A National Decision Point: Effective Testing and Screening for Covid-19

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Executive Summary

The Covid-19 pandemic is still spreading throughout the United States. Over 30,000 Americans continue to test positive daily, and hundreds are dying every day.

Economic activity has plunged and a record number of Americans are out of work. Millions of jobs may have disappeared forever. Most of the nation's school children have not returned to classrooms full time this fall, straining families as well as employers.

Many universities have returned to online-only classes after outbreaks caused sudden closures. Nursing homes and other long-term care facilities have been decimated by disease with their residents locked in isolation. A vaccine could bring relief, but its wide availability and impact is months away if not longer. In the meantime, few institutions have broadly-accepted plans for reopening safely.

This must change. The best tools for shifting back to some form of normalcy are effective masking and distancing measures to mitigate spread, coupled with sufficient Covid-19 tests paired with sophisticated strategies for their effective use. This report describes how to offer the latter in ways that can be tailored to local circumstances and risk tolerances. The goal is to give schools, businesses, and other critical institutions a pathway toward operating safely even for higher-risk populations and with continuing community spread.

There are four basic elements to a testing strategy that can contain outbreaks, inform public health decision-making, and respond to local Covid-19 prevalence rates:

- Assessments of the risks of infection and death depending on local spread and population characteristics.
- Meaningful and measurable goals for acceptable infection reduction through screening and surveillance.
- Calculation of budgetary and administrative constraints.
- Adequate supplies of sufficiently reliable tests.

Challenges in achieving this last element have long been a critical concern. Supply constraints have largely limited Covid-19 testing to symptomatic and essential workers. But that is changing with the development of growing supplies of rapid and low-cost tests for regular screening. Screening holds the potential to protect nursing homes, reopen schools, and detect and contain outbreaks in at-risk work and community settings.

The United States needs far more tests because the United States has far more Covid-19 infections. At present infection rates, a basic screening strategy will require approximately 200 million tests each month for students and staff at the nation's primary and secondary schools and residents and staff at nursing homes for them to open safely and in stages. But fewer than 25 million Covid-19 tests are now reported monthly in the United States. Even if infection rates decline, the testing needed in just schools and nursing homes exceeds the nation's entire capacity now.

But the nation's capacity to conduct screening tests is rising, and is projected to grow much further. By October 2020, based on recent and announced expected market entry, point-of-care tests will rise to at least 70 million tests per month. By January, that number could rise to almost 200 million tests per month. More growth is possible - if additional tests enter the market, if additional research laboratory capacity is recruited and supported, and if manufacturers make further investments to increase supply. To get this done, the federal government must provide more guidance, assistance and advance funding to manufacturers and payers, and should take further steps to coordinate these efforts with state and local governments. Without further steps to implement

and achieve a national testing strategy, state and local governments supported by the private sector and initiatives like that of The Rockefeller Foundation must step in.

These initiatives require a basic assessment of market needs, and that starts with three steps:

1. The federal government should issue guidelines that state, and local officials can use to refine their local protocols for regular diagnostic, screening, and surveillance testing for active infections.

2. Federal, state, and local governments should expand pilot testing initiatives to build the real world evidence base on test accuracy and on effective testing strategies for the range of risk settings and populations.

3. The federal government should develop a short- and long-term plan to procure and distribute tests to states, localities, and businesses and share and coordinate these plans with relevant stakeholders to ensure that receiving entities can plan to meet their testing needs and to allow manufacturers to better understand the demand for testing in the coming months.

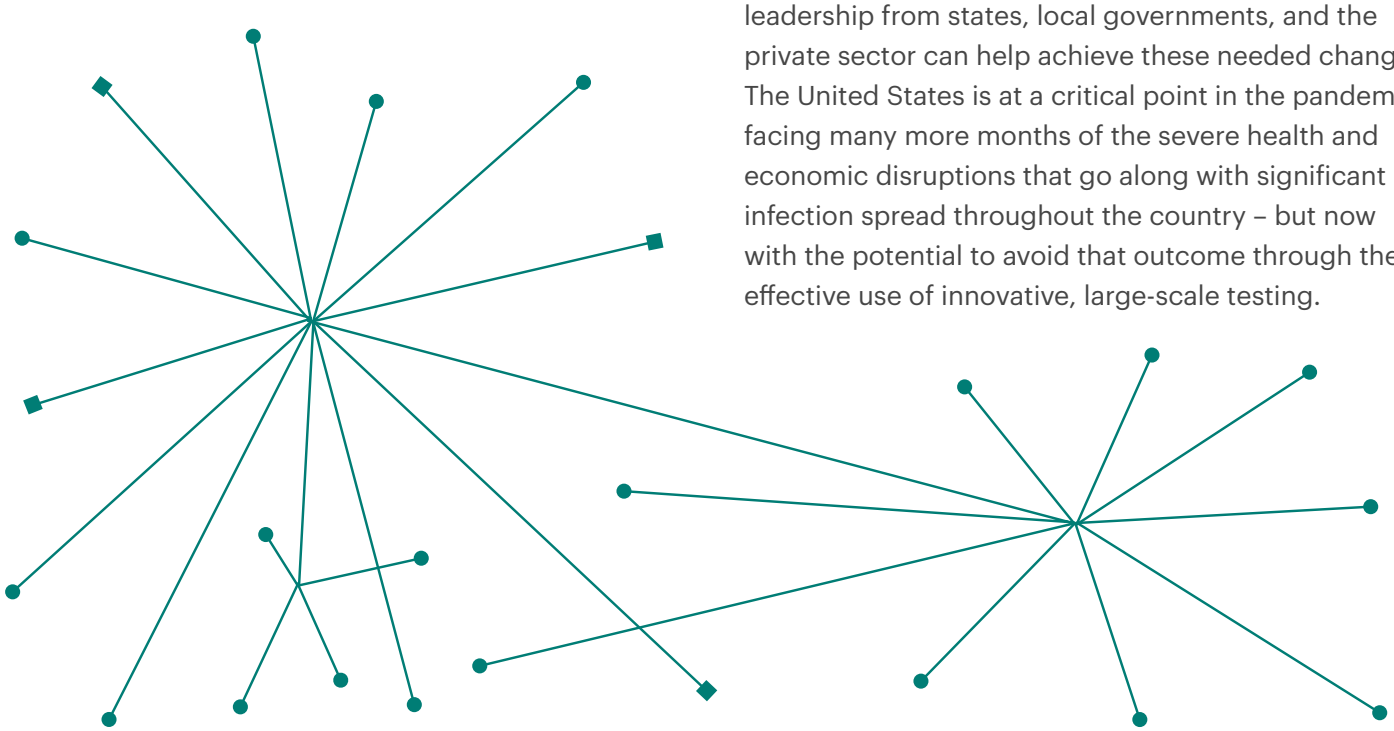
Beyond the market assessment, new supports must be provided to increase both the number and types of tests available in order to offer appropriate routine screening of asymptomatic individuals. Among the steps:

1. The Food and Drug Administration, the Centers for Medicare and Medicaid Services, and the Centers for Disease Control and Prevention should issue clearer written guidance about regulatory flexibility, pathways, templates, and other tools to support screening and surveillance.

2. The federal and state governments should support advance purchase contracts to assure needed testing capacity is available for priority populations for the remainder of the pandemic, including testing relevant to a vaccine. Our estimates suggest that several billion dollars per month in additional spending commitments for testing for the coming months could close the testing gap.

3. Use information provided by manufacturers and key suppliers to increase manufacturing capacity of key supplies and reagents, especially for laboratory tests.

In the absence of further Federal action, continued leadership from states, local governments, and the private sector can help achieve these needed changes. The United States is at a critical point in the pandemic, facing many more months of the severe health and economic disruptions that go along with significant infection spread throughout the country – but now with the potential to avoid that outcome through the effective use of innovative, large-scale testing.



Introduction

Diagnostic testing for Covid-19 infection is critical to identifying people who are ill, directing them to appropriate treatment, and initiating contact tracing. But more broadly, screening tests are key to suppressing the community transmission of the virus.

When the SARS-CoV-2 virus infects people, there is typically a lag before they experience symptoms of infection, and many people will not exhibit symptoms at all. In fact, 30%-60% of infected people are potential "silent spreaders", people who are contagious without realizing they have the virus.[1] Routine testing of non-symptomatic individuals – "screening" tests – identifies those who are infected, and enables them to be isolated from others, and then allows for the tracing of their contacts to determine who else may have become infected. Collectively, these actions constitute well-established public health strategies to break the chain of infection and contain outbreaks.

As of the publication of this brief, approximately 5 million Covid-19 tests are being reported weekly.[2] However, not all states report rapid test results.

A growing number of screening tests are now being performed on at-risk asymptomatic populations, and those who work with them. This includes those who live or work in settings that allow for rapid spread, such as staff and residents of nursing homes, hospital workers, patients scheduled for elective procedures, and students and faculty at certain universities and schools. The increase in screening tests reflects growing evidence that regular screening, using appropriate tests, may reduce outbreaks in at-risk populations. Ongoing, regular testing has allowed some universities to reopen succesfully.[3] Recent reports have recommended substantial increases in testing to continue to battle the virus and its spread, including a recent Rockefeller Foundation recommendation that the nation undertake at least 30 million tests per week.[4] Others have argued for even larger-scale testing.[5] These recommendations are well above current testing rates.

So far, however, the nation is not on a clear path to achieving such widespread testing. Although new tests are entering the market and the federal government has both been supporting new test development and purchasing much of the available supply, there have not been enough tests to routinely screen all at-risk populations. The strain on the available supply of tests between those who are ill and need diagnostic tests for clinical decision-making, and those who aren't symptomatic but may require screening tests for the protection of others, has led to delays in test results for those who are infected and already ill. While the Centers for Disease Control and Prevention (CDC) has produced recommendations on diagnostic testing for those with symptoms of Covid-19, its guidance for testing of asymptomatic individuals is not clear: it notes that testing should occur in some higher-risk settings, especially in areas where there is significant spread of Covid-19, but simply states that state and local public health authorities or medical experts should guide such testing. As a result of the uncertainty about test availability and lack of clear guidance on testing protocols, many organizations that could benefit from increased testing are not implementing it. Without clarity on future needs and support for testing, test manufacturing capacity and availability is not ramping up adequately to meet such needs.

