Return to on-site SARS-CoV-2 testing protocols

color

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Executive Summary

The purpose of Color's SARS-CoV-2 testing protocols is to create a framework that can be used by institutions and employers to quickly detect and prevent SARS-CoV-2 outbreaks in their populations, while protecting the health and wellbeing of individuals.

Testing of symptomatic individuals and individuals with known or suspected exposure to COVID-19 is important for containing outbreaks in workplaces and institutional settings, but is not sufficient on its own.

A proactive testing strategy can be used to effectively identify and isolate individuals who are infected, but not currently showing symptoms, and remove them before other individuals become infected.

To demonstrate the value of proactive testing, we used an extended SEIR epidemiological model (SEIRS+) to evaluate the impact different testing cadences would have on mitigating SARS-CoV-2 outbreaks in workplace settings of 100 and 1,000 individuals.

Based on our model, a once per week proactive testing cadence of all individuals can greatly reduce the chance of an outbreak event, with minimal disruption to daily operations.

The use of a semi-weekly proactive testing cadence reduces the chance of an outbreak even further and may be useful in populations with high-risk or vulnerable populations and/or settings where administrative modifications and mitigation strategies cannot be implemented.

Proactive testing for early identification of SARS-CoV-2 will be essential for containing outbreaks in workplaces, institutions, and other congregate settings to help mitigate widespread transmission in the community.

Background

Coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The high transmissibility of SARS-CoV-2 has resulted in governments around the world issuing shelter in place orders and restrictions on travel. In March of 2020, SARS-CoV-2 was declared a global pandemic by the World Health Organization.[1]

SARS-CoV-2 is primarily spread from person-to-person through respiratory droplets.[2] In addition, infected individuals can spread the virus without having symptoms, with peak infectiousness occurring a few days before or at symptom onset, and many individuals presenting with mild or no symptoms.[3,4]

Indoor environments that promote prolonged, close contact between individuals, facilitate transmission of SARS-CoV-2 and can lead to superspreading events.[5,6] These types of high-risk environments are common in workplaces, academic institutions, and other community settings.[7,8] Superspreading events in these types of settings produce large numbers of cases in a short period of time, placing a huge burden on the surrounding communities and health-systems. Therefore, the effectiveness of mitigation measures used in these types of settings is a major public health concern. Global efforts to develop therapeutic interventions and vaccines for SARS-CoV-2 infection are currently underway, however, it will likely be months to years before either of these become widely available. Until then, the use of widespread SARS-CoV-2 viral testing and mitigation strategies will be essential for allowing institutions to re-open and will play a crucial role in preventing superspreading events in communities.

SARS-CoV-2 testing for institutions

There are two types of SARS-CoV-2 tests:

1. **Viral tests** (nucleic acid or antigen tests), which are used to diagnose current infection, and
2. **Antibody tests**, which are used to identify whether an individual was previously infected.

Institutions intending to use SARS-CoV-2 viral testing for their population, should ensure the privacy and confidentiality of individuals is protected, and that testing procedures are consistent with all applicable laws and regulations.

For employers, the US Equal Employment Opportunity Commission (EEOC) has stated that viral testing is permissible under the American Disability Act (ADA) and employers may require their employees to undergo viral testing to detect active infections. At this time (07/08/2020), the EEOC has determined that antibody testing does not meet the ADA's "job related and consistent with business necessity" standard for medical testing and therefore cannot be required by employers. As such, antibody testing is not included in these protocols. Further information on the use of antibody testing in the workplace can be found in the appendix (Appendix A).

Here, we outline the following use cases for SARS-CoV-2 viral tests to ensure a safe return to on-site transition: 1) symptomatic testing, 2) re-entry testing, and 3) proactive testing. Workplaces, academic institutions, and other settings where individuals are in close quarters for long periods of time may use these testing protocols to mitigate and contain SARS-CoV-2 transmission in their population, while maintaining safe operations.

