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An Analytic Tool for Constructing & Evaluating Testing Strategies for COVID-19

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Abstract

This paper describes the utilization of a mathematical modeling tool for evaluating alternative testing cadences for the SARS-CoV-2 virus that are applicable to any well-contained congregate setting. These settings include long-term care facilities, and public-school systems.

Variables analyzed include population sizes, contagion factor, and unique testing objectives that congregate settings might have (e.g., differing susceptibilities, or varying underlying health conditions). The tool helps evaluate cost vs benefit for a range of testing cadences (e.g., daily, every 2 days, every 3 days, every week, every 2 weeks, every 3 weeks, and every 4 weeks) based on use of a commercially available antigen testing kit that costs $5 per test.

Our method allows public health officials, site managers and/or on-site healthcare workers to generate effective testing plans that align with available resources and support fact-based decision making. We also discuss how this tool can work with vaccine roll-out both in the United States and elsewhere.

Keywords: COVID-19; Mathematical model; Testing tool; Cost-benefit analysis

Introduction

A key lesson learned from the COVID-19 pandemic is that a substantial increase in the rate of testing has the potential to mitigate the impact and potential re-emergence of the pandemic, and its associated toll on humanity. An inability to test the population rapidly and effectively obscures the true scope of the pandemic, prevents an effective coordinated response, results in tremendous loss of life, and significantly impacts economic activity. In June 2020, the U.S. House Energy & Commerce Subcommittee chairman Diana DeGette stated, "If we're going to give the American public confidence so they can resume familiar activities and safely return to work, we need to expand testing to more people, including asymptomatic people" [1]. Today in 2022, as we enter the third year of COVID-19 infections, and as the number of COVID cases from the Delta, Lambda, and Omicron variants escalates [2], test kits are again in short supply as demand for testing surges.

In July 2020, the Rockefeller Foundation [3] pointed out that $50B to $75B would be needed to carry out levels of testing that would contain the spread of COVID-19 in the U.S. It is important, however, to delineate carefully the nature of testing for viral infections in a pandemic, particularly to distinguish between screening testing, diagnostic testing, and surveillance testing [4]. Screening testing is intended to identify infected people who are asymptomatic and do not have known, suspected, or reported exposure to SARS-CoV-2. Diagnostic testing is intended to identify accurately any currently infected patients when those individuals have symptoms consistent with COVID-19, or when that person is asymptomatic but knows they have recently been exposed to SARS-CoV-2. Public health surveillance is the ongoing, systematic collection, analysis, and interpretation of health-related data essential to planning, implementation, and evaluation of public health reporting. Surveillance testing is performed on de-identified specimens, and thus, results cannot be used for individual decision-making.

Screening testing of asymptomatic individuals to detect people who are likely infectious has been critically underused in the COVID-19 pandemic, yet it is one of the most promising tools to combat the pandemic [5]. Successful population screening for SARS-CoV-2 depends on understanding both the spread of the virus between individuals and the spread within the body of a given individual.

SARS-CoV-2 can spread from individuals who are pre-symptomatic, symptomatic, or asymptomatic [6-8] Therefore, diagnosis and isolation based on symptoms alone will not help control the spread of the virus [9-11], primarily because in the early stages of the COVID-19 pandemic, approximately 59% of the spread of the virus resulted from pre-symptomatic or asymptomatic individuals [12]. In addition, asymptomatic patients make up roughly 80% of infected individuals, and the viral loads of these asymptomatic patients are like those of symptomatic patients [13]. Further, children can harbor high levels of SARS-CoV-2, but rarely are symptomatic or express severe disease [14]. Recent information suggests that this is true even for the Delta variant [15] or the Omicron variant [16]. For this reason, it is critical that asymptomatic individuals be tested as part of a comprehensive testing strategy.

The average level of contagion of the wild-type virus, or R_0, was approximately 2.3 [17]. The R_0 parameter represents, on average, how many people an infected person will infect. For this study we used R_0 values of less than 3, which correlate to pandemic values most relevant to 2020. Current data, however, shows that the value of R_0 for mutated variants of the SARs-CoV-2 virus can range from 2.7 to 7 or even higher, as is being seen in the Delta and Omicron variant that is creating havoc now [18-21]. On the other hand, wearing a mask and social distancing has been shown to decrease the value of R_0 for COVID-19 to 1.0-1.5 [17].

The spread of the SARS-CoV-2 virus was seen to be highly clustered and follow the "the law of vital few" or the 80/20 rule [22]. Approximately 20% of the infected cases were observed to be responsible for 80% of all new cases, and ~ 69% of infected individuals do not transmit the SARS-

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CoV-2 virus to anyone else [23]. Identification and isolation of the few potential "super spreaders" is thus of critical importance to control the spread of the virus.

Confirmation that symptomatic individuals are infected by the SARS-CoV-2 virus is done most accurately by using nucleic acid-based tests such as qPCR [24]. These tests, however, are quite expensive (~ $100), require special laboratory resources, and have sample-collection-to-results times of 24-48 hours. Alternative formats for nucleic-acid testing such as isothermal amplification, or use of CRISPR are available, but these tests are also expensive (~ $50) and require special laboratory resources [25,26]

Serologic testing indicates the presence of SARS-CoV-2 antibodies. These antibodies signify the existence of prior infections but cannot be used to establish the presence or absence of acute SARS-CoV-2 infection [27].

On the other hand, tests for viral antigens are inexpensive (~ $5) and provide results in 30 minutes or less, but they do suffer from low analytical sensitivity (i.e., they require greater amounts of viral material to register a positive detection of COVID-19) [5,28,29]. This lack of high sensitivity was one of the reasons that prevented the antigen test kits from being extensively used for testing at the outset of the COVID-19 pandemic. However, the lower sensitivity of the results obtained with the antigen test kits can be overcome by increasing the frequency of testing [11,30].