The Rockefeller Foundation and others have previously called for a smart testing strategy that would increase routine screening in areas of the country with high, ongoing community spread of the virus.[4] This strategy would include protocols that provide clearer guidance

on screening tests in areas of greatest risk, and a clearer signal and support for test manufacturers to provide the tests. To assist local, state, and federal policy makers in devising these "smart testing" strategies and protocols, this report describes the different purposes for Covid-19 testing, the different types of tests available, and why some tests may be better suited to certain purposes than others. It also describes how testing strategies can be tailored to local areas, and how those who devise these strategies can balance such factors as rates of viral spread and availability of funding to carry out testing.

This report provides examples of how testing needs can be estimated for various settings, such as schools. It also discusses how these needs may evolve as the pandemic continues. Finally, this report also provides recommendations on a number of measures to increase the supply of tests, such as advanced purchase commitments to encourage manufacturers to invest in expansions and clarifying guidance on the use of academic and research laboratories to conduct certain types of testing. Without these changes, it is unlikely that the nation will make the necessary headway to suppress the virus until effective vaccines become available and widely used.

Table 1 – Testing purposes and characteristics

Testing Type	Purpose	Priority Characteristics	Required Sensitivity and Specificity
Diagnostic Testing[6,7]	Diagnosing symptomatic individuals and close contacts of those infected for clinical decision-making.	Highly accurate results with a short enough time to results for appropriate clinical treatment (if required) and effective isolation and contact tracing.	>95% Sensitive >99% Specific
Screening Testing[8]	Routine testing of individuals without symptoms or any reason to suspect exposure. The objective is to reduce infection spread by isolating potentially infected individuals faster to protect public health. Screening tests can also be used less frequently or on random subsets of a population to determine prevalence.	For regular routine screening, frequency of retesting and time to results is more important than highly accurate tests; confirmatory tests may be needed for individual clinical decision-making.	>70% Sensitive >90% Specific (higher specificity is required if used in low prevalence settings)
Surveillance Testing	Understanding prevalence in a community to inform workplace, local, or regional policies; individual results are not returned.	Frequency and time to results should be appropriate to allow timely decision-making and course adjustment.	Because these tests are not used for individual decision-making, less accurate tests can be used if highly validated to allow for appropriate statistical adjustments.

A Brief Overview of Covid-19 Testing

As noted above, there are multiple reasons and numerous testing technologies to carry out testing for active Covid-19 infection (see Table 1). Every testing strategy must start with diagnostic testing of individuals who are showing symptoms or have been in close contact of someone with Covid-19. However, a critical component of smart testing strategies will include routine screening tests for at-risk populations that don't have specific reason to think they are infected to reduce the silent spread of the disease by asymptomatic and pre-symptomatic individuals. In addition, less frequent screening or surveillance testing may be used by communities and individual settings to understand the prevalence (the number of active infections) within their populations to know if their current mitigation measures are suppressing viral spread or if escalation is needed.

There are multiple testing technologies, which each have different typical performance and time to receive a result (see Table 2) and therefore may be more or less appropriate for the different testing purposes listed in

Table 2 – Testing technologies

Test Type	Where Test Happens	Sample Taken By	Time from Sample to Result	EUA Sensitivity or PPA*	EUA Specificity or NPA*	Price (Sept 2020) $$$, $$, $	EUAs Reported Sept 7, 2020
PCR	Central Lab	HCP or Self	1-3+ days	100%	100%	$$$	175+
NGS	Central Lab	HCP or Self	2-3+ days	97-100%	98-100%	$$	3
CRISPR	Central Lab	HCP or Self	1-2+ days	95-100%	100%	$$	2
LAMP	Central Lab	HCP or Self	1-2+ days	100%	98-100%	$$$	9
LAMP	POC	HCP or Self	30-60 minutes	100%	90-100%	$$	2
Antigen	POC	HCP or Self	15-30 minutes	84-97%	90-98%	$/$$	4
Other Non-Antigen Rapid Systems	POC	HCP or Self	15-60 minutes	80-100%	90-100%	$$/$$$	1
Antigen in Development	At Home/ DIY	Self	15-30 minutes	70-97%**	90-98%**	$/$$	N/A

Legend: EUA – Emergency Use Authorization PPA – positive percent agreement NPA – negative percent agreement POC – point of care HCP – healthcare professional

*For an EUA, a manufacturer may sometimes report positive and negative percent agreement between its test results and the results of a previously validated PCR test. Since the samples used in the study may differ from those collected in other settings, test sensitivity and specificity may be different in actual use.

**Estimate for tests in development

Table 1. Arizona State University's Testing Commons has a curated database describing more than 1,600 (as of press time) testing technologies that are on the market or in development.[9]

Two of the most common diagnostic test technologies that look for active infection with the SARS-CoV-2 virus are: (1) "PCR" tests that detect the virus's genetic material, and (2) "antigen" tests that detect specific proteins on the surface of the virus. There are also other molecular testing technologies including loop mediated isothermal amplification (LAMP), next generation sequencing (NGS), CRISPR, and other novel technologies in development. Samples for tests are often collected by trained medical personnel, although some tests allow self-collection under the observation of a medical professional. In addition, some manufacturers have developed tests that enable people to collect their own samples at home without supervision. Point of care (POC) tests do not require sending samples to a lab.

Testing Accuracy

No medical test is perfectly accurate. All tests have varying degrees of "sensitivity," which is the likelihood that infected or sick individuals are correctly identified as such (true positives), and "specificity," which means the likelihood that non-infected or healthy individuals are correctly identified as such (true negatives). As shown in Table 2, these characteristics can vary by test technology, such that some types of tests are generally more sensitive or specific than others. PCR tests analyzed in clinical laboratories are considered the current gold standard for having very high sensitivity and specificity. Because PCR is considered the gold standard, performance of other types of tests is often stated as positive percent agreement (PPA) with a PCR test and negative percent agreement (NPA) with a PCR test, rather than sensitivity and specificity. These other types of tests may be somewhat less accurate but may be more readily available and able to produce actionable information faster. It should also be noted that tests may have significant differences in performance under real-world conditions compared to clinical studies. While PCR tests are generally considered 100% sensitive and specific under laboratory conditions, they do return both false negatives and false positives in clinical practice. If at all possible, testing strategies should draw on performance evidence from real world use.

Both false negatives and false positives can be problematic in different ways. False negatives are not problematic if the reason for the negative test is that the person is not infectious, i.e., a concentration of the virus may be present but is very low in an individual that is recovering. But false negatives in people who are actually infectious can lead people to behave in ways that continue to spread the virus. For diagnostic testing, high sensitivity is critical for isolation and clinical decision-making. However, the main objective of frequent routine screening is to reduce the overall risk of infection spread within a community. Infection risk can be substantially reduced without requiring every infected individual without symptoms to be detected, and therefore tests with somewhat lower sensitivity may be appropriate and highly effective. In addition, frequent routine screening means that a person that received a false negative may test positive on the next test, allowing isolation at that point.

False positives in diagnostic testing may lead to inappropriate decisions related to isolation and care, but that can be mitigated by understanding clinical signs and symptoms. In screening, false positives may lead people who are uninfected to spend time unnecessarily in isolation and, if confirmatory testing is required, use potentially scarce diagnostic testing.

As prevalence of active infection within a community increases, the likelihood that a positive result is false falls even though the sensitivity and specificity of the test itself doesn't change. For example, if there is zero infection in the population, by definition any test that produced a positive result would be a false positive, so 100% of positive results are false. On the other hand, if everybody is infected, then 0% of positive results are false. Positive predictive value (PPV) is the percentage of true positives from all positive results.

Devising Appropriate Testing and Screening Strategies

Especially with limited testing availability and cost concerns, state and local policy makers and others who make decisions on testing strategies need protocols that guide the allocation of testing to most effectively decrease the risk of viral spread. Risk-based protocols should reflect existing testing guidance:

- Anyone showing symptoms of Covid-19 should be tested for diagnostic purposes and to guide decisions about isolation and care. The CDC recommends that individuals remain isolated for at least 10 days after symptoms appear, regardless of test results. However, for certain essential workers who test negative and whose symptoms are mild and abate faster than 10 days, a protocol may consider if one or more highly sensitive test may be sufficient to allow an early return to work. This is especially important as the country enters allergy, cold and flu season.
- Anyone known to have been in close contact* with someone with a confirmed diagnosis should generally be quarantined and tested as soon as possible if there is significant spread in the community, or the person is or will be in an at-risk setting with vulnerable individuals, such as in a nursing home. If the test result is positive, the person should be treated like other Covid-19 cases.
- Universal testing or screening of all asymptomatic individuals is not recommended, but routine screening and/or surveillance testing for active infection may be necessary in appropriately selected populations to detect and limit viral spread.[10] As we have noted, such testing is likely to be valuable in at-risk congregate settings, such as nursing homes and schools, especially if contact tracing has proven difficult. Therefore, designing a smart testing strategy for asymptomatic individuals depends on determining setting-specific transmission risk and the ability of a particular testing protocol to reduce risk.

Assessing the need for, and dimensions of, a screening test strategy thus requires considering three different factors that will help to determine appropriate testing protocols: (1) **the likelihood of infection** in a given location or area; (2) **the likelihood of viral transmission** in that same location or area; and (3) **the consequences of transmission** if it occurs.

Likelihood of infection should be assessed by, first, understanding the community prevalence in a given location or area. Prevalence is typically judged by such factors as the number of daily confirmed positive tests per 100,000 people, combined with the test positivity rates – the share of Covid-19 tests performed that have been positive. Innovative approaches in determining community prevalence and providing early warnings of outbreaks within a community are also coming into use, such as screening wastewater to determine whether people have been "shedding" the virus in their urine or stool[11,12] or using data sources such as symptom reports for local surveillance. While community prevalence will be the primary determinant of risk of an infected person coming into a setting (see Figure 1), other factors may increase or reduce risk within a population. For example, patterns of commuting by workers, students, or others in a given location or area; their typical living situations, such as whether they live in large or multi-generational houses; and if employees are likely to have multiple jobs. Furthermore, the extent to which contact tracing systems are in place can increase or reduce risk within a population. For example, if a worker or customer is exposed outside of the workplace, are they likely to be notified and quarantined?

