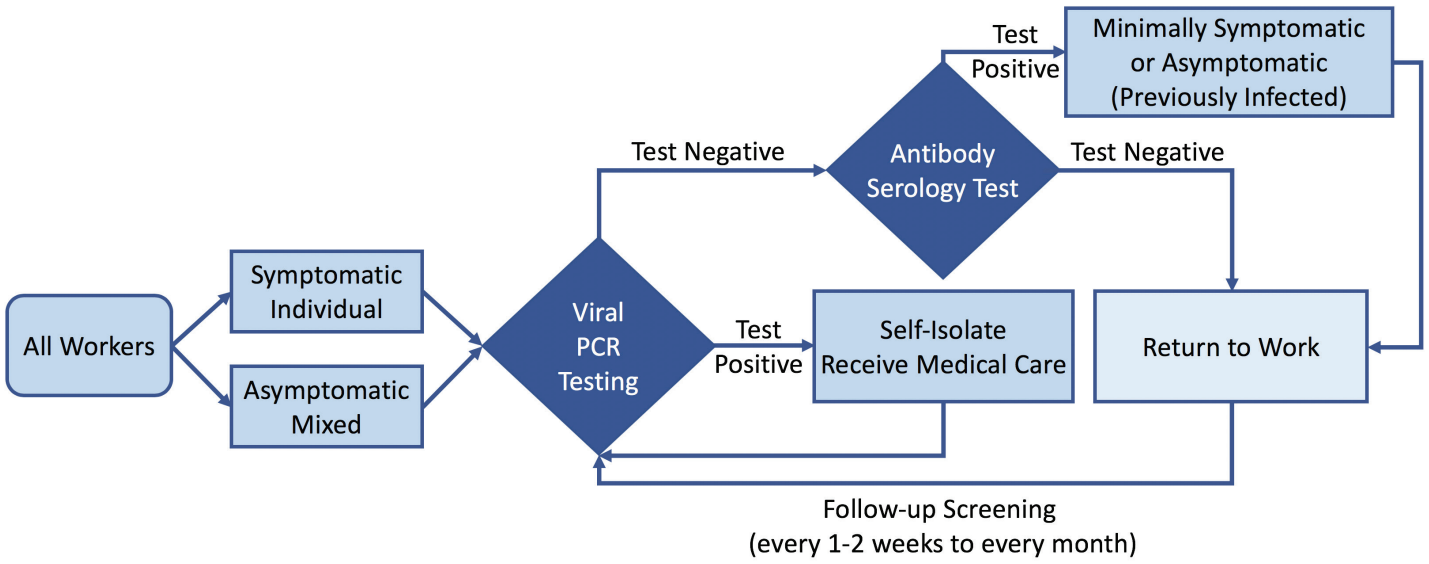


Figure 6-1. A testing strategy based on viral RT-PCR and antibody serology tests on returning workers.

A series of steps is outlined below for executing closed-loop testing at scale to enable returning to work.

1. Perform SARS-CoV-2 viral RT-PCR test on every worker. A worker who is symptomatic gets the viral RT-PCR testing as an individual. Viral swab from a worker who has no symptoms will pool with swabs from other asymptomatic workers in the so-called mixed or group RT-PCR testing. Mixed testing will increase efficiency and capacity. The goal is to identify those who are actively harboring the virus whether they have symptoms or not. If the cross-sectional community studies carried out in Los Angeles and Santa Clara Counties in California and in Telluride, Colorado are correct, the infected rate is 10 times or more than that of the case rate ascertained by the viral RT-PCR test.[19] Since we have only been testing symptomatic patients, the asymptomatic or minimal symptomatic subjects may account for the overwhelming majority, perhaps as high as 90% of the infected population. A key reason for testing is to identify these minimally symptomatic or asymptomatic subjects. Since the viral RT-PCR test only identifies active infection, we will supplement the viral RT-PCR test with an antibody serology test. The proposal is to do the SARS-CoV-2 viral antigen test on everyone first, and test for serology on those who tested negative on the viral RT-PCR test second. The sum of people without symptoms who test positive for SARS-CoV-2 by RT-PCR or antibody = minimally symptomatic or asymptomatic population. People with symptoms who test positive for SARs-CoV-2 RT-PCR = symptomatic subjects. People who test negative by both RT-PCR and antibody = unaffected population.