Considering the aforementioned factors, we chose the BinaxNOW antigen test kit from Abbott Laboratories for calculations in our analytic tool that is delineated below. Its requisite specificity (i.e., low levels of false positives), sensitivity (i.e., low levels of false negatives), rapid response (~15 minutes), and low cost (~ $5) makes it a useful screening test in public settings for the SARS-CoV-2 virus [31,32]. Importantly, these kits are easy-to-use and are being produced by Abbott at a rate of roughly 50 million tests per month [33]. They are also commercially available in retail pharmacies but the price of an individual test at a pharmacy is higher (~ $25) than the price of bulk-packed tests that would be procured for ongoing screening [34]. Two important additional features of these kits are first that each test card contains an RFID code that can be used to support the digitization of the tests results, and second, the antibodies used on the test card to detect the presence of SARS-CoV-2 are directed at the nucleocapsid proteins, not the spike proteins. Thus, this antigen test should effectively detect the known variants of SARS-CoV-2 [35].

Methodology

Understanding the clinical picture of COVID-19

We conducted a literature search to create a clinical picture of the SARS-CoV-2 virus in symptomatic individuals. The key information collected were: 1) the time course of viral load of the wild-type SARS-CoV-2 virus in the nasal passages of infected individuals, 2) the time course of viral-associated symptomology, 3) the probability of transmission of this virus over this time course, and 3) the ability for screening for these viruses using both nucleic acid tests (e.g., qPCR) and antigen tests (e.g., BinaxNow, Abbott). A summary of this meta-analysis is presented in the Results section below.

Scenario modeling

To conduct our analysis, we customized the publicly available computer code [36] in the R programming language that was originally written to implement the SEIR model of Paltiel et al. [37] Our customization of this code allowed us to expand the output parameters and to examine the costs and benefits of varying specific epidemic parameters or changing specific attributes with respect to testing. Our implementation of this computational code can be accessed publicly [38].

For the data presented in this paper, we used a given set of parameters that remained invariant, and then tested the impact of different test cadences, different R_0 values, and different population sizes on the costs and benefits of these testing cadences. The parameters that we kept as invariant in the tool for our calculations were as follows:

1. Number of times per day testing will be done: 1
2. Number of days per week: 5
3. Days of incubation: 3 [39,17]
4. Time to recovery: 10 days [40]
5. Percent asymptomatic advancing to symptoms: 30% [41-43]
6. Test sensitivity: 80% [31,32,44]
7. Test specificity: 98% [31,44]
8. Antigen test kit cost: $5.00 [33]
9. Testing horizon: 80 days

An additional important parameter is that the model allows for "exogenous shocks." That is, it allows the introduction of infections to the population at prescribed intervals and of prescribed size. Unless otherwise noted, we allowed 10 new infections per week into the test populations.

Assumptions for carrying out these tests are as follows. All individuals who test positive will be retested, and if they retest positive, they will be sent home for quarantine for 10 days. We define these individuals as true positives. Individuals who retest negative will be allowed to resume normal activities. They are assumed to be false positives. True positives after quarantine return to normal activities and are not tested again. False positives will remain in the "susceptible" pool and tested according to the scheduled cadence.

Our analytical tool is flexible and allows the user to compare test cadences of daily, every 2 days, every 3 days, weekly, every 2 weeks, every 3 weeks, and every 4 weeks. Moreover, these different test cadences can be repeated for two different test regimens. Thus, over the 16-week test period, the user can try a primary test regimen of any or all the seven cadences listed above and concatenate a secondary test regimen that includes any or all these seven cadences.

For the purposes of this paper, we analyzed the results from four scenarios.

Scenario 1: We used a population size of 30,000 individuals to test three different test regimens. This population size is typical of the total student and staff population of the public school system in a mid-sized county in the United States. The three test cadences examined using the antigen test kit were as follows: 1) daily testing for a given time (i.e., 1 to 15 weeks) followed by a second test regimen of testing every 4 weeks for the remainder of a 16-week test horizon, 2) testing every 2 days for a given period of weeks followed by every 4 weeks, and 3) testing every 3 days for a given period of weeks followed by every 4 weeks.

Scenario 2: We compared the results for three different R_0 values in the model. An R_0 of 2.3 was chosen because it represents the wild-type strain of SARS-CoV-2 [17]. The R_0 of 3.0 was chosen because some variants (e.g., the Delta variant) have an R_0 that is bigger by a factor of 0.3 to 0.7 [18]. The R_0 value of 1.5 was chosen because this is the rate of

spread observed when the population in consideration actively wears masks, practices social distancing, and maintains hand hygiene [17].

Scenario 3: We evaluated a testing strategy for population sizes of ten thousand, one hundred thousand, and 1 million people, respectively. This allowed us to test the scalability of our analytical model.

Scenario 4: We evaluated a testing strategy for a typical long-term-care facility. The size of the population tested in this facility was assumed to be 100 considering both the patients and staff. We assumed that a large percentage of the patients in long-term-care facilities likely have significant underlying health conditions, and therefore, keeping the number of infections to a minimum within the facility is a high priority. Moreover, since visitor access to these facilities is restricted, we assumed that this reduces the possibility of asymptomatic but infected individuals carrying the virus into the facilities. Our computations for long-term care facilities employed the following test parameters: two new outside infections into the facility every four weeks, R_0 of 1.5 (as increased safety protocols are more likely), and a mortality level of infections of 8% [45].