Assessing the **likelihood of transmission** involves examining the activities under way in a given setting and the interactions and movement among people. For example, are workers in frequent and sustained

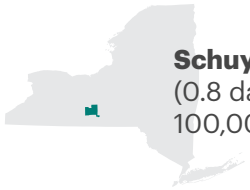
* A close contact is defined by the CDC for Covid-19 as "any individual who was within 6 feet of an infected person for at least 15 minutes starting from 2 days before illness onset (or, for asymptomatic patients, 2 days prior to positive specimen collection) until the time the patient is isolated."

close contact with other workers or customers in the setting in question? This assessment should consider mitigation measures that have been put into place, such as whether workers are stationed at least six feet apart, or separated by specially devised plastic screens. It should also realistically assess compliance with those measures: there may be distance markers on the ground, but are workers staying appropriately distanced throughout the day and on breaks?

Assessing the **consequences of transmission** requires answering several key questions. If the virus spreads within a given setting, are there high-risk or vulnerable populations in the setting who are likely to experience especially adverse outcomes, such as severe illness or death? Is there potential for infection transmission within the setting to spread broadly into the community? What would be the consequences if a business or other activity needed to be shut down for several days for extensive cleaning, or because a

Figure 1† – Chance of infected individuals present in group settings at different risk levels

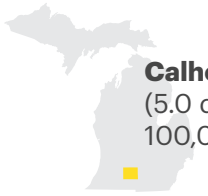
Green
(<1 daily new case per 100,000 people)



Schuyler County, NY
(0.8 daily new cases per 100,000 people)

Group Size	Chance of At Least 1 Infected Individual
25	3%
100	11%
500	43%
1000	68%

Yellow
(1 – 10 daily new cases per 100,000 people)



Calhoun County, MI
(5.0 daily new cases per 100,000 people)

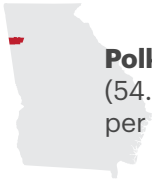
Group Size	Chance of At Least 1 Infected Individual
25	17%
100	52%
500	97%
1000	>99%

Orange
(10 – 25 daily new cases per 100,000 people)

Oklahoma County, OK
(17.0 daily new cases per 100,000 people)

Group Size	Chance of At Least 1 Infected Individual
25	46%
100	91%
500	>99%
1000	>99%

Red
(> 25 daily new cases per 100,000 people)



Polk County, GA
(54.3 daily new cases per 100,000 people)

Group Size	Chance of At Least 1 Infected Individual
25	81%
100	>99%
500	>99%
1000	>99%

† Definitions of geographic area risk levels (green, yellow, orange, and red) are based on Harvard University Key Metrics for COVID Suppression. Risk levels were assigned based on daily new cases per 100,000 as of August 27, 2020 using New York Times data. The Interactive COVID-19 Event Risk Assessment Planning Tool was used to determine the likelihood that at least one individual in these group settings could be infected with Covid-19.

significant fraction of the workforce, school, or other population became ill or required isolation?

Risk assessments carried out in each of these three categories – likelihood of infection, likelihood of transmission, and consequences of transmission – allows for settings to be distinguished between low-risk, medium-risk, and high-risk locations. Settings also may move between the categories over time if community prevalence or other factors change.

In addition, these risk assessments may yield even more refined distinctions that delineate significant differences among populations within a single setting. For example, in schools, teachers and staff may face different levels of risk than students due to older age or having other risk-factors for adverse outcomes if infected.

Devising Appropriate Testing Strategies Based on Settings, Populations, Risk Levels, and Types of Tests

Because of the varying risk, different testing strategies must be tailored to both settings and populations, and depending if the purpose of the testing is to reduce transmission or simply to understand prevalence. Prevalence can be determined through less frequent screening tests, randomized tests, or surveillance testing, and can inform decisions like whether to change a testing or a reopening strategy. Costs and availability of tests are also a key consideration, as well as logistical challenges in implementing these testing programs. As organizations develop and implement testing strategies, it is critical to observe the results and make adjustments to improve performance of the strategy.

We consider two primary settings for this report: (1) nursing home and other residential care facilities that provide care and (2) public schools from grades K-12. Repeated screening is also likely to be beneficial for certain essential workers and other high-risk congregate settings as supply increases, and resources become available.

Nursing homes are high-risk sites with residents likely to have complications or die should they become infected. The goal of a testing strategy should be to sharply reduce infection transmission. In such a setting, modeling studies suggest that frequent screening tests of both residents and staff are required; we describe these in more detail below.[8,13] The Centers for Medicare and Medicaid Services (CMS) recently released guidance that recommended nursing homes routinely screen staff every 1-4 weeks (depending on community prevalence) and conduct system-wide testing of all individuals (residents and staff) every three to seven days after a confirmed infection on-site until 14 days after no new infections are found.[14] To facilitate this screening, the U.S. Department of Health and Human Services (HHS) is now procuring tests to facilitate on-site testing in more than 14,000 nursing homes nationwide.[15] These tests may be less sensitive than PCR tests but results are received the same day, allowing rapid isolation.

It is critical that schools reopen for a more complete learning experience as well as social supports for many children and enable many parents to return to regular work. Depending on reopening goals, surveillance testing may be appropriate in some districts – for example, where there has been only limited return to school (e.g., in-facility teachers with students online) or in districts with low reports of daily new infections and a low test positivity rate. This information will inform decision-makers of the need to maintain or escalate precautions. In areas with a significant risk of outbreaks and transmission, an effective testing strategy along with other mitigation steps may allow schools to reopen more broadly than would be sustainable in the absence of testing.

While the report focuses on K-12 schools and nursing homes, other essential workers and the communities in which they live have also been affected by outbreaks. Many health care settings have already implemented routine testing for their workers and for all new patients.[16,17] Some cities and states are deploying mobile testing centers to essential workplaces like firehouses or food processing facilities, as well as to

congregate settings like prisons or shelters, and to communities where outbreaks have been observed.[18] If testing capacity is limited, such rapidly deployable screening capacity paired with early-warning surveillance based on the approach we describe here can limit outbreaks, particularly among low-income populations and communities of color that have been disproportionately affected by the pandemic.

Effective prioritization and implementation of such testing strategies can benefit from modeling the likely performance of the testing strategy chosen, given the results of the risk assessment, and the feasibility of obtaining the needed testing capacity at a time of limited supply.

Achieving Goals in Lowering Viral Transmission Through Different Testing Strategies

Multiple strategies are available that may be more or less feasible, given resources available to pay for testing and availability of tests. Here, we describe an approach to determining testing impact that policymakers, communities, and organizational leaders can use to determine the feasibility of a desired goal. The testing goal can then be assessed alongside the available resources, the local capacity to implement testing programs and support actions based on test results, and the size of their available budgets, to choose appropriate protocols and testing types.

We use computer simulations to help quantify the tradeoffs between different testing strategies, based on available evidence on the accuracy and typical time to results of the test used. We have collaborated with a research team from the University of Colorado Boulder who developed one such model to investigate a range of testing strategies and their impacts on viral transmission.[8]

This model, built on the evidence available about the progression of SARS-CoV-2 growth and over the course of an infection, combined with extensive simulations (see Appendix A), sheds light on the required frequency of testing, as well as test sensitivity and specificity, that are required to achieve transmission reduction goals. At the broadest level, increasing the frequency of testing and reducing the test turnaround time will more rapidly and effectively reduce transmission.

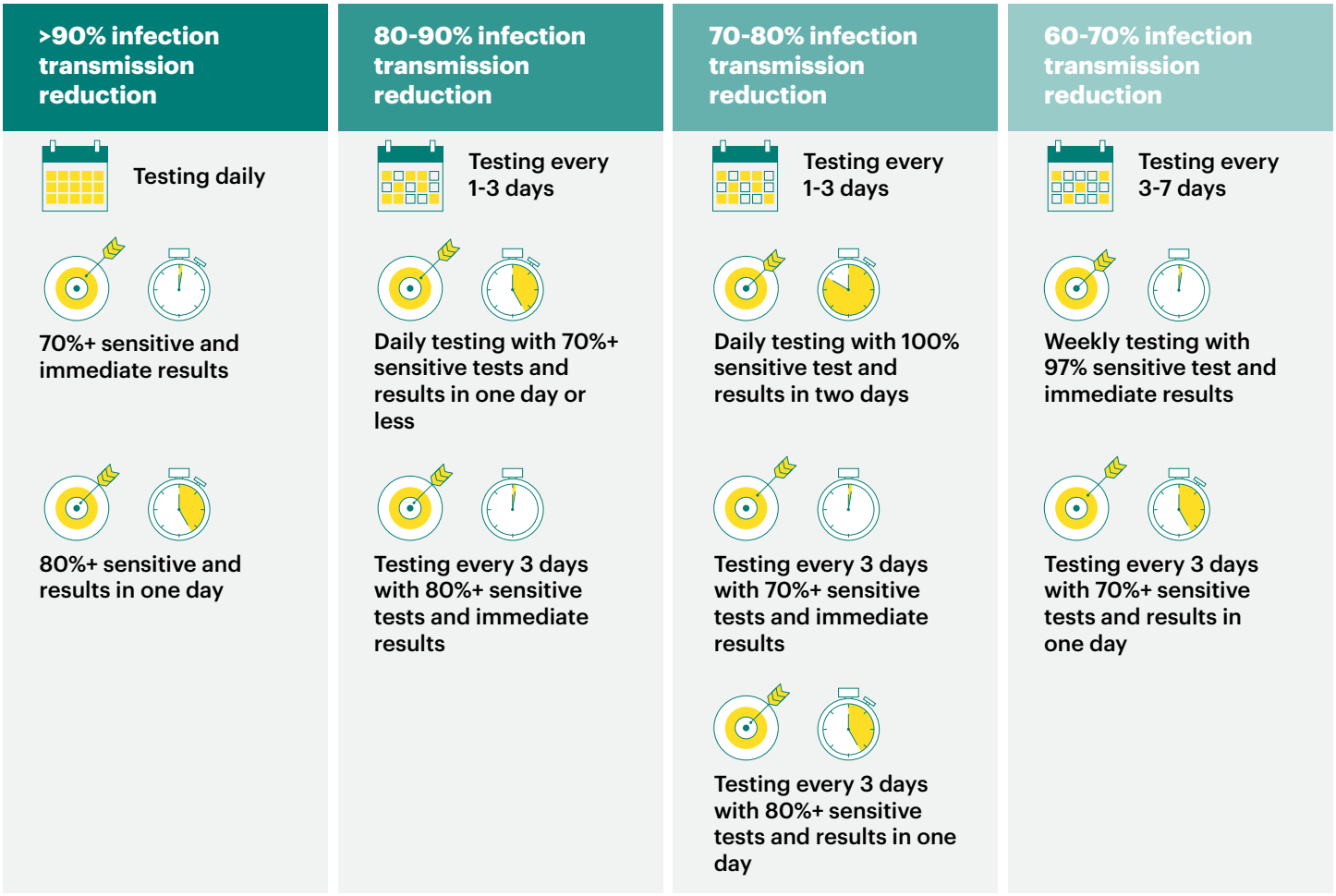
Epidemiologists measure whether an epidemic is growing or shrinking using the reproductive number (R), which is defined as the average number of additional infections caused for each current infection. When R is above 1, each infection replaces itself with, on average, more than one new infection, causing accelerating community spread. When R is below 1, each infection causes, on average, less than 1 new infection, leading to decelerating community spread. Existing testing, mask wearing, good ventilation, extensive sanitation, and social distancing are all mitigation factors that reduce the reproductive number to near, or even below, 1. When these mitigation strategies are not enough, or are very disruptive, screening test protocols may be able to achieve significant enough reductions in transmission to contain potential outbreaks and cause local collapses in case counts.