2. Minimally symptomatic or asymptomatic individuals can return to work in a phased manner as proposed above. They may not need to be retested because they have the antibody against the virus and may be immunized. However, it is not known at this time whether they are truly immunized or how long such an immunity can last if they are immunized against reinfection.

3. Symptomatic people can be retested upon new occurrence of symptoms. This need for repeat testing will be rare because we think that reinfection is very rare. That being said, there have been reports of reinfection in Asia and the United States. The root cause is not clear: are these true reinfections, or reappearance of viral antigen, or was the preceding viral antigen test a false negative?

Vulnerable Populations

4. Vulnerable populations can be considered those who are at high risk for adverse outcomes of COVID-19 infection (named "medically vulnerable") and those who are vulnerable because of job loss or risk thereof ("economically vulnerable"). Based on what we know now from CDC reports, those at high-risk for severe illness from COVID-19 are people 65-years-old and older, and people who live in a nursing home or long-term care facility. Medically vulnerable are also people of all ages with underlying medical conditions, particularly if not well-controlled, such as chronic lung disease, moderate to severe asthma, serious heart conditions, immunocompromised, obesity, diabetes, chronic kidney disease undergoing dialysis, and liver disease based on CDC reports.[20]

   In addition, mental stress, anxiety and depression constitute another group of vulnerability (stressed group). There is clearly overlap among the three groups. The medically vulnerable group should continue to telecommute, if still in the workforce, until an effective vaccine is available or until the work environment has been tested and shown to be relatively safe. The economically vulnerable people will return when the jobs return at all levels. The stressed group will need counseling and societal help.

   There is a fourth group which are racially minority populations ("vulnerable minority"). The health disparity and COVID-19 disease and adverse burden are high. African Americans and Latinos are overrepresented nationally in terms cases and deaths in addition to being overrepresented in many areas hardest hit by the

COVID-19 pandemic such as New York City where age-adjusted death rates for African Americans are more than double those for Caucasians and Asians.[21] Furthermore, Johns Hopkins University and American Community Survey report in the United States that the COVID-19 infection rate is more than three times higher and the death rate is six times higher in predominately black counties than in predominately white counties.[22] More or at least equally available testing, tracing and isolation as well as new medical treatment needs to be offered. This fourth group is likely at triple jeopardy -- medically, economically and psychologically. Attention must be paid to this fourth group.

In the initial "pilot" phase we suggest allowing only approximately 1/4 of the associates to return to the workplace at a time, then allow 14 days to pass, while monitoring daily for new COVID-19 cases. Note that a recent Rhode Island study suggested a 14-day downward trend in the number of cases or a 14-day trend in stable or declining hospitalizations.[23] If an acceptable level is reached (ideally 0 new cases), then allow the next 1/4 of associates to return to work, and so forth. In the best scenario, all associates would be back to work within eight weeks. We think this approach would result in an informed way to monitor the organization's health while minimizing the health risk of a potential spike in infections following re-entry. In none of these early phases should a gathering of more than five individuals be permitted per CDC guidelines. This guideline can be increased as evidence evolves to permit larger group gatherings.

Contact Tracing

Employers will have to evaluate the feasibility of implementing contact tracing for their employees. Contact tracing may reduce risk in the workplace and may improve the quality of life for elderly or vulnerable citizens.

Advanced information technology could be deployed for contact tracing. Apple and Google announced plans to partner to develop a contact tracing app to validate if an individual has tested positive or negative and when.[24] Such a tool may potentially offer a "good health validation" that might be adopted by employers or might be used by individuals to ascertain the risk of entering an area. University of Washington and Microsoft have teamed to develop the CovidSafe app that promises to alert people automatically if they've been in close proximity to a COVID-19 infected person.[25] Once potentially exposed, it is recommended an individual self-quarantine for 14 days.

A formal contact tracing process should be considered for Connecticut utilizing students and trained unemployed people to physically trace potential contact paths associated with new cases. Competing issues of personal privacy and public health may arise with contact tracing. It remains to be seen whether data collected by contact tracing apps could be shared with the state of Connecticut and its corps of contact tracers.