Results

Understanding the clinical picture of COVID-19

A meta-analysis of information summarized from seven published papers is presented in Table 1. Columns 1-5 in Table 1 show the typical daily rates of viral growth in the nasal passages of individuals infected with the SARS-CoV-2 virus (as measured by qPCR), the level of symptomology, and the probability of disease transmission during these time intervals. In the qPCR tests, the virus is detectable in nasal swabs as soon as 1.5 to 2 days post infection, it remains detectable for many days, and usually wanes to undetectable levels by 2 weeks after infection. The nucleic acid assay is, therefore, not necessarily effective as a screening test for infectious virus because the assay can also detect the presence of viral RNA (not necessarily intact viruses), which implies that for certain infected individuals the nucleic acid test will be positive for weeks (if not months) after infection [11,46]. Moreover, the results of the nucleic acid test are typically communicated back to the user 24 to 48 hours after the swab sample is taken.

Thus, decisions based on nucleic acid tests are effectively displaced by 24 to 48 hours from the data shown in Column 5 of Table 1 [47,48]. The typical pattern of viral load in an infected individual as measured by the BinaxNOW antigen test is presented in column 6 of Table 1. These data were adapted from Perchetti et al. [31] and James et al. [44]. This antigen test is not as sensitive as nucleic acid tests for detecting the extremely low viral loads present at the early onset of a SARS-CoV-2 infection. The likely limit of detection of this antigen test is about 100 times less than the qPCR tests (~10E5 cp/ml). Perchetti, et al. [31] have shown that the BinaxNOW card has an analytical sensitivity approximately equivalent to a generic qPCR cycle threshold value of 29 to 30. This antigen test, however, does appear to detect the virus in what could be described as the "Goldilocks" zone, which is the period when an infected individual is most likely to be infectious (i.e., 4-7 days post infection; see Table 1, column 3). Also noteworthy is that antigen tests revert to identification of weak or negative results once the individual's immune system is actively killing the virus and the risk of transmission is low. The analytic specificity of the BinaxNOW card exceeds 98% [44,31]. Different laboratories have determined the level of sensitivity of the BinaxNOW test, and results vary from 52% for asymptomatic persons (83% for symptomatic persons) [44] to 96.5% (95% confidence interval 90.0% -99.3%) [32]. As shown by Paltiel et al. [37] and Larremore, et al. [11], the level of false negatives can be limited by testing at frequent intervals-that is, daily, every 2 days, or every 3 days.

Scenario modeling

Detailed below are results of modeling using the tool we developed for four different scenarios that are described above in the Methods section and which are easily obtained by simply adjusting the different parameters within the tool.

Scenario 1: Table 2 compares three different primary test cadences and one secondary test cadence on 30,000 people, which is, as noted above, typical of the total student and staff population of a mid-sized county public school system in the United States. The data in Table 2 shown in bold font highlight the test conditions that resulted in the best outcomes from combinations of the cadences in terms of low cost, low numbers of people in quarantine, large numbers of infections prevented, and the lowest costs per case averted. The best outcomes occur around weeks 4 to 6 of daily testing followed by every 4-week testing, or around 6 to 8 weeks of every 2-day testing (followed by 4-week testing), or around 9 to 11 weeks of every 3-day testing (followed by every 4-week testing). Comparing these three test cadences shows that primary testing daily would be the most expensive approach both in terms of total cost (~ $4.0M) and cost per case averted (~ $170). The lowest cost alternative is the cadence that uses every 3-day initial testing followed by every 4-week testing. This approach saves about $300K relative to the every-2-day cadence, and about $1.5M relative to the daily cadence. These results demonstrate the value of this modeling approach in providing policymakers with an analytical means of comparing different potential testing scenarios to determine the most efficacious outcomes for the circumstances or available resources. **Scenario 2:** A comparison of output using three different R_0 values in the model is summarized in Table 3. Table 3 includes only those ranges of testing cadences that resulted in the best outcomes in terms of low cost, low numbers of people in quarantine, large numbers of infections prevented, and the lowest costs per case averted.

Results suggest that good hygiene would save approximately $400K in testing costs (i.e., comparing R_0 2.3 to R_0 1.5). If a new variant has an R_0 of 3.0, however, the cadence of testing every 3 days followed by testing every 4 weeks is never able to decrease infections below 45% of the tested population. Remember that in this model, we are allowing new infections to enter this population at rate of 10 new cases per week. In this scenario, one would have to increase the rate of primary testing to every 2 days to see a decrease in new cases to below 20% of the tested population (see Table 3). The every-2-day regimen for a period of 10-12 weeks reduces the infection rate to below 20% at a cost of roughly $4M. Unfortunately, variants with R_0 in the range of 4-7 already have been identified [18, 20, 49,50]. We also tested an R_0 of 6 in our model using the same conditions stated for Table 3, and the only testing cadence that impacted the degree of infection significantly (i.e., 79% of cases averted) was daily testing. The cost of this daily testing schedule was $9,835,355. Clearly, variants with an R_0 greater than 3.0 will be very expensive to manage.

Scenario 3: To determine if the results change appreciably if testing

Days of infection	Viral load/ml typical case [47, 48]	Symptoms for typical case [11, 48]	Transmission probability [11, 48]	Nucleic acid test [47]	Antigen test [44, 31]
1	1.00E+03	None	0%	Weak	Negative
2	1.00E+05	None	<1%	Weak to positive	Weak
3	1.00E+07	None	10%	Positive	Weak to positive
4	1.00E+08	Weak	40%	Positive	Positive
5	1.00E+09	Weak	80%	Positive	Positive
6	1.00E+08	Weak	>80%	Positive	Positive
7	1.00E+07	Yes	60%	Positive	Positive
8	1.00E+06	Yes	50%	Positive	Positive
9	1.00E+05	Weak	20%	Positive	Weak
10	1.00E+05	Weak	<10%	Positive	Weak
11	1.00E+04	None	<10%	Positive	Negative
12	1.00E+04	None	<10%	Positive	Negative
13	1.00E+03	None	<10%	Weak to positive	Negative
14	1.00E+03	None	<10%	Weak to positive	Negative
15	1.00E+03	None	<10%	Weak to positive	Negative
16	1.00E+02	None	<10%	Weak to positive	Negative
17	1.00E+02	None	<10%	Weak to positive	Negative
18	1.00E+01	None	<10%	Negative to weak	Negative
19	1.00E+01	None	<10%	Negative to weak	Negative
20	1.00E+01	None	<10%	Negative to weak	Negative

Table 1: Meta-analysis of clinical study results for COVID-19 tests for symptomatic individuals.