For these reductions in transmission to be realized, however, procedures will need to be in place to promptly isolate individuals that test positive, and to ensure that other mitigation measures remain in place. Testing strategies must include considerations for what will be done in the event of a positive test, including potential false positive tests.

The model suggests that there are multiple options to reduce infection transmission by greater than 90%, although all involve testing daily: using tests that are between 70-80% sensitive and reporting results immediately or using tests that are at least 80% sensitive and results that are reported by the next day (Table 3). The choice of which strategy to use may be one of budget, availability of one test over an another, minimizing complexity of administering the protocol or other locally relevant factors.

Conducting tests of varying levels of sensitivity – for example, rapid RT-PCR testing, RT-LAMP, and antigen

Figure 2 – Model results of testing strategies to reduce Covid-19 transmission



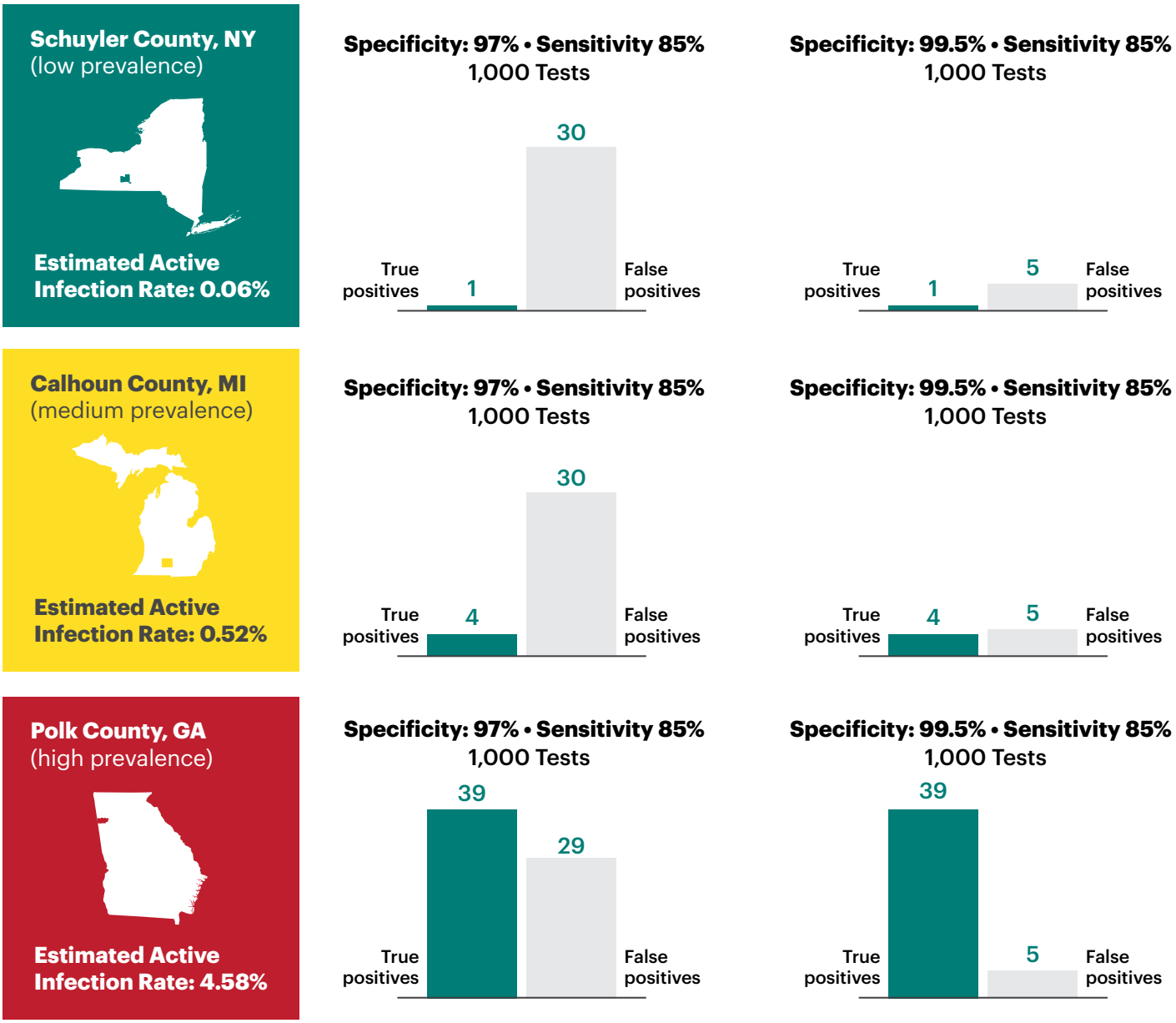
testing – can each yield similar reductions in the overall rate of transmission when these tests are performed frequently and with rapid turnaround times (Figure 2). These results agree with recent modeling by researchers at Yale University and Massachusetts General Hospital, which showed that testing asymptomatic individuals every 2-3 days, with tests results reported within 8 hours, would be necessary to prevent mass infection on a mid-size college campus.[13]

In lower-risk settings, a routine testing strategy is unlikely to achieve worthwhile benefits in transmission reduction relative to costs, including costs of managing false-positive results. Testing everyone in a population monthly, or even more frequent testing of only a small subset of a population does not break lines of transmission effectively, and therefore will not by itself cause large reductions in transmission. However, this type of testing can be useful in understanding how prevalence may be changing within a community, so relevant authorities can determine if they need to start more routine testing or if current mitigation techniques are effective. Surveillance in combination with rapid, surge testing can reduce infection transmission, as seen recently at the University of Arizona where over 300 students in a dorm were tested in response to a positive Covid-19 signal in their wastewater surveillance system.[19] All students were screened with a rapid antigen test. Two positives were returned, both individuals were asymptomatic and immediately isolated which stopped a potential hot spot from occurring.

Testing strategies must also account for false positive tests. Figure 3 below gives examples of the number of true and false positives that might be expected in communities with different active infection rates if tests similar to those available today were used to screen 1,000 people. As can be seen, protocols will need to have procedures in place to account for the high

number of false positives when the active infection rate is low, either by relying on surveillance testing that can be adjusted for prevalence, or if using routine screening, by using tests with very high specificity. If using very specific tests for repeat and rapid screening is not feasible, the costs of managing false positive tests can be reduced by limited use of high-sensitivity, high-specificity tests like PCR lab tests for confirmation. For example, individuals testing positive could be asked to isolate pending results of a confirmatory test. Individuals who test negative on the confirmatory test could be released from isolation if they have not developed symptoms in the interim. This would limit the impact of false-positive tests with much less use of diagnostic lab tests than would be required if such tests were used in regular screening to reduce false positives.

Figure 3 – How estimated active infection rate and test specificity affect the ratio of true and false positive test results‡



‡ Estimated active infection rates were determined using 10-day cumulative case rates from New York Times data as of August 27, 2020, in accordance with the Interactive COVID-19 Event Risk Assessment Planning Tool's methodology and CDC advice on duration of Covid-19 infectious periods. This 10-day cumulative case load was multiplied by 10 to correct for under-reporting due to ascertainment bias.

Our analysis highlights the importance of developing better evidence on test performance in actual practice. Initiatives such as The Rockefeller Foundation's Testing Solutions Group are sharing their experiences with different tests and testing strategies. Those learnings, as well as evaluations of testing strategies being adopted in pilots across the country, will lead to refined guidance as experience with screening increases.[20]

How Many Tests are Required for Screening and Surveillance?

While testing capacity and resources are still limited, the growing array and volume of test technologies and strategies increases the feasibility of large-scale, more routine screening protocols. A smart testing plan will consider setting-specific factors and an ever-changing local Covid-19 prevalence. Higher local prevalence generally means more testing is required to achieve a given level of in-person operation of schools and other critical activities. If prevalence declines in more areas of the country, fewer tests will be needed to prevent uncontrolled spread in essential and critical settings. In that case, more testing could be available to support additional reopening.