Summary

This section provides a set of factors to consider and recommendations for returning to work and protecting the vulnerable in the state of Connecticut. These recommendations span dramatic increases in testing that comprise viral RT-PCR and antibody serology; staggered reopening and reassessment based upon monitoring of local COVID-19 infection rates and trends; implementation of patient tracking and contact tracing; ensuring availability of sufficient supplies of masks, hand sanitizers, and disinfectant wipes; enforcement of preventative measures such as wearing masks and social distancing; and enhanced cleaning and sanitizing of buildings.

SECTION 7

Need for Outpatient Medical Treatment

It would be desirable if not a major key for reopening society, to have an efficacious drug, antibody or decoy receptor for the virus that is implemented early in the disease course, or a vaccine prior to virus exposure. **An effective outpatient treatment would have an enormous public-health impact even apart from vaccine availability**. Hospital treatment is a limited resource that is many orders of magnitude more expensive and treats the disease at a point when its mortality is at least 10-fold greater than with outpatient treatment. Many general approaches to treatment that target the viral infection are being pursued in academic, industrial and government laboratories as well as in the clinical setting. These include the screening of approved drugs in an effort to repurpose them. While formal randomized controlled trials are ongoing or still in planning stages, physicians are dependent on the available body of medical scientific evidence available from various inpatient and outpatient studies around the globe. Without a more detailed look at these studies as a whole, it is easy to jump to the wrong conclusions regarding either efficacy or risks. Often no distinction is made with regard to inpatient versus outpatient use in evaluating the potential efficacy of a particular drug or combination of drugs. Additionally, risks cannot be dismissed but need to be understood in the context of an individual patient's particular medical condition. In this section, we discuss what is currently known from the most relevant studies for consideration in the ongoing evaluation of these various treatments. Most importantly, we advocate for the need for development of outpatient medical treatment and effective means for sharing best practices among physicians providing care for COVID-19 patients. Treatment at an early stage of symptom onset may be especially helpful given that viral load appears to be highest before or near appearance of symptoms.

Discussion of Relevant Studies [1]

In the inpatient context, the anti-viral remdesivir has been shown in one study to be an effective anti-viral drug by shortening the recovery time in hospitalized COVID-19 patients from 15 days to 11 days.[2] This was accomplished by a multi-site placebo controlled randomized trial involving over 1,000 COVID-19 patients. Thus, it is the first drug to receive emergency use authorization (EUA) by the FDA that was proven by a convincing established scientific process. While these anti-viral therapy results are encouraging, it is administered via intravenous infusion which is more easily carried out in an inpatient setting. However, a short course of its intravenous infusion in the outpatient setting is not out of the question. Outpatient infusion such as via a subcutaneous route is often done for other illnesses such as cancer or dermatological conditions. At this writing, Gilead, the developer of remdesivir, has indicated that the company is actively developing subcutaneous and other formulations suitable for outpatient treatment. However, the FDA has not approved remdesivir for outpatient use, and empirical data on such use are not yet available.

The other drug option is hydroxychloroquine (HCQ) with azithromycin (AZ) (HCQ/AZ) or HCQ/doxycycline. Evidence for efficacy or risk of adverse events of HCQ used alone or in inpatient settings is unclear and is insufficient to justify such treatment approaches in comparison to outpatient use of HCQ/AZ or HCQ/doxycycline. The medical scientific evidence for HCQ/AZ used in outpatient settings is good, but not yet "proven" at the level of randomized controlled trial (RCT). One controlled but not randomized study found significant, 50-fold decreased viral shedding in outpatient nasopharyngeal swabs, seven-fold better than HCQ used alone, key evidence of the anti-viral effect of the combined medications.[3] Another controlled but not ran-

domized trial found significantly less hospitalization outcomes with the combined medication treatment.[4] Two large series of cases involving approximately 1500 treated high-risk outpatients resulted in a total of seven deaths.[5] HCQ and AZ are known to promote QTc prolongation, and carefully monitored inpatient studies[6] have documented some 11-12% of hospitalized COVID-19 patients treated with the combination have so-called critical prolongation of QT Corrected (QTc), a disturbance of the heart electrical cycle that can cause rare occurrences of death. No fatal arrhythmias occurred in those studies, nor did the case series studies or the non-randomized trials involving in total more than 2000 treated patients terminate treatment for any of treated patients because of QTc lengthening. Very large database studies[7] (Lane et al., 2020) also do not show any excess cardiac arrhythmia mortality or all-cause mortality with HCQ or HCQ/AZ use, with the caveat that these database analyses average the use of HCQ and HCQ/AZ across individuals of varying risks of QTc prolongation.