High risk environments that are susceptible to superspreading

Workplaces

Academic Institutions

Other High-density Settings

Testing protocols for mitigating SARS-CoV-2 transmission

01 - Symptomatic testing

Individuals who report current symptoms are tested

02 - Re-entry testing

Individuals without symptoms are tested before entering a specified environment or setting

03 - Proactive testing

Individuals without symptoms are tested regularly at a specified cadence

Symptomatic testing

The US Centers for Disease Control and Prevention (CDC) recommends viral SARS-CoV-2 testing for any individual with signs or symptoms compatible with COVID-19. Individuals with COVID-19 report a wide-range of symptoms, including fever, cough, fatigue, shortness of breath, and loss of taste or smell.[9,10] However, no single symptom or spectrum of symptoms is sufficiently sensitive or specific to reliably diagnose or exclude COVID-19. Therefore, individuals reporting symptoms of illness are recommended to stay home, separate themselves from others, and should be evaluated by a healthcare provider to determine whether SARS-CoV-2 viral testing is warranted.

Re-entry testing

Re-entry testing involves testing asymptomatic individuals prior to returning on-site in order to minimize the risk of introducing SARS-CoV-2 cases. The testing protocol and criteria for re-entry should be dependent on the reason and length of time of an individual's absence. Below we describe three different re-entry testing protocols to return to site.

Initial testing before re-entry to site

Initial viral testing of all individuals prior to returning on-site reduces the probability of immediately introducing SARS-CoV-2 cases. Institutions implementing an initial testing before re-entry program should have all individuals undergo SARS-CoV-2 viral testing one to two days before their intended re-entry date. A negative test result should be required prior to returning on-site. In addition, individuals should be symptom free and have no recent exposure to individuals with a known or suspected COVID-19 diagnosis (Figure 1).

Figure 1. Suggested re-entry criteria for individuals returning on-site

In some cases, institutions may choose to require two viral tests prior to re-entry in order to further reduce the possibility of introducing SARS-CoV-2 cases on-site (Appendix B).

This re-entry protocol can be used to clear individuals at initial return to site and for any subsequent re-entry events — such as returning on-site after traveling, holiday breaks, or any other extended period of time (e.g., more than seven days).

Re-entry after COVID-19 exposure

Current CDC guidance recommends testing all asymptomatic individuals with close contact to a known or suspected COVID-19 case.[11] In most cases, asymptomatic individuals who have been in close contact with a known or suspected COVID-19 case should self-quarantine for 14 days in order to prevent transmission.

In workplace settings, critical infrastructure employees who have been exposed to a known or suspected COVID-19 case may continue to work as long as they remain symptom free and additional precautions are in place, per CDC guidelines.[12] These additional precautions may include, but are not limited to: regular symptoms monitoring, the required use of face masks, and temperature checks. Employees should adhere to these additional precautions for at least 14 days after the last exposure. In addition, employers may also choose to use a serial testing strategy (e.g., testing employees every three days) as an added precaution to monitor exposed employees and reduce transmission in the workplace.[12]

Re-entry after isolation for individuals with COVID-19

Institutions should have clear protocols in place for how to modify operations in the event that an individual tests positive for SARS-CoV-2 viral infection. The rapid identification, isolation, and support of individuals who test positive for SARS-CoV-2 will be essential for preventing further transmission in both the institution and community. The CDC currently provides guidance for three strategies for discontinuing isolation of individuals who have tested positive for SARS-CoV-2 (Figure 2).[11] Institutions should determine which de-isolation strategy or combination of strategies would be most appropriate to implement in their facility.

Figure 2. Strategies for discontinuing isolation of individuals with COVID-19

De-isolation strategies for individuals who have **not had symptoms**	De-isolation strategies for individuals who have **had symptoms**
Test-based strategy: • Two consecutive negative SARS-CoV-2 viral tests from at least two respiratory samples collected ≥ 24 hours apart	**Test-based strategy:** • Two consecutive negative SARS-CoV-2 viral tests from at least two respiratory samples collected ≥ 24 hours apart
Symptom-based strategy: • At least 10 days since first positive SARS-CoV-2 viral test • No symptoms	**Time-based strategy:** • At least 10 days since first symptoms appeared • At least 24 hours have passed since resolution of fever (without using fever reducers) and improvement in symptoms

Notes: CDC guidance current as of 07/19/2020[11]