Here we present a reference testing strategy for limiting outbreaks in K-12 schools and nursing homes and residential care facilities, to estimate the number of tests required for screening as prevalence across the U.S. changes. For K-12 schools, we started with the Harvard University Key Metrics for COVID Suppression recommendations regarding community prevalence risk levels and a phased grade-based school reopening plan, as shown in the example testing strategy in Figure 4.[21] With the heightened risk of adverse outcomes for residents of nursing homes and residential care facilities, ongoing screening should be performed even in low prevalence areas, as detailed in a recently updated CMS guidance which forms the basis of the testing strategy in Figure 4.[14]

We then estimated the national number of screening tests required using three different scenarios of the percentage of the relevant population that would be in each risk category. Scenario A reflects the share of the US population living in counties at each of these risk levels on the week of September 2, 2020 (see Appendix B). Scenarios B and C reflect declining case counts as smart testing strategies and more effective mitigation and treatment strategies are implemented to help contain the pandemic. The figure highlights how much community prevalence influences the amount of testing needed to contain spread.

Our preliminary analysis shows that testing capacity must increase in order to limit outbreaks while reopening schools and controlling infection spread in nursing homes. If Covid-19 prevalence across the United States remains at 2020 levels, approximately 193 million tests are needed to support reopening with limited spread under modified conditions including no in-person classes in "red" communities and limiting in-person attendance to grades K-5 in "orange" communities. (Individual school testing needs will vary: particular schools may be able to implement more or less effective mitigation strategies, and some schools may not reopen for other reasons.) In contrast, if Covid-19 infection rates can be reduced significantly, broader school reopening while controlling outbreaks will require less than half as much testing – but testing requirements to avoid significant outbreaks would still be substantial. Further, even when the country achieves substantially better control, significant testing needs will be needed to limit risk of further outbreaks in other at-risk populations.

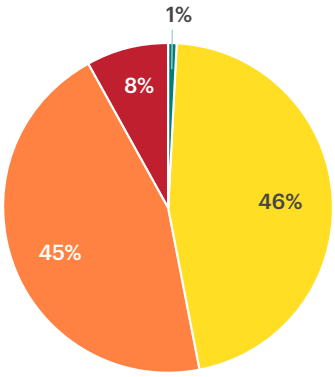
There are over 80 million essential workers in the country, inclusive of nursing home and public education staff, disproportionately including low-income and minority populations, many of whom work closely together and have experienced significantly elevated risk of Covid-19 infection, complications, and death.[22] The methods we have applied here suggest that 66 million tests would be required to substantially limit spread for every 10% of the essential workforce working and residing in high prevalence, higher-risk settings where twice weekly screening would be appropriate. Another 16.5 million tests would be required for every 10% of essential workers working in settings that only require testing every other week.

Figure 4 – Scenarios of varying community risk and tests per month

	K-12 Testing Strategy	Nursing Home and Residential Care Facility Testing Strategy
Green (<1 daily new case per 100,000 people)	Teachers, staff, and all students are able to return to in-person school. Mitigation measures with optional environmental or pooled surveillance.	Staff are tested monthly. Staff and residents are "surge tested" if an active infection is found, meaning they are tested every 3-7 days until 14 days after no new infections are found.
Yellow (1 – 10 daily new cases per 100,000 people)	Teachers, staff, and all students are able to return to in-person school. Students and staff are tested once every 2 weeks.	Staff tested weekly. Staff and residents are "surge tested" if an active infection is found.
Orange (10 – 25 daily new cases per 100,000 people)	Teachers, staff, and K-5 students are able to return to in-person school. Students and staff are tested twice a week.	Staff tested twice per week. Residents are "surge tested" if an active infection is found.
Red (> 25 daily new cases per 100,000 people)	Teachers and staff return to school to facilitate remote instruction under strict mitigation measures and are tested once every 2 weeks.	Staff tested twice per week. Residents are "surge tested" if an active infection is found.

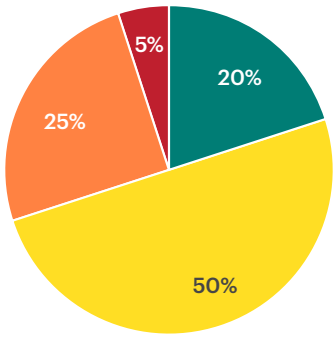
Monthly tests needed based on the % population in each risk category

Scenario A



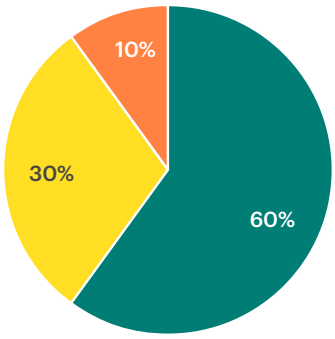
School Staff Tests: 42 M
K–5 Student Tests: 107 M
6–12 Student Tests: 27 M
Nursing Home Staff Tests: 8 M
Nursing Home Resident Tests: 9 M
Monthly Tests: 193 M

Scenario B



School Staff Tests: 28 M
K–5 Student Tests: 72 M
6–12 Student Tests: 29 M
Nursing Home Staff Tests: 6 M
Nursing Home Resident Tests: 8 M
Monthly Tests: 143 M

Scenario C



School Staff Tests: 13 M
K–5 Student Tests: 33 M
6–12 Student Tests: 18 M
Nursing Home Staff Tests: 4 M
Nursing Home Resident Tests: 4 M
Monthly Tests: 72 M

Even when the country returns much further toward a "green" level of Covid-19 transmission risk where most essential workers would not be tested regularly (scenario C), substantial testing would be required.

How to Meet the Need for Covid-19 Testing

Although the number of Covid-19 tests performed has risen dramatically since the start of the pandemic, when the United States struggled to conduct 10,000 tests per day, the nation is still testing at rates well below the optimal level. As noted in early September 2020, when much of the country was experiencing significant rates of community spread, we estimated that students and staff in public K-12 school settings as well as residents and staff at nursing homes and residential care facilities require 193 million tests per month (roughly 45 million per week). Even when the country returns much further toward a "green" level of Covid-19 transmission, just over 70 million tests per month will be needed to avoid outbreaks in just those two settings. Additional testing capacity is required to limit outbreaks among other essential workers and other high-risk populations.

Assuming that aggressive, accurate, and efficient testing and tracing can be achieved and paired with continued social mitigation measures, testing demand will decline over time, as described in the previous section. Lower case counts will decrease diagnostic testing requirements as fewer close contacts will need to be tested. However, screening testing should increase as more students return to school and employees return to the workplace. Later, assuming that effective vaccines against Covid-19 are developed and administered nationwide, there will still be an ongoing need for testing to establish vaccine efficacy and achievement of population immunity against the SARS-CoV-2 virus.

Table 3 shows current manufacturing capacity and expected growth in the production of rapid POC tests based on press releases, earnings reports, and conversations with the companies. POC testing capacity is increasing rapidly with the recent and expected addition of new tests. To date, the vast majority of POC testing capacity has been directed to the United States, and we expect similar patterns with future growth. Additional platforms not currently included in our overall supply estimate could add 50 million or more tests per month to US capacity by late 2020, and potentially up to 100 million more tests by mid-2021. But this is dependent on effective supporting policies being implemented, such as more clarity about federal, state, and local willingness to purchase additional tests that meet performance and price criteria. The majority of this additional capacity is expected to come from POC antigen tests, supplemented by other POC technologies. Some of the companies that may be part of this capacity growth include several of the National Institute of Health's Rapid Acceleration of Diagnostics (RADx) award recipients including MatMa Corp, Maxim Biomedical, MicroGEM International, NOWDiagnostics, STOPCovid, Talis Biomedical, and others.

While POC tests may not be able to fully meet testing demand within the next several months, additional laboratory testing capacity will fill some of the remaining gap. Existing CLIA laboratory testing capacity is constrained, but novel high-throughput testing techniques such as **pooled samples for screening and surveillance** are being deployed by some universities and other labs. For example, **the University of Illinois-Champaign** has implemented such an approach using a saliva-based testing system; a simplified extraction-free system has been developed by Yale University, and the **Broad Institute** is performing testing for many New England universities.[23,24,25] Next-generation sequencing and CRISPR also may support a substantial capacity increase. However, advance planning and financial commitments will be required to assure that adequate laboratory supplies are available and mechanisms are in place to address costs. The state of California's initiative to use advance-purchase contracts **to recruit significant additional laboratory testing capacity** for individuals with Covid-19 symptoms is an example of this approach.[26]

There have been several challenges to increasing the supply of rapid POC tests. The Food and Drug Administration (FDA) requires that rapid tests for active infection show a high level of agreement with PCR test

results. While this standard is appropriate for clinical testing, and point of care tests used for screening are becoming more accurate, it is an unnecessarily high standard for tests designed for use in a routine screening protocol. The FDA does not yet have a set of standards related to screening tests specifically. This is in part because the federal government has produced few guidelines for the use of screening protocols for transmission reduction in at-risk settings. Finally, POC tests also have supply chain issues such as supplies of packaging needed for sterile distribution.

Alongside steps to address these regulatory and planning issues, the financial costs of supporting effective screening must be addressed – several billion dollars per month are required, based on currently available testing technologies and prices. The health and economic benefits in terms of confident reopening of schools and workplaces provided by much better infection control in hard-hit communities and populations are far greater.

Table 3 – Estimated Planned Monthly Manufacturing Capacity of Select Point of Care Tests (in millions)

Test	Test Type	September 2020	October 2020	January 2021	April 2021
Abbott ID Now (EUA March 2020)	LAMP POC	2 M	2 M	2 M	2 M
Mesa Biotech Accula (EUA March 2020)	PCR POC	0.2 M	0.3 M	0.5 M	0.9 M
Quidel Sofia (EUA May 2020)	Antigen POC	6 M	6 M*	6 M*	11.7 M*
BD Veritor (EUA July 2020)	Antigen POC	6 M	8 M*	8 M*	12 M*
Abbott BinaxNOW (EUA August 2020)	Antigen POC	20 M	50 M	50 M	50 M
LumiraDx SARS-CoV-2 (EUA August 2020)	Antigen POC	2 M	4 M	10 M	10 M
LuminUltra GeneCount Q-16 (EUA submission expected Q3)	PCR POC	N/A	16 M^	40 M	60 M
OraSure OraQuick Coronavirus Rapid Antigen Self Test (EUA submission expected Q4)	Antigen Self-Test	N/A	1.4 M**^	2.3 M**	2.3 M**
Roche SARS-CoV-2 Rapid Antigen Test (EUA submission expected Q4)	Antigen POC	N/A	40 M^	80 M	80 M
Total		**36.2 M**	**70.3 M+ ^**	**198.8 M**	**228.9 M**

* Figures provided as tests per week and extrapolated to month. ** Figures provided as tests per year and extrapolated to month.
^ Dependent on EUA timing, and therefore not included in the total.