That being said, complete proof of a beneficial role of HCQ/AZ in COVID-19 patients in the ambulatory setting awaits results of placebo controlled RCTs, of which five are ongoing to answer this question. We expect trial outcomes to be available starting September of this year. FDA and NIH have both issued warnings on the use of HCQ/AZ, though not of HCQ/doxycycline, and limited HCQ/AZ recommended use to hospitalized or registered clinical trial settings, though there are opposing viewpoints by distinguished physician groups elsewhere.

Comments Regarding Physician Practice

In the real world of physician practice, physicians are free to prescribe both or one of the HCQ/AZ medications in off-label use, and many physicians in Europe are already doing so. Given the uncertainty of cardiac risks, physicians should measure QTc and guard against concomitant medical conditions such as kidney disease, low potassium and magnesium, and use of other medications such as for heart failure or fluid retention (diuretics or water pills), depression or other psychiatric conditions, and fungal infections. Such coexisting medical conditions or medication use, if not correctable, are considered contraindications to HCQ/AZ use and alternative treatments should be sought.

In any event, risk of more serious disease progression indicates that individuals with suspected COVID-19 infection should seek immediate physician care. At the present time of low influenza prevalence, two or more of the recognized signs and symptoms of COVID-19 infection may be sufficient to seek care: fever or chills, cough, headache, loss of taste or smell, nausea or diarrhea, myalgia, shortness of breath doing mild activities of walking or moving around. The last-mentioned may be sufficient by itself. Individuals should not lose time trying to confirm their condition or feel that they can just withstand the discomfort. They should seek immediate medical care.

SECTION 8

Urgency of Reopening the Full Healthcare System

The COVID-19 pandemic has severely tested United States healthcare systems.[1,2,3] Connecticut has experienced the third-largest epidemic in the U.S. based on deaths per capita (after New York and New Jersey) as of mid-May. As in the rest of our nation and globe, our health system has pivoted to meet the challenges of caring for these patients in inpatient, outpatient and community settings, the latter through telemedicine. COVID-19 patients often require urgent and sometimes prolonged hospitalization with attendant rapid preparation for surge capacities and coping with unprecedented ICU and ventilator demands. In this context, "full-service" medical services such as elective – but often vital – outpatient and inpatient health visits and procedures were largely suspended.[4] Hence, many patients have voluntarily deferred or been asked to delay seeking medical attention for their heart, cancer, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular illnesses, and other chronic illnesses. Even required care has been delayed due to concerns of the novel coronavirus (SARS-CoV-2) infection risks in healthcare settings.

Impact of Declining Clinical Services

The volume of clinical services in Connecticut and in the U.S. has declined substantially during the expansion of COVID-19. For example, in March 2020 versus March 2019, Connecticut witnessed marked decreases in both inpatient and outpatient services. Examples include, but are not limited to, decreases of hospital discharges of newborns and neonates (-12.0%), adult service lines such as adult medicine, surgery, cardiology/vascular, neurosciences, orthopedics, oncology and OB-GYN (-12.1%). Connecticut also saw decreases in outpatient services such as emergency department (-25.0%), urgent care (-32.6%), outpatient observation (-29.9%), surgical extended recovery (-47.3%), ambulatory surgery (-30.6%), outpatient gastroenterology (-41.3%), outpatient cardiac catheterization (-27.9%), outpatient coronary angioplasty (-16.6%), outpatient electrophysiology (-35.9%), outpatient pacemakers and ICD (-14.9%), outpatient vascular procedure (-13.2%), outpatient MRI scans (-22.4%), outpatient chemotherapy (increase of 4.9%), and outpatient psychiatry (-25.7%).