Proactive testing

Proactive testing is a powerful control measure that can be used to head off the spread of SARS-CoV-2 in workplaces, academic institutions, and other congregate settings.[13] Individuals infected with SARS-CoV-2 may not show symptoms because they are asymptomatic carriers or they are in the presymptomatic phase of the infection. The aim of proactive testing is to identify and isolate these individuals, who are infected but not currently showing symptoms, and remove them before other individuals become infected. To date, several health systems have used proactive testing strategies to successfully identify and isolate asymptomatic individuals, preventing further transmission through early containment.[14,15]

For institutions implementing a proactive testing strategy, one of the most important decisions to make is how often to perform testing. To be effective, testing must be frequent enough that new introductions and asymptomatic/presymptomatic cases of SARS-CoV-2 are detected and removed before transmission occurs. Many factors contribute to choosing an appropriate testing cadence, including population size and setting, the types of controls and mitigation measures implemented to reduce transmission, and the prevalence of infection in the community. To demonstrate the utility of proactive testing in high-density settings, we used an extended SEIR epidemiological model (SEIRS+) to evaluate different proactive testing cadences in a workplace setting of 100 and 1,000 people.

SEIRS+ model description

Mathematical models, such as the SEIR model, are frequently used to model the spread of disease in a population. Standard SEIR models are compartmental models, meaning they track the proportion of the population in different disease states over time. SEIR models include compartments for susceptible (S), exposed (E), infectious (I), and recovered (R) individuals. Over time, individuals within the population move between these compartments at rates determined by the disease parameters. When susceptible (S) individuals become infected, they are not immediately infectious and are placed in the exposed (E) compartment. Once individuals become infectious, they progress to the infectious (I) and, eventually, recovered (R) compartments.

Here we used the SEIRS+ model, developed by Ryan McGee, Carl Bergstrom, and colleagues at the University of Washington, to evaluate proactive testing cadences in the workplace. The SEIRS+ model is an extended SEIR model, which incorporates the effects of stochastic dynamics, network structure, SARS-CoV-2 testing, and additional interventions in the workplace. Further information and code for the SEIRS+ model can be found at https://github.com/ryansmcgee/seirsplus. Using this model, we evaluated the impact of weekly and semi-weekly proactive testing as a mitigation strategy, within a large (n = 1,000) and small (n = 100) workplace.

Proactive testing strategies evaluated in models

01 - Semi-weekly proactive testing

All individuals are tested twice per week, every three to four days.

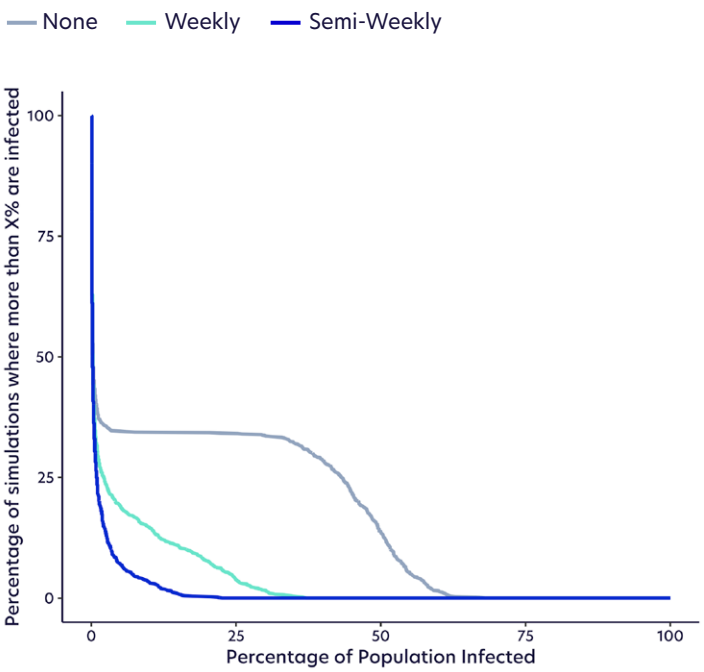
02 - Weekly proactive testing

All individuals are tested once per week, every seven days.

03 - No proactive testing

Individuals with sufficient symptoms quarantine and are evaluated by a healthcare provider.