Recommendations

Our analysis shows that the U.S. will likely need very large numbers of all types of Covid-19 tests well into 2021 to contain outbreaks while returning toward normal activity, with a particular need for more screening tests that have very fast turnaround times. Testing capacity and test capabilities are improving, but further steps are needed by government, businesses, and manufacturers to close the gaps.[27] There is uncertainty about the precise levels of demand for various types of tests, as well as uncertainty about payment for screening tests.

To address this, the federal government should build on its support for testing, to provide the guidance and additional advance funding to eliminate this uncertainty and the major gaps in access to testing in the months ahead. In the absence of further federal actions, actions by state and local governments supported by the private sector and initiatives like that of The Rockefeller Foundation will remain critical.

A. *To better define the number and types of tests that are needed:*

1. Building on the approach discussed in this report, the federal government should issue guidelines that state, and local officials can use to refine their local protocols for regular diagnostic, screening, and surveillance testing for active infections.

Additional specific, evidence-based federal guidance like that developed here is needed to serve as the basis for local protocols for routine screening and surveillance in settings of public health importance (e.g. nursing homes, public schools). An example is the previously discussed CMS guidance on screening staff and residents in nursing homes. Guidelines in support of developing protocols for K-12 schools should be prioritized, as well as for other congregate settings such as universities and prisons and essential workplaces like food processing plants in which outbreaks are common and can spread through the community. Screening public service workers, such as first responders, who are at risk of both being exposed and exposing others due to close contacts should also be a priority. While federal guidelines should set out clear objectives for such testing, they should allow for local customization, particularly with respect to local mitigation steps, risk of spread, and the equitable distribution of testing resources. Such specific guidance will facilitate state and local protocols that specify the type and number of tests, and will provide more meaningful national estimates for testing needs in the months ahead.

Enhanced access to routine screening tests will help reduce outbreaks, reducing the need for intensive testing to avoid substantial outbreaks in high-priority settings like schools. With reduced community spread, testing needs will ease in these high-priority settings, as illustrated in our estimates above that show testing demand going from 193 million to 72 million for K-12 public schools as the country moves from mostly "orange" to mostly "green." With greater containment and sufficient testing capacity, state and local governments can maintain efforts to limit community spread as well as shift more testing capacity to other priority settings, such as supporting business activity and increased testing in neighborhoods. Even when immunization with effective vaccines becomes available, it will likely take some time to reach and sustain herd immunity levels, where enough people have immunity to protect susceptible people from local infections, in most communities. Well into 2021, there will continue to be demand for screening and active virus surveillance testing to contain potential outbreaks in additional work settings where risk of transmission is high, as well as high-risk neighborhoods.

2. Federal, state, and local governments should expand pilot testing initiatives to build the real world evidence base on test accuracy and on effective testing strategies for the range of risk settings and populations.

Some of the uncertainty around large-scale implementation of routine testing lies in the lack of real-world evidence regarding the performance of the different available and emerging tests in various settings and populations. While testing capacity is building, studies and pilot sites should be funded to build an evidence base on the ability for rapid POC

tests to accurately test asymptomatic individuals in real-world conditions. This includes more evidence of diagnostic test sensitivity and specificity measured against a consistent set of reference samples that reflect different real-world testing conditions. Evidence should also be developed and disseminated on how to improve implementation and increase the effectiveness of promising testing strategies. The Rockefeller Foundation is working with a cohort of cities and states to start pilot testing protocols developed in conjunction with researchers at Duke-Margolis and John Hopkins University, in order to build evidence-based protocols for settings of public health interest. Federal and state governments can support such efforts in conjunction with providing additional tests. The evidence-based recommendations on tests and testing strategies from these efforts should be disseminated to facilitate Covid-19 containment and personal decision-making.

3. The federal government should develop a short- and long-term plans to procure and distribute tests to states, localities, and businesses and share and coordinate these plans with relevant stakeholders to ensure that receiving entities can plan to meet their testing needs and to allow manufacturers to better understand the demand for testing in the coming months.

In addition to **purchasing and distributing testing supplies** for nursing homes, **HHS also announced** that the department has bought and will deploy 150 million rapid tests from Abbott. [15,28] **News reports** about the purchase mention their potential use in assisted living sites, as well as schools and first responders.[29] Clarity on whether these tests are earmarked for certain purposes or will be sent to the states to prioritize distribution is critical, as well as how many and what tests states should expect, not just for this purchase but for future purchases as well. Without transparent, advance reporting on federal plans for test procurement and distribution, it is challenging for states to work with manufacturers to procure additional tests or to plan for implementing testing plans with confidence. The federal government could announce and regularly update a more predictable distribution plan for each state based on clearer testing guidance, which would enable states to meet their priority needs based on local factors and patterns of spread. Such transparency is critical for states, localities and private entities to understand how they can test effectively

B. To support development of increased capacity for the numbers and types of tests that are needed, especially for appropriate routine screening of asymptomatic individuals:

1. FDA, CMS, and CDC should issue clearer written guidance about regulatory flexibility, pathways, templates, and other tools to support screening and surveillance.

FDA has provided **useful guidance and templates** on testing for asymptomatic individuals and for pooled PCR testing, and CMS has provided **useful regulatory flexibility** during the pandemic for screening and surveillance testing programs.[23,30] But uncertainty remains regarding how flexible FDA will be regarding the performance of tests – sensitivity, specificity and overall accuracy – that are meant to be used not for one-time diagnosis in an individual but as part of routine repeated screening protocols in an at-risk population. Similarly, the Centers for Disease Control and Prevention (CDC) should provide further written guidance to support effective screening in schools and work settings, as experience accumulates.

2. The federal and state governments should support advance purchase contracts to assure needed testing capacity is available for priority populations for the remainder of the pandemic, including testing relevant to a vaccine.

A key strategy for increasing testing supplies will be devising and adopting advance purchase contracts, under which the federal and state governments would commit to purchasing large numbers of tests from manufacturers. The federal government should also support manufacturer investment in additional production facilities, as it has done for **some point of care tests**.[31] Our report shows that testing capacity is already on track to increase rapidly. In conjunction with our other recommendations, a clear commitment by the federal government of several billion dollars per month for the coming months appears sufficient to create a robust supply of screening tests. These

commitments would complement federal initiatives like **Rapid Acceleration of Diagnostics (RADx) Initiative** to promote better tests and accelerate widespread availability of reliable, fast, and cost-effective testing platforms.[32] The combination of support for development and advanced purchasing contracts has led to far greater investments by manufacturers of vaccines and some therapeutics as part of Operation Warp Speed, the federal effort to jumpstart countermeasures against the virus. **Steps to address the testing shortfall** have been more limited and shorter-term – not sufficient to generate the needed large-scale capacity.[7]

In lieu of or in addition to further federal commitments to purchasing tests, **advance purchase contracts** for tests by collaborations of state and local governments or school districts with testing manufacturers and suppliers could also create a clearer signal of support for a more robust testing market. That is, instead of a pay-as-you-go, per-test approach, the contracts would provide availability for a large pre-specified number of tests to reliably meet a population testing need.[7] The Rockefeller Foundation and a bipartisan group of states have engaged in a **cooperative interstate compact** to generate sufficient purchasing power to order millions of rapid point of care antigen tests to generate the incentives and guarantees that private manufacturers require in order to rapidly expand capacity.[33]

Federal, state, and local advance arrangements would provide more certainty to test manufacturers and suppliers to make additional investments in production facilities and supplies, and could expand the availability of innovative testing platforms. By forming multi-state purchasing collaboratives, based on clearer testing protocols, states would signal to manufacturers that the future market for tests will be larger for some time, encouraging further investments in capacity. In contrast, short-term contracts without a coordinated strategy in the pandemic simply result in states competing against each other – or the federal government – for a limited supply of tests and testing supplies. To support formation of these collaboratives, the federal government could provide subsidies to states, along with guidance on entering into advance purchasing arrangements through 2021. These multi-state collaboratives allow for an exchange of information and experience to better inform future policy decisions.

3. Use information provided by manufacturers and key suppliers to increase manufacturing capacity of key supplies and reagents, especially for laboratory tests.

The federal government receives ongoing information from test manufacturers and from other manufacturers in the testing supply chain about the availability of sample collection materials, testing materials, and reagents. While individual supplier information is often proprietary, aggregate information on current and projected capacity could and should be shared more publicly, to facilitate public-private planning for increased testing capacity.

These federal reports about the supply chain, developed in collaboration with the testing industry, could be used as a basis for advance purchase contracts for key testing supplies and reagents. If necessary, the federal government could also invoke the Defense Production Act to address supply chain-related choke points in increasing testing capacity. State and local governments experiencing supply shortages would benefit from action by the federal government that spurs more development of supply and could expand upon that to build out their capacity.

Conclusion

The United States is at a critical point in the pandemic. Even with rapid progress on therapeutics and vaccines, the nation faces potentially many more months of significant community spread, hospitalizations and deaths, and disrupted schools and businesses. However, testing capacity is increasing substantially – including for tests suitable for repeat screening to limit the spread of Covid-19. Consequently, there is an urgent need for federal action to provide more clarity about testing protocols and testing needs, to provide reliable and predictable funding for screening tests and on how to use the tests effectively in high-priority settings. We have outlined such measures here. They would build on existing federal efforts to develop new

tests and support the procurement of new tests – steps that have been helpful, but that do not yet amount to a national testing strategy and clear path to implement it. In the absence of federal actions, state and local governments and the private sector, working with supporters like The Rockefeller Foundation, can take further, meaningful steps to enable smarter, more extensive testing to contain the pandemic.

Appendix A: Modeling Screening Strategies

The Duke-Margolis Center research team collaborated with Dr. Daniel Larremore, a computer scientist and infectious disease modeler at the University of Colorado Boulder, to project the effects of various screening strategies on reducing the reproductive number, R, of the Covid-19 pandemic.[8] The reproductive number is the average number of infections expected to be generated by a single infection in the absence of any population immunity.