In the U.S., investigators at Harvard University and Phreesia, a healthcare technology company, compiled and analyzed data on decreases due to COVID-19 in visit volume from mid-March through mid-April of 2020 for the more than 50,000 providers who are Phreesia clients. Data sources, analyses and study limitations are provided in their Data and Analyses section.[5]

In the U.S., dramatic decreases have been seen in the number of visits in all regions of the country. New England and the mid-Atlantic states saw the largest reductions of clinical volume, as might be expected given the New York City epicenter. As the number of in-person visits dropped, telehealth visits increased but only partially offset the decrease in in-person visits. An estimated 30% of visits at the ambulatory practices are now provided via telemedicine. The decline in clinical outpatient visits was larger among surgical and procedural specialties than other specialties such as adult primary care, obstetrics/gynecology, oncology and behavioral health. From patients' perspective, the decline was largest among school-age children and older adults.
Finally, for training grounds of future generation of physician workforce, according to the Association of

American Medical Colleges (AAMC), academic faculty practices have witnessed a 30-60% decrease in their clinical volumes. This trend, if not corrected, will adversely impact the quality of future physician training and their clinical abilities.

SARS-CoV-2 infection itself is associated with lethality that is likely 5-10 times higher than seasonal influenza, but the virus can also contribute to increased morbidity and mortality of an elective surgery if contracted by such patients.[6] It is in this unfamiliar context, with a virus that persists for days on plastics or steel, that conservative measures have been adopted for elective visits and procedures. Environmental interventions in the health workplace such as personal protective equipment seem to have resulted in lower prevalence rates in health care workers in such diverse settings as the New York City and its metropolitan area[7] and Palo Alto, California[8] than in the general population, a truly remarkable achievement even as we acknowledge the hundreds of healthcare workers who have died in their line of duty.

As a result of avoided or deferred care,[9] the lethality associated with delayed medical care of serious or even non-serious chronic illnesses, including preventive screening, could be greater even than the harm caused by the virus itself. Returning the health system to near-full-functioning could mitigate the magnitude of unintended harms of deferred care for preexisting conditions. In addition, many healthcare workers, such as doctors, nurses and medical staff, have been laid off or furloughed, triggering early retirement, career shifts or departures, weakening the workforce and resulting in a loss of critical skillsets. If full-service care is not returned, patients, healthcare workers and systems will suffer increasingly, making our health system less prepared for not just routine and demanding clinical service, but also the next wave of infections. At the same time, unsafely opening our medical services could put healthcare workers, allied health staff, patients and families at risk.

Recommended Approach for Reopening

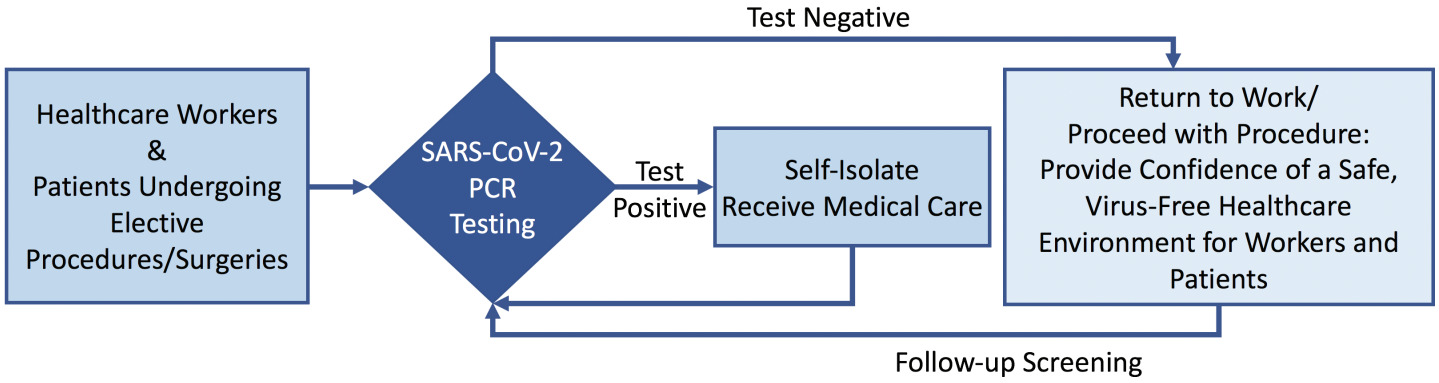


Figure 8-1. Suggested flow diagram for return-to-normalcy in healthcare settings in the COVID-19 era.