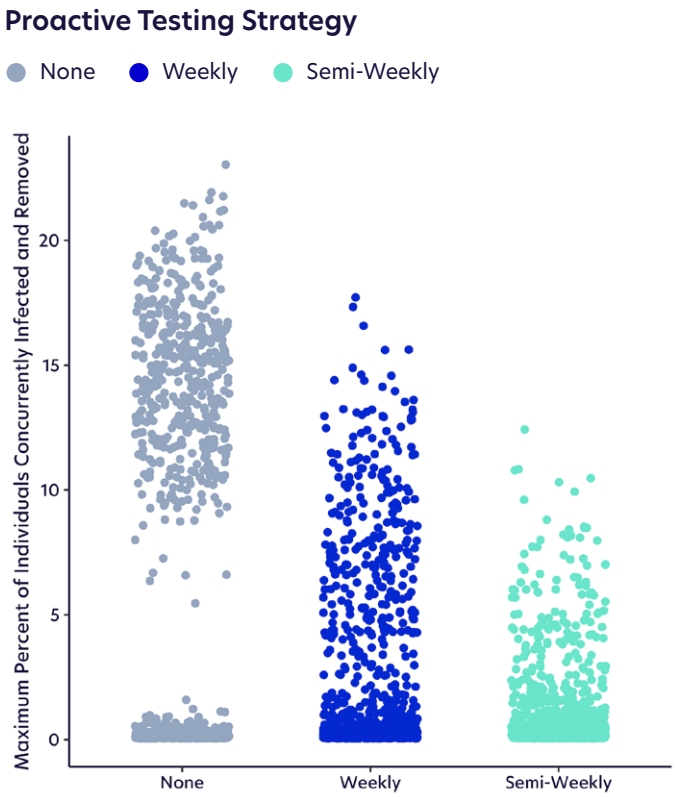
Figure 3. Total percent of a 1000-person workforce infected after a single SARS-CoV-2 case is introduced into the workplace under different testing conditions. The cumulative distribution of results from 1000 simulation runs are shown for each testing strategy.



Proactive testing for large populations (1,000 employees)

To evaluate the impact that proactive testing and subsequent quarantine would have on the size and frequency of SARS-CoV-2 outbreaks in an employee population of 1,000 individuals, we modeled three testing strategies using 1) a semi-weekly proactive testing cadence, 2) a weekly proactive testing cadence and 3) no proactive testing. We used a 1-day turn-around time for test results in the model. In each simulation, we modeled the path of an outbreak that would occur given the introduction of a single individual with SARS-CoV-2 into the population. To account for variability of possible outcomes, we ran 1,000 iterations for each testing strategy. We used two metrics to compare the effectiveness of each testing strategy: the total percent of the population infected over the course of an outbreak (Figure 3) as well as the maximum number of employees who would be concurrently infected and removed from work at any given time (Figure 4). We found that the use of proactive testing strategies improved both metrics compared to using no proactive testing.

Figure 4. Distribution of the maximum percent of employees concurrently infected and/or removed by proactive testing strategy (n = 1,000)



Simulations using a weekly or semi-weekly proactive testing strategy resulted in a lower total percent of the population infected compared to simulations using no proactive testing strategy (Figure 3). We found that when no proactive testing strategy was used, almost half (44.0%) of all of SARS-CoV-2 introductions resulted in outbreaks where 5.0% or more of employees were concurrently infected and/or removed from the workplace (Figure 4). The addition of weekly proactive testing in this population performed better, with less than a quarter (21.8%) of all introductions leading to 5.0% or more of the workforce being affected concurrently (Figure 4). The use of a semi-weekly proactive testing cadence was most effective in preventing large outbreaks, with only 6.3% of all introductions resulting in outbreaks where 5.0% or more of employees were concurrently infected and/or removed (Figure 4).

Figure 5. Total percent of a 100-person workforce infected after a single SARS-CoV-2 case is introduced into the workplace under different testing conditions. The cumulative distribution of results from 1000 simulation runs are shown for each testing strategy.