Briefly, a SARS-CoV-2 infection, whether symptomatic or asymptomatic, follows a typical viral trajectory: Immediately after exposure, the virus is undetectable at secondary sites like the nose and throat, or in the saliva. After a few days in this latent phase, the virus becomes detectable and viral loads enter a period of exponential growth before reaching a peak 2-4 days later. Peak viral load is followed by a longer, slower decline in virus concentrations at secondary sites before eventual clearance. As a consequence of this trajectory, the same test applied on different days of the infection may be more or less likely to return a positive result. And, two different tests applied on the same day could return the same or different results. The model of **Larremore et al** focuses on simulating how combinations of (i) test frequency, (ii) test limit of detection (LOD, the minimum detectable concentration of viral RNA, sometimes called "analytical sensitivity"), and (iii) test turnaround time (the time lag between test administration and return of results) interact with viral load trajectories to provide (or fail to provide) positive test results when isolation is still useful.

The model also considered (iv) sample sensitivity, which refers to the probability that the sample itself was collected correctly, reflecting known difficulties in sample collection. These sensitivities were included in addition to test limit of detection parameters to approximate sample collection and storage errors outside the biochemical properties of the test.

In each simulation, 1,000 SARS-CoV-2 viral load trajectories were simulated and subjected to a testing strategy specified by the four parameters described above. Test LOD values were drawn from the literature for RT-PCR, RT-LAMP, and antigen tests. Sample sensitivities were varied from 70%-100%, matching the Emergency Use Authorization (EUA) reported ranges of currently available tests. In the main results presented above and in Appendix Figure A1 below, the LOD values of the tests were held constant while varying sensitivity using EUA-reported data. Because this form of sensitivity is related to sample collection, storage, etc., its false negatives were considered to be independent of viral load. To ensure that this did not overly bias the calculations, a second set of calculations of infection transmission reduction were made, allowing LOD to vary with test type using common LOD values for PCR, LAMP, and antigen tests and similar patterns were seen.

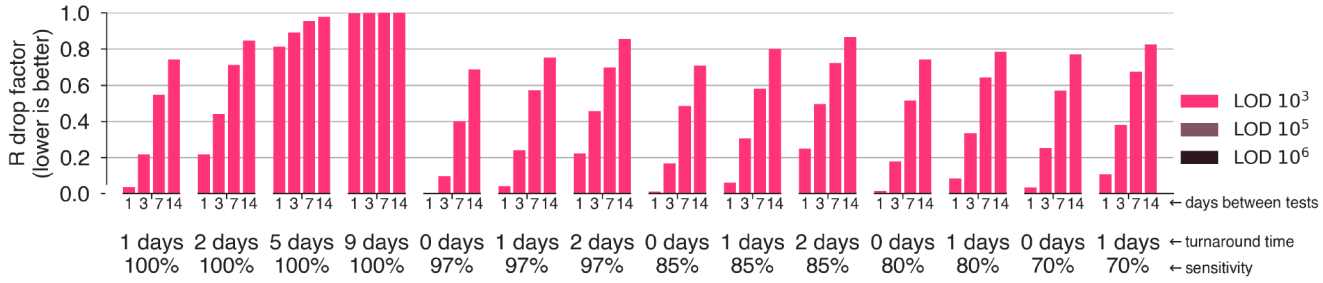
In the model, each infected individual's viral load was simulated, and their testing schedule was assigned at the frequency corresponding to the strategy under investigation. Their first day of testing was assigned at random within the prescribed frequency. A positive test result occurred when an individual received a test on a day when the viral load exceeded the test's LOD *and* the sample collection did not produce a false negative. Individuals receiving a positive test were assumed to quarantine with no further transmission. Individuals receiving a negative test (whether truly uninfected, or not detected by the test) continue to contribute to community infections and undergo the assigned test strategy until they receive a positive test. Some individuals were simulated to develop symptoms with 3 days of peak viral load, at which point they were assumed to self-isolate, unless they received a positive test result prior to symptom onset. Aggregated community viral load under each testing strategy was compared to no testing and used to determine reduction in Covid-19 basic reproductive number.

Figure A1 – Reduction in basic reproductive number resulting from alternative testing strategies

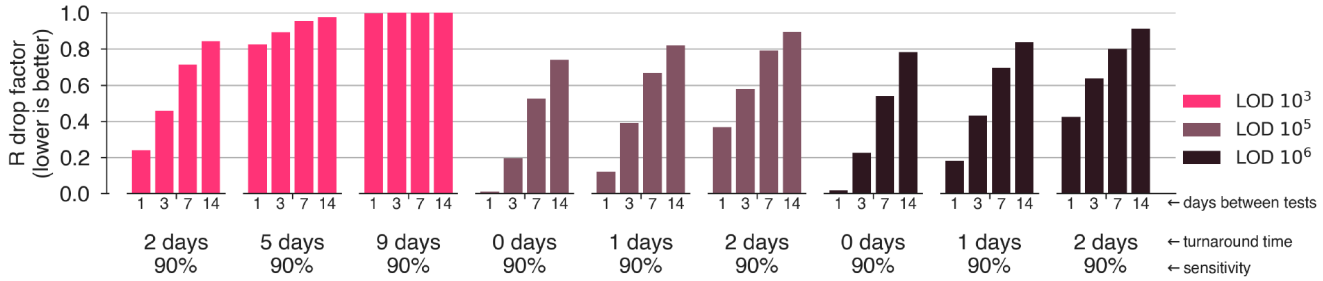
R drop factor is plotted on the y-axis and represents a multiplier applied to a population's basic reproductive number (R_0). For example, if a testing strategy yields 0.2 on the y-axis in a population with an R_0 of 2.5, implementation of that testing strategy is predicted to change R_0 to: 0.2 * 2.5 = 0.5.

LOD: limit of detection; R: effective reproductive number.

a.



b.



The impact of a testing strategy was calculated as the factor by which the reproductive number would be multiplied, were that strategy put in place. For instance, a calculated factor of 0.4 would mean that a pre-testing reproductive number of 1.5 would be reduced to 0.6 with testing.

Results from simulated analyses are presented here in Appendix Figures A1(a) and A1(b). Appendix Figure A1(a) shows base case results where LOD was held constant at 10^3, corresponding to RT-PCR, for each test and sensitivity was alone varied. Test frequencies examined included every 1, 3, 7, and 14 days, with TATs of 0-9 days. Appendix Figure A1(b) presents similar results, but varies LOD while holding sensitivity constant at 90%. The model assumes a LOD of 10^5 corresponds to an RT-LAMP assay and a LOD of 10^6 corresponds to a typical antigen test. This sensitivity analysis supports the main results presented previously in which more frequent and rapid tests generate relatively higher reductions in infectivity than slower but more accurate tests.

The model was developed and described in a paper by Larremore et al which demonstrated the relative importance of screening test frequency and turnaround time over sensitivity. These results used similar methods and showed that test frequency was the most significant factor in infection reduction, while test sensitivity had a much smaller impact. The reductions in R were further incorporated into two population-level epidemiological models to show effects of the examined testing strategies. The authors of these earlier modeling studies emphasized that less frequent testing strategies that allowed even one extra day of viral spread could have a significant impact in worsening the epidemic.[8]

A similar study, carried out by **Paltiel et al**, investigated testing strategies for a mid-sized college campus utilizing a compartmental model and assuming a test sensitivity of just 70%, without directly modeling viral load or test limit of detection. In this less complicated and more straightforward model, simulations revealed that testing students every 2-3 days was necessary to avoid uncontrolled outbreak. Analyses that varied test sensitivity and frequency across plausible ranges demonstrated a closer association of test frequency with infection control. The wide variety of tests with varying turn-around times and sensitivity allow for local authorities to choose multiple methods to achieve goals while respecting potential constraints such as budget availability.[13]

Modeling conducted by **Imperial College London**, and based on assumptions derived from the United Kingdom, reinforced that testing frequency is a primary driver in infection reduction. Using a micro-simulation model, the authors found that weekly testing of healthcare workers reduces R_0 by an additional 23% in addition to self-isolation of symptomatic individuals. Additionally, a large reduction in test sensitivity had relatively small impacts on reduction in infectiousness.[34]

Several assumptions and limitations were noted in these studies, principally around viral dynamics and its effect on test sensitivity, proportion of asymptomatic spread, as well as efficacy of isolation strategies after positive tests. However, in each case researchers utilized best available evidence and tested uncertainty through sensitivity analysis. In sum, across a wide variety of modeling techniques and research groups, test frequency is repeatedly shown to impact infection reductions more significantly than test sensitivity.

Appendix B: Testing Protocols and Estimation of Testing Needs

Nursing homes and residential care facilities house approximately 2.2 million residents and employ over 1.2 million workers.[35] There are approximately 50 million students in K-12 public schools and 8.2 million Americans are employed by public schools including 5.5 million teachers.[36,37]

Table B1 lists the testing strategies for both K-12 and nursing homes/residential care facilities for the estimate of testing needs for each scenario of population risk. The testing strategy for K-12 schools incorporates recommendations that schools consider prioritizing reopening grades K-5, whose students are not able to learn as efficiently online, to allow for a partial reopening in the orange risk level, but not fully reopening until the school district is considered to be lower risk. The nursing home and residential care facility testing strategy reflect recently released CMS guidance on nursing home testing, which focuses on screening staff regularly and surge testing facilities when an active infection is found.