To restore the healthcare systems while continuing to mitigate the risk of new COVID-19 infections, we recommend the testing strategy illustrated in Figure 8-1 and described as follows:

- All healthcare workers who are clinical employees will be tested by an FDA-approved viral test. If test shortages prevail, the priority sequence will be for persons involved in more urgent elective procedures and surgeries and chronic illness management, and then those involved in preventive care. This includes doctors, dentists, nurses, technicians, technologists, emergency medical technicians, medical and dental assistants, operating room staff, receptionists, volunteers, housekeepers (especially those first responders in rooms vacated by infected patients), orderlies and others.

Goals here include:
  - Rule out viral infection including workers who might be asymptomatic carriers. This will protect patients and colleagues and provide confidence among the workers themselves that they are not infected; however, precautions will still be universal to avoid infecting others.
  - Alongside environmental hygiene and patient management measures described below, provide confidence to patients of a virus-free healthcare environment, per best practices.[4,10,11]
  - In the absence of symptoms, follow-on viral testing will continue but at a frequency determined by the virus incubation period and to determine asymptomatic carrier status.
- Virus-positive workers will be required to self-isolate, receive care, and return to work per CDC guidance without risking job loss, with staggered return by risk status such as age and underlying co-morbidities.
- Patients undergoing elective procedures/surgery will be tested including those with ≤3 days post any plausible exposure to anyone who might harbor SARS-CoV-2. Goals here include:
  - Rule out infection, noting that 25-50% of infectious persons may be asymptomatic.
  - Provide confidence of no increased risk for exacerbating non-COVID-19 illnesses.
  - Allow healthcare providers the confidence to proceed with evaluation and management, medical or surgical, of non-COVID-19 patients.
  - In the absence of symptoms, perform follow-up viral reverse transcription-polymerase chain reaction (RT-PCR) or antibody testing based on clinical and epidemiological considerations.
  - Care of COVID-19 recovered patients will continue, and such patients will be assessed very carefully prior to elective surgery or procedure (e.g., lung capacity).
  - Patients for ambulatory visits also need to have viral testing if they have any symptom consistent with COVID-19 infection or if they are at high risk for adverse outcome, such as those older than 65 and/or with coexisting medical conditions. Ideally, testing will be widely available, alongside contact tracing.
- Both healthcare workers and patients will continue to practice and ensure hygienic precautions, such as distancing, checking of temperature and symptoms, and wearing masks (surgical or cloth face covering, respectively).[12]
- Preparation and care for infected patients will continue in segregated sections of hospitals such as Non-COVID Care zones.
- Facilities will need more thorough and aggressive sanitization of operating rooms and rooms vacated by infected patients, perhaps aided by in situ simulation. Goals include:
  - Proper air ventilation including negative pressure application and biocontainment for rooms that might harbor virally infected persons.
  - Personal protective equipment (PPE) must be obtained for healthcare personnel performing elective procedures and operations. Sufficient quantity and quality of PPE is required for a full-service system.
- Staggered return to normalcy and reopening of full-service activities will be based on background epidemiological characteristics of viral transmission in the local community such as uncontained spread.

To mitigate harm of needed healthcare delayed or avoided, we must gradually and safely restore our full-service healthcare systems. The speed of such a restoration will depend upon the background epidemiology of local transmission. Failing to restore healthcare presents potential harms that may equal or exceed those of the viral infection itself. Coordination with local and state public health departments is critical, as is engagement of community healthcare providers and community organizations, ensuring transparent and consultative decision-making. We believe rigorous infection control and hygienic processes[10,11] radically expanded viral antigen testing, strategic patient flow strategies, and full PPE availability will make full-service healthcare possible throughout Connecticut.

SECTION 9

Key Concepts and Recommendations

On May 20, 2020, Connecticut initiated the first phase of reopening with limited relaxation of earlier mitigations. The seven-day moving average of new cases has declined to about half of the earlier peak but is declining slowly. COVID-19 is likely now endemic, meaning that it is part of our disease ecology, destined to surge and wane as does influenza. SARS-CoV-2 has spread globally. Even those countries that have effectively contained it at the start will be at risk of reinfection as businesses and borders are reopened.