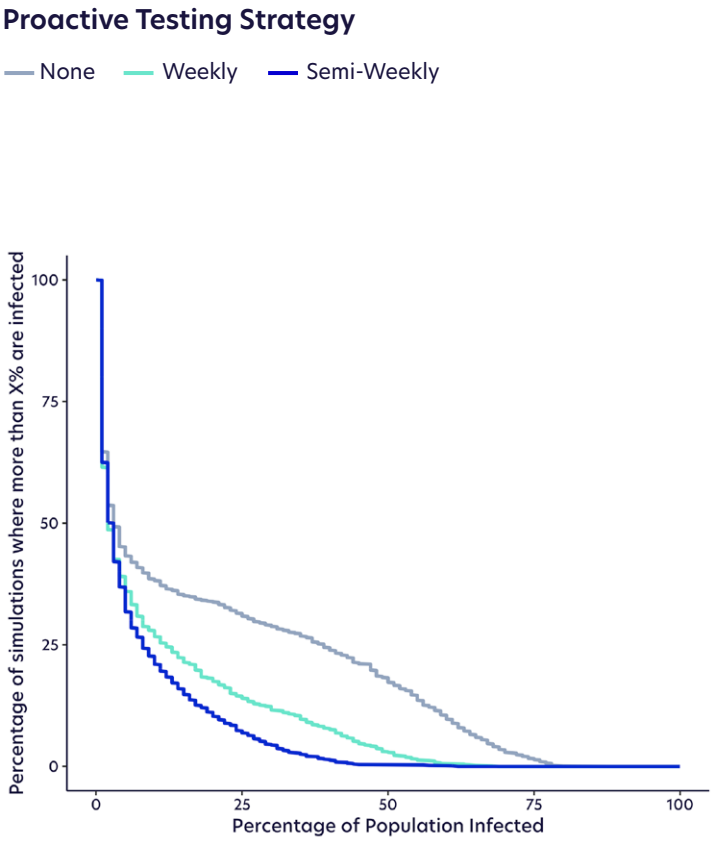
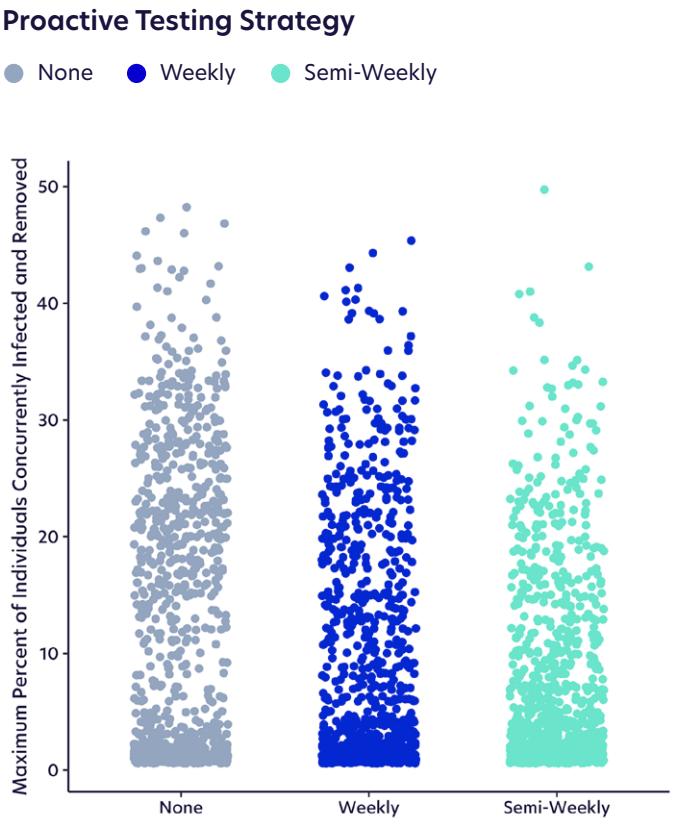