Cadence of primary testing	Weeks of primary testing	Cadence of secondary testing	Total persons tested	Average number In quarantine	Average % true positives in quarantine	Total testing cost	Total infections	Percent infected	Cases averted	Cost per case averted
Daily	1	Every 4 Weeks	2,25,000	1,379	96.70%	$ 1,174,290	29,123	99%	277	$ 4,239
Daily	2	Every 4 Weeks	3,78,834	792	89.20%	$ 1,947,280	22,175	75%	7,225	$ 270
Daily	3	Every 4 Weeks	5,19,963	523	76.80%	$ 2,659,125	12,633	43%	16,767	$ 159
Daily	**4**	**Every 4 Weeks**	**6,56,447**	**455**	**65.70%**	**$ 3,352,295**	**8,117**	**28%**	**21,283**	**$ 158**
Daily	**5**	**Every 4 Weeks**	**7,91,786**	**438**	**56.70%**	**$ 4,041,065**	**5,601**	**19%**	**23,799**	**$ 170**
Daily	**6**	**Every 4 Weeks**	**9,26,660**	**442**	**49.40%**	**$ 4,728,030**	**3,951**	**13%**	**25,449**	**$ 186**
Daily	7	Every 4 Weeks	10,61,250	456	43.60%	$ 5,413,870	2,836	10%	26,564	$ 204
Daily	8	Every 4 Weeks	11,95,639	477	39.10%	$ 6,098,890	2,078	7%	27,322	$ 223
Daily	9	Every 4 Weeks	13,29,872	504	35.60%	$ 6,783,260	1,568	5%	27,832	$ 244
Daily	10	Every 4 Weeks	14,63,980	533	32.80%	$ 7,467,090	1,229	4%	28,171	$ 265
Daily	11	Every 4 Weeks	15,97,982	564	30.60%	$ 8,150,440	1,009	3%	28,391	$ 287
Daily	12	Every 4 Weeks	17,31,891	597	28.80%	$ 8,833,365	869	3%	28,531	$ 310
Daily	13	Every 4 Weeks	18,65,717	631	27.30%	$ 9,515,895	784	3%	28,616	$ 333
Daily	14	Every 4 Weeks	19,99,465	665	26.00%	$ 10,198,045	736	3%	28,664	$ 356
Daily	15	Every 4 Weeks	21,33,140	699	24.80%	$ 10,879,835	713	2%	28,687	$ 379
Every 2 Days	1	Every 4 Weeks	1,47,126	1,441	97.90%	$ 779,545	29,323	100%	77	$ 10,124
Every 2 Days	2	Every 4 Weeks	2,23,717	1,167	95.80%	$ 1,166,695	28,300	96%	1,100	$ 1,061
Every 2 Days	3	Every 4 Weeks	2,97,344	833	91.80%	$ 1,535,370	23,878	81%	5,522	$ 278
Every 2 Days	4	Every 4 Weeks	3,66,784	589	85.30%	$ 1,883,135	16,959	58%	12,441	$ 151
Every 2 Days	5	Every 4 Weeks	4,33,293	454	77.20%	$ 2,218,215	11,022	37%	18,378	$ 121
Every 2 Days	**6**	**Every 4 Weeks**	**4,98,186**	**389**	**69.20%**	**$ 2,546,870**	**7,139**	**24%**	**22,261**	**$ 114**
Every 2 Days	**7**	**Every 4 Weeks**	**5,62,247**	**362**	**62.40%**	**$ 2,872,335**	**4,806**	**16%**	**24,594**	**$ 117**
Every 2 Days	**8**	**Every 4 Weeks**	**6,25,866**	**354**	**57.10%**	**$ 3,196,110**	**3,411**	**12%**	**25,989**	**$ 123**
Every 2 Days	9	Every 4 Weeks	6,89,229	357	53.00%	$ 3,518,885	2,560	9%	26,840	$ 131
Every 2 Days	10	Every 4 Weeks	7,52,427	366	49.80%	$ 3,840,995	2,030	7%	27,370	$ 140
Every 2 Days	11	Every 4 Weeks	8,15,507	379	47.30%	$ 4,162,610	1,699	6%	27,701	$ 150
Every 2 Days	12	Every 4 Weeks	8,78,497	393	45.30%	$ 4,483,830	1,493	5%	27,907	$ 161
Every 2 Days	13	Every 4 Weeks	9,41,411	409	43.50%	$ 4,804,710	1,368	5%	28,032	$ 171
Every 2 Days	14	Every 4 Weeks	10,04,260	425	42.00%	$ 5,125,285	1,298	4%	28,102	$ 182
Every 2 Days	15	Every 4 Weeks	10,67,050	442	40.60%	$ 5,445,580	1,264	4%	28,136	$ 194
Every 3 Days	1	Every 4 Weeks	1,14,368	1,553	98.50%	$ 613,835	29,401	100%	undefined	undefined
Every 3 Days	2	Every 4 Weeks	1,64,176	1,437	97.50%	$ 867,630	29,302	100%	98	$ 8,853
Every 3 Days	3	Every 4 Weeks	2,12,825	1,249	96.20%	$ 1,113,725	28,694	98%	706	$ 1,578
Every 3 Days	4	Every 4 Weeks	2,59,674	1,024	94.10%	$ 1,348,765	26,641	91%	2,759	$ 489
Every 3 Days	5	Every 4 Weeks	3,04,403	812	91.20%	$ 1,572,165	22,624	77%	6,776	$ 232
Every 3 Days	6	Every 4 Weeks	3,47,099	649	87.30%	$ 1,785,670	17,530	60%	11,870	$ 150
Every 3 Days	7	Every 4 Weeks	3,88,161	541	82.80%	$ 1,991,960	12,762	43%	16,638	$ 120
Every 3 Days	8	Every 4 Weeks	4,28,057	478	78.40%	$ 2,193,415	9,090	31%	20,310	$ 108
Every 3 Days	**9**	**Every 4 Weeks**	**4,67,172**	**446**	**74.60%**	**$ 2,391,730**	**6,579**	**22%**	**22,821**	**$ 105**
Every 3 Days	**10**	**Every 4 Weeks**	**5,05,774**	**433**	**71.60%**	**$ 2,587,980**	**4,977**	**17%**	**24,423**	**$ 106**
Every 3 Days	**11**	**Every 4 Weeks**	**5,44,034**	**433**	**69.40%**	**$ 2,782,835**	**4,001**	**14%**	**25,399**	**$ 110**
Every 3 Days	12	Every 4 Weeks	5,82,057	438	67.60%	$ 2,976,685	3,425	12%	25,975	$ 115
Every 3 Days	13	Every 4 Weeks	6,19,909	448	66.20%	$ 3,169,775	3,099	11%	26,301	$ 121
Every 3 Days	14	Every 4 Weeks	6,57,628	459	65.00%	$ 3,362,255	2,925	10%	26,475	$ 127
Every 3 Days	15	Every 4 Weeks	6,95,240	470	63.80%	$ 3,554,230	2,844	10%	26,556	$ 134