Fortunately, there is also a global effort to develop treatments and vaccines to address this disease. More than 1,000 clinical trials have been registered in the U.S. National Institutes of Health (NIH) registry site, most for repurposed, existing drugs and biologics, and more than 100 vaccines are currently in development. The extent to which efforts to mitigate have blunted pandemic and local spread remains uncertain and whether alternative approaches would have been better adopted unknown; hindsight itself is biased and the disease continues to be very dynamic. The shutdowns have helped, but the toll has been massive. The economic toll of the extensive stay-at-home orders has been devastating with nearly 40 million people filing first-time unemployment claims in the past nine weeks in the U.S. The health impacts of these shutdowns are only now becoming more evident.

We must pivot to a different approach to managing this disease, one that is more adaptive and targeted. Rather than prolonged and repeated universal shutdowns of "non-essential" businesses and activities, we can effectively deploy the tools of physical distancing, PPE, hand/face/surfaces hygiene, outdoor alternatives, antigen testing, contact tracing and teleworking and extended workhours to reopen in an adaptive fashion. We can do this in a way that continues to safeguard public health. We need to take full advantage of monitoring and modeling local conditions to fine-tune mitigations and continue protecting the vulnerable. This is a feedback control approach instead of an on/off switch. As we move forward together through these unchartered waters, these seven imperatives must guide a new strategy built on **COURAGE**:

Caution is warranted. We do not know how this disease will evolve and what future waves will look like. The possibility of exponential growth requires readiness for early action. As the current wave recedes, vigilance will be key to contain potential future outbreaks before they can spread broadly once again. Social cooperation in reasonable efforts to reduce viral spread (e.g., mask use, handwashing and physical distancing) is needed.

Open the full healthcare system. Our health systems have been nearly singularly focused on meeting the challenges of caring for COVID-19 patients. As a result, many people have deferred elective and even required care due to concerns for infection risks. They have waited to seek medical attention for their heart, cancer, chronic obstructive pulmonary disease, chronic kidney disease, cerebrovascular illnesses, and other chronic diseases. This presents a significant health risk of a different type and must be addressed. We recommend a systematic SARS-CoV-2 antigen testing strategy for healthcare workers and for patients undergoing elective procedures. This screening combined with diligent PPE use and thorough sanitization of facilities will enable the safe restoration of our full-service healthcare systems.

Understanding comes from effective monitoring of the current situation. Antigen testing must be adequate, accessible, and accurate. The current levels of testing are not enough, but the levels needed

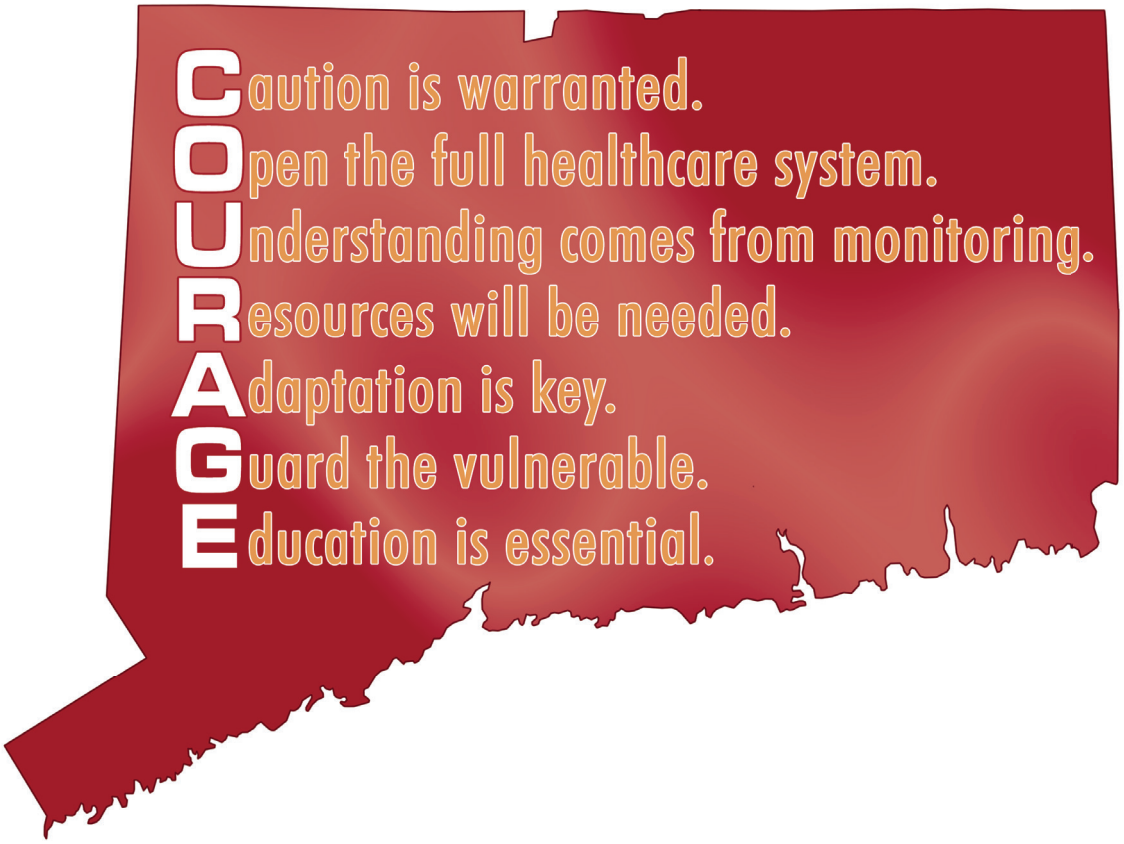
are not massive. Connecticut is on a good path to reaching the weekly antigen testing volume required for effective response. Volume of testing will vary depending on the extent of the disease spread, and guidance regarding scaling that volume is provided in this report. Diagnostic testing to see if someone currently has the disease is actionable and should be widely available; antibody testing can provide useful insight regarding disease prevalence over time, but it is not actionable because we do not yet know that it correlates with immunity. Tracking the spread of the disease depends on both creative surveillance strategies and the capability to trace contacts of those who are infected. Automated privacy-preserving approaches for contact tracing when adopted broadly can augment but not replace traditional manual efforts.