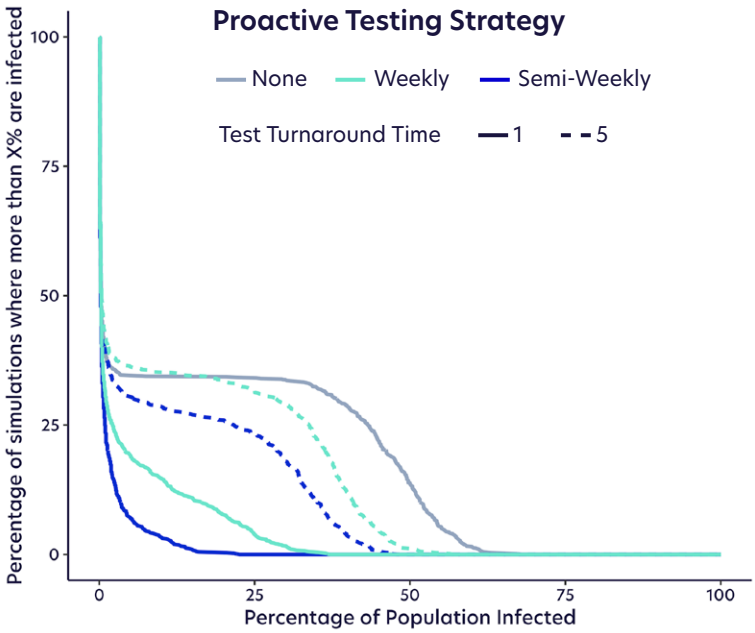
Figure 6. Distribution of the maximum percent of employees concurrently infected and/or removed by proactive testing strategy (n = 100)



Proactive testing for small populations (100 employees)

In small institutions with fewer individuals, introductions of SARS-CoV-2 can easily result in outbreaks that concurrently affect a large proportion of the workforce. Using the same assumptions and three testing protocols as those in the above model, we evaluated the impact of proactive testing in a workplace with a population of 100 employees. Results were similar to those found in the larger population of 1,000 employees, with more frequent proactive testing resulting in a lower total percent of the population infected (Figure 5). When no proactive testing strategy was used in this population, we found that 45.0% of SARS-CoV-2 introductions would lead to 10.0% or more of employees being concurrently infected or removed from the workplace (Figure 6). Using a weekly or semi-weekly testing strategy, outbreaks affecting 10.0% or more of employees resulted from 35.0% and 28.3% of SARS-CoV-2 introductions, respectively (Figure 6).

Figure 7. Impact of turnaround time and proactive testing strategy on the distribution of total infections in an outbreak under different testing strategies (n = 1,000)



Testing turnaround time

Test turnaround (TAT) time is defined as the length of time between specimen collection and return of results. For proactive testing, a short test TAT is necessary to effectively mitigate and contain outbreaks. Delays in TAT can lead to increased levels of SARS-CoV-2 infection in the population, as it may not be feasible to preemptively quarantine those without symptoms. Therefore, short test TAT's are essential for identifying and isolating infectious individuals, and in turn, containing outbreaks. To evaluate the importance of test TAT, we modeled different testing cadences and test TAT's, in a population of 1,000 individuals, using the same assumptions as those used in the previous models. For simulations where no proactive testing was used, we assume that individuals with sufficient symptoms will quarantine and be evaluated by a healthcare provider.

Here we simulate the potential outcomes of using no proactive testing strategy, compared to using a proactive testing strategy at a semi-weekly testing cadence, with both a short test TAT (one day) and a long test TAT (five days). When no proactive testing strategy was used, almost half (44.0%) of all introductions resulted in outbreaks affecting 5.0% or more of the population (Figure 7). In comparison, using a proactive testing strategy at a semi-weekly testing cadence with a short test TAT (one day), resulted in only 6.3% of introductions affecting 5.0% or more of all individuals (Figure 7). However, when the test TAT was increased to five days, the benefit of using a more frequent semi-weekly proactive testing cadence was lost. Similar to simulations where no proactive testing strategy was used, semi-weekly testing with a five day test TAT resulted in 41.5% of introductions producing outbreaks that affected 5.0% or more of individuals (Figure 7). These results suggest that longer test TAT's can dramatically reduce the effectiveness of proactive testing strategies, due to delays in identifying and removing infectious individuals.