Note: [a] Parameters for this simulation are as follows: initial susceptible population=29,400, initial infected population=600, testing horizon=80 days, cycles per day=1, days per week=5, R_0=2.3, time for virus incubation=3 days, time to recovery=10 days, asymptomatic advancing to symptoms=30%, symptom case fatality=2.0%, test sensitivity=0.8, test specificity=0.98, exogenous shock=yes, frequency of exogenous shock=every 5 days, new infections per shock=10, secondary cadence=yes, new R_0=2.3.

Table 2: Comparison of three different primary test cadences and one secondary test cadence on 30,000 people[a].

Numbers of people	Cadence of primary testing	Weeks of primary testing	Cadence of secondary testing	Total persons tested	Average number in quarantine	Average % true positives in quarantine	Total testing cost	Total infections	Percent infected	Cases averted	Cost per case averted
1.5	Daily	1	Every 4 Weeks	251,235	327	83.2%	$ 1,256,175	4,399	15%	25,001	$ 50
1.5	Daily	2	Every 4 Weeks	389,579	285	68.6%	$ 1,947,895	2,102	7%	27,298	$ 71
1.5	Daily	3	Every 4 Weeks	525,686	300	58.8%	$ 2,628,430	1,497	5%	27,903	$ 94
1.5	Every 2 Days	1	Every 4 Weeks	178,619	272	85.1%	$ 893,095	4,408	15%	24,992	$ 36
1.5	Every 2 Days	2	Every 4 Weeks	245,207	236	75.8%	$ 1,226,035	2,866	10%	26,534	$ 46
1.5	Every 2 Days	3	Every 4 Weeks	310,761	224	67.2%	$ 1,553,805	1,987	7%	27,413	$ 57
1.5	Every 3 Days	1	Every 4 Weeks	150,781	369	90.7%	$ 753,905	7,291	25%	22,109	$ 34
1.5	Every 3 Days	2	Every 4 Weeks	194,745	291	84.3%	$ 973,725	4,706	16%	24,694	$ 39
1.5	Every 3 Days	3	Every 4 Weeks	236,990	252	77.7%	$ 1,184,950	3,214	11%	26,186	$ 45
2.3	Daily	1	Every 4 Weeks	249,249	379	85.7%	$ 1,246,245	5,736	20%	23,664	$ 53
2.3	Daily	2	Every 4 Weeks	387,928	310	71.3%	$ 1,939,640	2,653	9%	26,747	$ 73
2.3	Daily	3	Every 4 Weeks	523,487	318	61.3%	$ 2,617,435	1,817	6%	27,583	$ 95
2.3	Every 2 Days	1	Every 4 Weeks	174,592	394	90.1%	$ 872,960	7,449	25%	21,951	$ 40
2.3	Every 2 Days	2	Every 4 Weeks	241,762	336	83.3%	$ 1,208,810	5,161	18%	24,239	$ 50
2.3	Every 2 Days	3	Every 4 Weeks	307,358	305	76.2%	$ 1,536,790	3,643	12%	25,757	$ 60
2.3	Every 3 Days	3	Every 4 Weeks	230,865	428	87.3%	$ 1,154,325	7,225	25%	22,175	$ 52
2.3	Every 3 Days	4	Every 4 Weeks	271,737	406	84.1%	$ 1,358,685	6,023	20%	23,377	$ 58
2.3	Every 3 Days	5	Every 4 Weeks	311,855	394	81.1%	$ 1,559,275	5,117	17%	24,283	$ 64
3.0	Daily	7	Every 4 Weeks	1,054,270	544	53.1%	$ 5,271,350	9,398	32%	20,002	$ 264
3.0	Daily	8	Every 4 Weeks	1,188,067	530	45.5%	$ 5,940,335	5,814	20%	23,586	$ 252
3.0	Daily	9	Every 4 Weeks	1,321,454	538	40.1%	$ 6,607,270	3,630	12%	25,770	$ 256
3.0	Every 2 Days	10	Every 4 Weeks	734,399	525	66.0%	$ 3,671,995	7,341	25%	22,059	$ 166
3.0	Every 2 Days	11	Every 4 Weeks	795,082	517	62.5%	$ 3,975,410	4,955	17%	24,445	$ 163
3.0	Every 2 Days	12	Every 4 Weeks	855,403	524	60.1%	$ 4,277,015	3,719	13%	25,681	$ 167
3.0	Every 3 Days	13	Every 4 Weeks	558,825	1,117	88.1%	$ 2,794,125	16,790	57%	12,610	$ 222
3.0	Every 3 Days	14	Every 4 Weeks	586,474	1,141	87.7%	$ 2,932,370	14,513	49%	14,887	$ 197
3.0	Every 3 Days	15	Every 4 Weeks	612,812	1,172	87.5%	$ 3,064,060	13,318	45%	16,082	$ 191