Resources will be needed. They will be needed to scale up the state's testing and contact tracing capabilities. Public and private entities alike will need to keep investing in research for treatments, therapeutics and vaccines. Increased capacity of and coordination among our public health organizations and hospitals are critical to confront future risks of outbreaks.

Adaptation is key. We need to continue to learn and apply that learning. We will need to keep adjusting our response in a thoughtful and timely way. Here the key is to balance the benefits, costs, and risks appropriately. By using more targeted approaches to mitigations, one can achieve similar positive outcomes while minimizing the unintended negative consequences. Adaptation requires being able to anticipate trends correctly; however, past projections have varied so widely as to limit their utility for guiding mitigations and even future testing strategies. Along with the understanding gained from increased testing, useful Connecticut-tailored epidemiological models need to be developed and regularly updated with the latest information and data. Such models would also be invaluable in assessing the effectiveness of mitigation policies and guidelines.

Guard the vulnerable. It is unconscionable that so many have died in nursing homes, often alone. We must do better. A careful policy review is needed as to how many nursing patients could have been moved back home, to hotels, or to small pods of persons with highly limited mixing with others. There is much that can be learned and adopted from successful healthcare practices. The diligent use of PPE has enabled hospitals to significantly reduce spread among their staff and patients as compared to the population at large. Homeless shelters were spared the worst of the crisis when they decompressed their populations into empty hotels with individual rooms and bathrooms. We can keep our vulnerable safe while still affording them much needed contact with those that love them. We must take the time to understand true root causes and develop lasting solutions to protect the health of the most vulnerable groups in our state.

Education is essential. We need to equip the people of Connecticut with a practical understanding of risk and mitigation that enables them to adjust appropriately their everyday routines rather than being fearful of daily activities. For example, the concept of contact intensity, which includes duration of contact, number of contacts and physical separation distance, is much more useful than the current simplistic and rigid six-foot social distancing guidance. A clear differentiation of risks in different types of indoor and outdoor settings provides important insights on how best to conduct business and social activities without unduly compromising public health. Here too, models for disease transmission and analysis of various risks, particularly in indoor settings, can usefully guide policy makers. As decisions are made, communication of policies must be clear, consistent, and transparent without politicization. Without buy-in, even mandatory measures will fail. With buy-in, even simple guidance can be effective.


Caution is warranted.
Open the full healthcare system.
Understanding comes from monitoring.
Resources will be needed.
Adaptation is key.
Guard the vulnerable.
Education is essential.

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Executive Summary

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Section 9: Key Concepts and Recommendations

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