Table B1 – Example screening strategy by risk level for selected populations

Risk Level	Public Education Teachers and Staff	Public Education - Students K-5	Public Education - Students 6-12	Nursing Home and Residential Care Facility - Staff	Nursing Home and Residential Care Facility - Residents
Green	Ongoing diagnostic testing as needed and general community surveillance	Ongoing diagnostic testing as needed and general community surveillance	Ongoing diagnostic testing as needed and general community surveillance	Tested monthly. Surge tested when an active infection is found (estimated as requiring an additional 3 tests per person per year)	Surge tested when an active infection is found (estimated as requiring an additional 3 tests per person per year)
Yellow	Tested once every two weeks	Tested once every two weeks	Tested once every two weeks	Tested weekly (no surge testing because CMS guidelines state "surge testing" can be performed every 3-7 days)	Surge tested when an active infection is found (estimated as requiring an additional 52 tests per person per year)
Orange	Tested twice a week	Tested twice a week	Ongoing diagnostic testing as needed and general community surveillance	Tested twice per week (no surge testing required)	Surge tested when an active infection is found (estimated as requiring an additional 52 tests per person per year)
Red	Tested once every two weeks	Ongoing diagnostic testing as needed and general community surveillance	Ongoing diagnostic testing as needed and general community surveillance	Tested twice per week (no surge testing required)	Residents surge tested when an active infection is found (estimated as requiring an additional 52 tests per person per year)

We estimated current Covid-19 county level risk as determined by prevalence on of September 2, 2020 by accessing data from the Harvard Global Health Institute COVID Risk Levels Dashboard.[38] We downloaded county-level risk levels and matched county risk level to population as determined by the 2010 U.S. Census population estimates for 3,111 of 3,144 U.S. counties or county equivalents. Each county had one of four color coded risk levels, as defined by the Harvard University Key Metrics for COVID Suppression "bucket" risk levels of green, yellow, orange, and red.[21] We summed county population for each risk level and found the percentage of total identified population for each risk level. This current prevalence constitutes the baseline Scenario A. Scenarios B and C are predicated on improved infection transmission control resulting in lower levels of community spread and decreasing risk throughout the nation.

Using the nursing home, residential care, and K-12 population number above, assuming proportional distribution across the country, and utilizing the testing strategies outlined in Table B1, we are able to estimate the number of tests required monthly for both K-12 public schools (Table B3) and nursing homes and residential care facilities (Table B4), rounded to the nearest 100,000.

Table B2 – Percent of the relevant population in each risk category for the three scenarios

Risk Level	Scenario A	Scenario B	Scenario C
Green (< 1 daily new case per 100,000 people)	1%	20%	60%
Yellow (1 – 10 daily new cases per 100,000 people)	46%	50%	30%
Orange (10 – 25 daily new cases per 100,000 people)	45%	25%	10%
Red (> 25 daily new cases per 100,000 people)	8%	5%	0%

Table B3 – Estimated monthly testing needs for K-12 public schools

Risk Level	Scenario A Test Needs	Scenario B Test Needs	Scenario C Test Needs
Green	0	0	0
Yellow	57,200,000	62,200,000	37,300,000
Orange	117,400,000	54,700,000	23,800,000
Red	1,400,000	1,300,000	-
Total	**176,000,000**	**118,100,000**	**61,100,000**

Table B4 – Estimated monthly testing needs for nursing homes and residential care facilities

Risk Level	Scenario A Test Needs	Scenario B Test Needs	Scenario C Test Needs
Green	<100,000	500,000	1,400,000
Yellow	6,800,000	7,400,000	4,400,000
Orange	9,000,000	4,600,000	2,000,000
Red	1,600,000	1,400,000	-
Total	**17,400,000**	**13,900,000**	**7,800,000**

Endnotes

1 Huff, H.V. and A. Singh, *Asymptomatic Transmission During the Coronavirus Disease 2019 Pandemic and Implications for Public Health Strategies*. Clinical Infectious Diseases, 2020.

2 The COVID Tracking Project, *US Historical Data*. 2020; Available from: https://covidtracking.com/data/national.

3 Duke Today Staff, *Duke Reopening FAQ*. 2020; Available from: https://today.duke.edu/2020/07/duke-reopening-faq.

4 The Rockefeller Foundation, *Covid-19 National Testing & Tracing Action Plan*. 2020, The Rockefeller Foundation.

5 Jha, A., *America Needs to Radically Rethink Our Covid-19 Testing Approach*, in *Time Magazine*. 2020.

6 Kretzschmar, M.E., et al., *Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study*. The Lancet Public Health, 2020. 5(8): p. e452-e459.

7 McClellan, M., C. Rivers, and C. Silcox, *Legislative and Regulatory Steps for a National COVID-19 Testing Strategy*. 2020, Duke-Margolis Center for Health Policy.

8 Larremore, D.B., et al., *Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance*. medRxiv : the preprint server for health sciences, 2020: p. 2020.06.22.20136309.

9 Arizona State University, *Testing Commons - COVID-19 Diagnostic Commons*. 2020 [August 31, 2020]; Available from: https://chs.asu.edu/diagnostics-commons/testing-commons.

10 Gottlieb, S., et al., *National coronavirus response: a road map to reopening*. AEI Paper & Studies, 2020.

11 Bogler, A., et al., *Rethinking wastewater risks and monitoring in light of the COVID-19 pandemic*. Nature Sustainability, 2020: p. 1-10.

12 Wu, F., et al., *SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases*. medRxiv : the preprint server for health sciences, 2020.

13 Paltiel, A.D., A. Zheng, and R.P. Walensky, *Assessment of SARS-CoV-2 Screening Strategies to Permit the Safe Reopening of College Campuses in the United States*. JAMA network open, 2020. 3(7): p. e2016818-e2016818.

14 Centers for Medicare & Medicaid Services, *Interim Final Rule (IFC), CMS-3401-IFC, Additional Policy and Regulatory Revisions in Response to the COVID-19 Public Health Emergency related to Long-Term Care (LTC) Facility Testing Requirements and Revised COVID-19 Focused Survey Tool*. 2020 [August 31, 2020]; Available from: https://www.cms.gov/medicareprovider-enrollment-and-certificationsurveycertificationgeninfopolicy-and-memos-states-and/interim-final-rule-ifc-cms-3401-ifc-additional-policy-and-regulatory-revisions-response-covid-19.

15 U.S. Department of Health and Human Services, *Trump Administration Uses Defense Production Act to Aid Our Most Vulnerable*. 2020, U.S. Department of Health & Human Services.

16 New York State Department of Health, *DAL 20-14: Required COVID-19 Testing for all Nursing Home and Adult Care Facility Personnel*. 2020, New York State Department of Health.

17 Lennon, N.J., et al., *Comparison of viral levels in individuals with or without symptoms at time of COVID-19 testing among 32,480 residents and staff of nursing homes and assisted living facilities in Massachusetts*. medRxiv : the preprint server for health sciences, 2020.

18 Solis, S., *Coronavirus in Massachusetts: Mobile testing program now available for long-term care facilities where no one has COVID-19 symptoms*, in *MassLive*. 2020.

19 Peiser, J., *The University of Arizona says it caught a dorm's covid-19 outbreak before it started. Its secret weapon: Poop.*, in Washington Post. 2020.

20 The Rockefeller Foundation, *Covid-19 Testing Solutions Group*. 2020 [September 2, 2020]; Available from: https://www.rockefellerfoundation.org/covid-19-national-testing-solutions-group/.

21 Harvard Global Health Institute and Harvard Edmond J. Safra Center for Ethics, *Key Metrics for COVID Suppression*. 2020, Harvard Global Health Institute and Harvard Edmond J. Safra Center for Ethics.

22 U.S. Bureau of Labor Statistics, *Occupational employment statistics, May 2019*. 2019 [September 3, 2020]; Available from: https://www.bls.gov/oes/tables.htm.

23 Centers for Medicare & Medicaid Services, *CLIA University Lab Testing FAQs*. 2020 [September 2, 2020]; Available from: https://www.cms.gov/files/document/clia-univeristy-lab-testing.pdf

24 Touchstone, L.A., *Illinois rapid saliva test for COVID-19 now operating under FDA Emergency Use Authorization*, in *Illinois News Bureau*. 2020.

25 Broad Institute, *Fall 2020 College and University Screening*. 2020, Broad Institute.

26 Office of Governor Gavin Newsom, *Governor Newsom Announces Major Plan to More than Double State's Testing Capacity, Reduce Turnaround Time*. 2020, Office of Governor Gavin Newsom.

27 Schneider, M., et al., *From Development to Market: Understanding COVID-19 Testing and Its Challenges*. 2020, Duke-Margolis Center for Health Policy.

28 U.S. Department of Health and Human Services, *Trump Administration Will Deploy 150 Million Rapid Tests in 2020*. 2020 [September 1, 2020]; Available from: https://www.hhs.gov/about/news/2020/08/27/trump-administration-will-deploy-150-million-rapid-tests-in-2020.html.

29 Kaiser Health News, *KHN Morning Briefing: Who Gets Rapid COVID Tests First? HHS Sending To States For Assisted Living Facilities, Schools*. 2020 [September 2, 2020]; Available from: https://khn.org/morning-breakout/who-gets-rapid-covid-tests-first-hhs-sending-to-states-for-assisted-living-facilities-schools/.

30 U.S. Food and Drug Administration, *FAQs on Testing for SARS-CoV-2*. 2020, U.S. Food and Drug Administration.

31 Becton, Dickinson and Company, *BD Partners with U.S. Government on $70 Million Manufacturing Infrastructure Project for Mass Vaccination Campaigns*. 2020, Becton, Dickinson and Company.

32 National Institutes of Health, *Rapid Acceleration of Diagnostics (RADx)*. 2020 [August 31, 2020]; Available from: https://www.nih.gov/research-training/medical-research-initiatives/radx.

33 The Rockefeller Foundation, *Arkansas and Rhode Island Join Bipartisan Interstate Testing Compact, Expanding Agreement To Ten States*. 2020, The Rockefeller Foundation.

34 Grassly, N.C., et al., *Comparison of molecular testing strategies for COVID-19 control: a mathematical modelling study*. The Lancet Infectious Diseases, 2020.

35 Harris-Kojetin, L., et al., *Long-term care providers and services users in the United States, 2015–2016*. Vital and Health Statistics, 2019. 3(43).

36 National Center for Education Statistics, *Fast Facts: Back to school statistics*. 2020; Available from: https://nces.ed.gov/fastfacts/display.asp?id=372.

37 U.S. Bureau of Labor Statistics, *A look at elementary and secondary school employment*. 2018; Available from: https://www.bls.gov/opub/ted/2018/a-look-at-elementary-and-secondary-school-employment.htm.

38 Harvard Global Health Institute and Harvard Edmond J. Safra Center for Ethics, *COVID Risk Levels Dashboard*. 2020, Harvard Global Health Institute and Harvard Edmond J. Safra Center for Ethics.