[a]Parameters for this simulation are as follows: initial susceptible population = 29,400, initial infected population = 600, testing horizon = 80 days, cycles per day = 1, days per week = 5, time for virus incubation = 3 days, time to recovery = 10 days, asymptomatic advancing to symptoms = 30%, symptom case fatality = 2.0%, test sensitivity = 0.8, test specificity = 0.98, exogenous shock = yes, frequency of exogenous shock = every 5 days, new infections per shock = 10, secondary cadence = Yes, new R_0 = same as primary testing

Table 3: Comparison of three R_0s on testing results of 30,000 people.

is scaled-up to handle screening of larger populations, we evaluated the same testing strategy as in the scenarios above, but used 10,000, 100, 00 and 1,000,000 individuals. Data in Table 4 shows that the best test outcomes occurred at different times depending upon the size of the population being tested. For example, in comparing the cost per case averted across across the three different population sets, the best test cadence consisted of primary testing every 3 days for a given period followed by secondary testing every 4 weeks (see Table 4). Also note that the times for primary testing that resulted in the best outcomes seemed to be 10 to 12 weeks for the 10,000 population, 8 to 10 weeks for the 100,000 population, and 7 to 9 weeks for the 1,000,000 population. Thus, the model helps provide flexible, actionable intelligence regardless of the size of the population being tested.

Scenario 4: Results from the model considering testing in a simulated long-term-care center is shown in Table 5. Data show that daily testing for 15 weeks still resulted in approximately 10% of the individuals at a typical long-term care center becoming infected; and testing resulted in a cost of approximately $30,000. Testing regimen of every 2 days or every 3 days resulted in 11%-15% of the individuals becoming infected while the costs for these testing regimens were approximately $16,000 and $11,000, respectively. Even though the mortality rate for these nursing home settings was set at 8%, this higher mortality rate did change the percent infection rate, or the cost of testing. Thus, this model helps provide information for fact-based decisions on testing even in the long-term-care facilities.

Numbers of people	Cadence of primary testing	Weeks of primary testing	Cadence of secondary testing	Total persons tested	Average number in quarantine	Average % true positives in quarantine	Total testing cost	Total infections	Percent infected	Cases averted	Cost per case averted
10,000	Daily	6	Every 4 Weeks	307,692	188	60.7%	$ 1,538,460	3,212	33%	6,588	$ 234
	Daily	7	Every 4 Weeks	352,520	182	53.2%	$ 1,762,600	2,336	24%	7,464	$ 236
	Daily	8	Every 4 Weeks	397,164	182	47.0%	$ 1,985,820	1,686	17%	8,114	$ 245
	Every 2 Days	8	Every 4 Weeks	207,460	149	66.4%	$ 1,037,300	2,469	25%	7,331	$ 141
	Every 2 Days	9	Every 4 Weeks	228,470	144	61.5%	$ 1,142,350	1,826	19%	7,974	$ 143
	Every 2 Days	10	Every 4 Weeks	249,345	143	57.6%	$ 1,246,725	1,383	14%	8,417	$ 148
	Every 3 Days	10	Every 4 Weeks	167,195	174	76.7%	$ 835,975	2,645	27%	7,155	$ 117
	Every 3 Days	11	Every 4 Weeks	179,739	171	74.5%	$ 898,695	2,101	21%	7,699	$ 117
	Every 3 Days	12	Every 4 Weeks	192,141	172	72.8%	$ 960,705	1,747	18%	8,053	$ 119
100,000	Daily	3	Every 4 Weeks	1,740,496	1,372	70.3%	$ 8,702,480	25,339	26%	72,661	$ 120
	Daily	4	Every 4 Weeks	2,194,135	1,217	57.1%	$ 10,970,675	11,742	12%	86,258	$ 127
	Daily	5	Every 4 Weeks	2,644,025	1,252	49.3%	$ 13,220,125	7,460	8%	90,540	$ 146
	Every 2 Days	5	Every 4 Weeks	1,449,716	1,255	72.3%	$ 7,248,580	24,812	25%	73,188	$ 99
	Every 2 Days	6	Every 4 Weeks	1,665,140	1,102	63.5%	$ 8,325,700	13,998	14%	84,002	$ 99
	Every 2 Days	7	Every 4 Weeks	1,878,233	1,064	57.2%	$ 9,391,165	8,749	9%	89,251	$ 105
	Every 3 Days	8	Every 4 Weeks	1,431,095	1,457	76.3%	$ 7,155,475	24,207	25%	73,793	$ 97
	Every 3 Days	9	Every 4 Weeks	1,561,639	1,375	72.5%	$ 7,808,195	17,089	17%	80,911	$ 97
	Every 3 Days	10	Every 4 Weeks	1,690,765	1,350	69.5%	$ 8,453,825	12,899	13%	85,101	$ 99