Conclusion

In the absence of a vaccine, frequent introductions of SARS-CoV-2 into an high-density setting and the ensuing outbreaks pose an ongoing threat to both the community's and the individuals' safety. Call centers, meat processing facilities, universities, and other congregate settings, provide favorable environments for SARS-CoV-2 transmission and have been tied to superspreading events around the world.[7,8] As a result, institutions will need to have clear policies and procedures in place to mitigate the risk of transmission when bringing individuals back on-site. Mitigation strategies, such as administrative and engineering controls, as well as viral testing for symptomatic individuals and testing for re-entry, can reduce the risk of transmission in these settings. Using the SEIRS+ model, we demonstrate that proactive testing, at a weekly or semi-weekly cadence, is a highly effective strategy for mitigating SARS-CoV-2 transmission in both small and large populations.

Taken together, the use of mitigation strategies and these viral testing protocols in institutional settings, such as workplaces and academic institutions, allows for the rapid detection and containment of SARS-CoV-2 outbreaks, while ensuring continuity of operations and maintaining the health and safety of individuals.

Appendix

A. Antibody testing in the workplace

Antibody tests, also known as serology tests, detect the presence of antibodies generated in response to SARS-CoV-2 infection. While the detection of SARS-CoV-2 specific antibodies may provide evidence of prior infection, at this time, it is unknown whether these results prove immunity or resistance to re-infection.[16] Validation and standardization of antibody tests for the purpose of informing use in the clinic and in public health applications, is still needed. Furthermore, the CDC's Interim Guidelines for Antibody Testing does not recommend the use of antibody testing for making decisions about whether employees return to work.[17] Based on these guidelines, the EEOC has determined that, at this time, antibody testing does not meet American Disabilities Act standards and employers cannot require employees to undergo antibody testing prior to entering the workplace.[18]

B. Repeat testing protocol for re-entry

Some employers may choose to require that employees undergo two SARS-CoV-2 viral tests prior to entering the workplace. The use of repeat testing further reduces the likelihood of introducing SARS-CoV-2 into the workplace. For employers utilizing the repeat testing protocol for re-entry, two viral tests should be administered 24 - 48 hours apart and as close to the start date as possible. Both tests should be administered no more than four days before returning to work, and one test must be administered two days before the employees start date. Under this protocol, employees for whom both SARS-CoV-2 tests are negative, as well as no symptoms or exposures are reported, are cleared to re-enter the workplace.

C. Epidemiological Model Parameters

For this analysis, we used a network model to simulate the infection dynamics of SARS-CoV-2. The code to perform these simulations is open source and can be found at https://github.com/ryansmcgee/seirsplus. For each testing cadence and population size, we performed the simulation 1000 times to observe the realized distributions of outcomes for each SARS-CoV-2 introduction into a population.

The network model allows us to simulate each individual person, their specific connections, and the stochastic nature of an outbreak. While classic SEIR models are deterministic and perform well when applied to large populations, they do not take into account random variability in infection dynamics, which can play a larger role in smaller populations. The network model allows us to simulate individual heterogeneity in infectiousness and recovery time across the population. Full details are available on Github, below is a table of key parameter averages used in the simulation:

Table C.1. Model parameters and values

Parameter	Mean Value	Description
R_0	2.0	The R_0, or reproductive number, is the expected average number of secondary infectious cases produced by a single infectious case.
Latent period	3.0 days	The time from exposure to when the individual becomes infectious to others.
Presymptomatic infectious period	2.2 days[19,20]	The period when an individual infected with SARS-CoV-2 is contagious but has not yetdeveloped symptoms.
Incubation period	5.2 days[19,21-24]	The total time from exposure to symptom onset — this is the sum of the latent period and presymptomatic period.
Infectious period	6.2 days[20,25-27]	The time period during which an infected individual is infectious to others. For symptomatic cases, this includes the presymptomatic period.
Test sensitivity	76% while presymptomatic, 80% during first 5 days of infectious period, and decreasing thereafter[28,29]	Probability that a single test will correctly identify an infectious individual as having SARS-CoV-2.
Percent asymptomatic	30%[30-33]	Percentage of individuals infected with SARS-CoV-2 who do not develop symptoms.
Percent symptomatic who self-quarantine	30%	Percentage of symptomatic individuals who develop sufficient symptoms (e.g., fever) that they call in sick and stay home from work.
Test turnaround time	1 day	Length of time between testing and isolation for individuals who receive positive results.

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