1,000,000	Daily	2	Every 4 Weeks	12,740,988	21,216	86.4%	$ 63,704,940	592,616	60%	387,384	$ 164
	Daily	3	Every 4 Weeks	17,434,893	12,113	66.2%	$ 87,174,465	174,295	18%	805,705	$ 108
	Daily	4	Every 4 Weeks	21,965,460	10,915	52.1%	$ 109,827,300	49,408	5%	930,592	$ 118
	Every 2 Days	4	Every 4 Weeks	12,317,679	15,198	80.8%	$ 61,588,395	396,023	40%	583,977	$ 105
	Every 2 Days	5	Every 4 Weeks	14,519,113	11,455	69.6%	$ 72,595,565	195,390	20%	784,610	$ 93
	Every 2 Days	6	Every 4 Weeks	16,669,612	10,207	60.6%	$ 83,348,060	98,525	10%	881,475	$ 95
	Every 3 Days	7	Every 4 Weeks	13,000,213	15,648	80.0%	$ 65,001,065	325,209	33%	654,791	$ 99
	Every 3 Days	8	Every 4 Weeks	14,328,241	13,984	75.2%	$ 71,641,205	216,881	22%	763,119	$ 94
	Every 3 Days	9	Every 4 Weeks	15,634,333	13,271	71.4%	$ 78,171,665	151,289	15%	828,711	$ 94

[a]Parameters for this simulation are as follows: testing horizon=80 days, cycles per day=1, days per week=5, R_0= 2.3, time for virus incubation=3 days, time to recovery = 10 days, asymptomatic advancing to symptoms=30%, symptom case fatality=2.0%, test sensitivity=0.8, test specificity=0.98, exogenous shock=yes, frequency of exogenous shock=every 5 days, new infections per shock=10, secondary cadence=yes, new R_0=2.3

Table 4: Influence of different population sizes of testing results[a].

Cadence of primary testing	Weeks of primary testing	Cadence of secondary testing	Total persons tested	Average number in quarantine	Average %TP in quarantine	Total testing cost	Total infections	Percent infected	Cases averted	Cost per case averted
Daily	1	Weekly	1,844	2	78.40%	$ 9,445	19	19%	79	$ 120
Daily	2	Weekly	2,231	2	74.40%	$ 11,420	18	18%	80	$ 143
Daily	3	Weekly	2,612	2	71.00%	$ 13,360	18	18%	80	$ 167
Daily	4	Weekly	2,991	2	68.00%	$ 15,295	18	18%	80	$ 191
Daily	5	Weekly	3,386	2	63.10%	$ 17,300	16	16%	82	$ 211
Daily	6	Weekly	3,763	2	60.00%	$ 19,225	15	15%	83	$ 232
Daily	7	Weekly	4,134	2	57.50%	$ 21,120	14	14%	84	$ 251
Daily	8	Weekly	4,503	2	55.30%	$ 23,000	14	14%	84	$ 274
Daily	9	Weekly	4,875	3	52.60%	$ 24,895	13	13%	85	$ 293
Daily	10	Weekly	5,243	3	49.80%	$ 26,770	12	12%	86	$ 311
Daily	11	Weekly	5,603	3	47.90%	$ 28,610	11	11%	87	$ 329
Daily	12	Weekly	5,962	3	46.30%	$ 30,440	11	11%	87	$ 350
Daily	13	Weekly	6,321	3	44.80%	$ 32,270	11	11%	87	$ 371
Daily	14	Weekly	6,674	3	44.20%	$ 34,070	9	9%	89	$ 383
Daily	15	Weekly	7,023	3	43.20%	$ 35,850	9	9%	89	$ 403
Every 2 Days	1	Weekly	1,600	2	79.00%	$ 8,205	19	19%	79	$ 104
Every 2 Days	2	Weekly	1,747	2	77.20%	$ 8,955	19	19%	79	$ 113
Every 2 Days	3	Weekly	1,893	2	75.50%	$ 9,700	18	18%	80	$ 121
Every 2 Days	4	Weekly	2,036	2	74.00%	$ 10,430	18	18%	80	$ 130
Every 2 Days	5	Weekly	2,185	2	71.90%	$ 11,185	18	18%	80	$ 140
Every 2 Days	6	Weekly	2,335	2	69.20%	$ 11,950	16	16%	82	$ 146
Every 2 Days	7	Weekly	2,477	2	67.40%	$ 12,670	16	16%	82	$ 155
Every 2 Days	8	Weekly	2,616	2	66.00%	$ 13,380	15	15%	83	$ 161
Every 2 Days	9	Weekly	2,756	2	64.50%	$ 14,095	15	15%	83	$ 170
Every 2 Days	10	Weekly	2,897	2	62.00%	$ 14,810	13	13%	85	$ 174
Every 2 Days	11	Weekly	3,032	2	60.60%	$ 15,500	13	13%	85	$ 182
Every 2 Days	12	Weekly	3,166	2	59.50%	$ 16,185	13	13%	85	$ 190
Every 2 Days	13	Weekly	3,300	2	58.40%	$ 16,865	13	13%	85	$ 198
Every 2 Days	14	Weekly	3,432	2	57.80%	$ 17,540	11	11%	87	$ 202
Every 2 Days	15	Weekly	3,561	2	57.10%	$ 18,200	11	11%	87	$ 209
Every 3 Days	1	Weekly	1,505	2	80.70%	$ 7,725	20	20%	78	$ 99
Every 3 Days	2	Weekly	1,574	2	79.60%	$ 8,075	20	20%	78	$ 104
Every 3 Days	3	Weekly	1,640	2	78.70%	$ 8,415	20	20%	78	$ 108
Every 3 Days	4	Weekly	1,705	2	78.00%	$ 8,745	19	19%	79	$ 111
Every 3 Days	5	Weekly	1,771	2	77.00%	$ 9,080	19	19%	79	$ 115
Every 3 Days	6	Weekly	1,840	2	75.60%	$ 9,430	18	18%	80	$ 118
Every 3 Days	7	Weekly	1,904	2	74.60%	$ 9,755	17	17%	81	$ 120
Every 3 Days	8	Weekly	1,966	2	73.80%	$ 10,070	17	17%	81	$ 124
Every 3 Days	9	Weekly	2,028	2	73.00%	$ 10,390	17	17%	81	$ 128
Every 3 Days	10	Weekly	2,090	2	71.80%	$ 10,705	16	16%	82	$ 131
Every 3 Days	11	Weekly	2,150	2	71.00%	$ 11,010	16	16%	82	$ 134
Every 3 Days	12	Weekly	2,209	2	70.30%	$ 11,310	15	15%	83	$ 136
Every 3 Days	13	Weekly	2,267	2	69.80%	$ 11,605	15	15%	83	$ 140
Every 3 Days	14	Weekly	2,324	2	69.40%	$ 11,895	15	15%	83	$ 143
Every 3 Days	15	Weekly	2,380	2	69.00%	$ 12,180	14	14%	84	$ 145

Note: Parameters for this simulation are as follows: Initial susceptible population=98, initial infected population=2, testing horizon=80 days, cycles per day=1, days per week=5, R0=1.5, time for virus incubation=3 days, time to recovery=10 days, asymptomatic advancing to symptoms=30%, symptom case fatality=8.0%, test sensitivity=0.8, test specificity=0.98, exogenous shock=yes, frequency of exogenous shock=every 21 days, new infections per shock=2, secondary cadence=yes, new R_0=1.5.

Table 5: Testing in simulated long-term care centres[a].

Discussion

The analytics tool we describe above provides decision makers in the healthcare sector critical information for making informed decisions for screening in congregate settings. For example, the cost for opening a typical school district of 30,000 students and staff could be ~$2.7 million per semester and still result in an infection rate of ~14% (see Table 2). Moreover, testing for viral variants with R_0 values of greater than 3 in this setting will be quite expensive likely $4.3 million per semester with a similar infection rate of ~13% (see Table 3). In long-term-care centers where it is critical to keep the infection rate as low as possible, one must use daily testing in conjunction with mandating mask wearing and social distancing. Still the costs will be ~$30,000 every 16 weeks, or ~$100,000 per year, in order to keep rate of infection below 10% (Table 5).

It is our view that at the outset of the COVID-19 pandemic, the U.S. failed to develop an appropriate national testing strategy, and going forward, policy makers have failed to develop a national roadmap for doing so. As COVID variants continue to present themselves, testing is re-emerging as a critical element to combating the spread of the pandemic. Lacking Federal guidance, states and local governments have been forced to author their own plans for testing. This is especially challenging, because the public health information can be confusing, and testing policies often transcend the jurisdiction or expertise of local or state agencies (e.g., the availability of resources for testing, vaccines, therapeutics, personal protection, assessing the risk of novel viral variants, assessing the long-term health consequences of COVID-19, among other issues). For example, in early 2021 in the U.S., several pathways for reopening schools were proposed [51-53], but the costs, resources and management infrastructure required for adopting such regimens were fragmented or unavailable at the time. The U.S. has no clear methodology for establishing an endpoint metric such as testing positivity rates or level of infections per 100,000 individuals. Moreover, the CDC defines test positivity rates based solely on nucleic acid amplification test results [54], which, in the early days of the COVID-19 pandemic were being collected mostly from symptomatic individuals. The CDC admits that high positivity results can be misleading because mostly those at greatest risk of infection within a community are being tested. Moreover, certain jurisdictions prioritize data collection for positive test results over negative results. In fact, there is little consistency in how U.S. states define, publish, and present COVID-19 data. One of the major aggregators of U.S. COVID-19 data from the earliest days of the pandemic, "The COVID Tracking Project", eventually stopped tracking COVID-19 positivity rates, in part because of these data inconsistencies [55].

The availability of vaccines has mitigated somewhat, but not eliminated, the need for large scale testing in the US. As of January 2022, data from the CDC showed that 63% of total US population is fully vaccinated; however, five states had less than 52% of their populations fully vaccinated. The rate of vaccination slowed considerably in the U.S. through the summer of 2021, and vaccine hesitancy appears to be the major cause of this slow down. The rapid rise of the Omicron variant in the U.S. was expected to curb some of this hesitancy. However, as of January 2022, the fully vaccinated rates in three states are still at or below 50% [56]

The availability of the tool described in this paper suggests a strategy for managing COVID-19 in both vulnerable and vaccine-hesitant populations. Individuals hesitant to be vaccinated and who are part of congregant settings within these areas (e.g., schools, work facilities, and hospitals) would be tested routinely (using a rapid antigen test not PCR) and allowed to return to school or work if negative and placed in quarantine if positive. This approach could also limit spread of infection in those countries where low levels of vaccination have resulted from resource limitations. It has been estimated that vaccines will not be available to many of the poorest nations until, at least, 2023 [57].

Conclusion

The availability of simplified analytic modeling tools that can help decision makers determine when and how to reopen certain congregate settings, like schools, is an absolute necessity. In this research, we offer a strategic analytic tool for utilization of low-cost antigen tests in a comprehensive, targeted testing strategy, which in our perspective as academics specializing in business and biotechnology management is critical and allows for effective use of the various planning and execution protocols. Furthermore, strategic deployments have the potential to improve dramatically the production, procurement, and distribution of test kits, and can be of critical help to control and mitigate the spread of the SARS-CoV-2 virus in the United States., and around the globe.

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Authors' Contributions

Kouri: Conceptualization, methodology, writing; warsing: Methodology, writing, reviewing, editing; Singh: visualization, data modeling; Thomas: Validation, Manuscript Review and Editing; Handfield: Validation, writing, reviewing editing.

Availability of Data and Materials

Results were generated using the computational tool available at https://ncsu-scrc.shinyapps.io/covid-19-screening/. The tool produces both summary results and detailed output at the request of the user. Only summary results appear in this manuscript.

Ethics Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing Interests

The authors declare that they have no competing interests.

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