**Asymptomatic testing strategies to limit COVID-19 introduction from shift-workers into congregate settings**

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## Introduction (413 words)

Since the early stages of the COVID-19 pandemic, outbreaks in congregate settings such as skilled nursing facilities [CITEs], homeless shelters (1–4), and carceral facilities (5) have been particularly devastating. Individuals living in these settings are limited in their ability to effectively isolate themselves from other potentially infected individuals, and certain facilities place many people in close proximity [CITE]. These conditions are highly conducive to the spread of SARS-CoV2, with estimated as high as 8.44 in one carceral facility (6), as high as 6.2 in homeless shelters (7), [other examples].

Preventing the importation of primary cases into congregate settings may therefore be the most effective way to protect vulnerable populations within these facilities. The transfer of infected residents from one facility to another has been implicated as the impetus of large outbreaks in carceral facilities (8,9), but reformed policies have now limited the frequency of such resident transfers. Furthermore, more effective testing and isolation procedures appear to have limited the SARS-CoV2 importation risk associated with such transfers [CITEs].

Spillover from the community to facility staff and subsequent introduction into resident populations remains a major risk to the health of congregate populations. Staff introductions have caused a number of outbreaks in congregate settings across the US (5,10,11). Routine testing of staff is essential to identify new cases and prevent such importations into resident populations. Prior analyses suggest that routine asymptomatic testing is an effective strategy to reduce transmission in homeless shelters (7), in healthcare settings (12), and prior to airline travel (13). Current guidance suggests…

Even as vaccination rates increase across the United States and the world, concerns over breakthrough variants and transmission among unvaccinated populations reiterate the importance of asymptomatic testing. Different testing strategies that consider the frequency and timing of testing in relation to staffing schedules and key transmission characteristics of SARS-CoV2 such as pre- and asymptomatic transmission and the duration of the latent period have not been systematically investigated. Here we draw on staffing and testing schedules from carceral facilities operated by the California Department of Corrections and Rehabilitation (CDCR) to fill this gap. We propose an analytic framework to estimate the effect of variable testing frequencies and delays on the reproduction number, . We then develop an individual-based model which incorporates CDCR staffing and testing schedules to simulate community acquisition of SARS-CoV2 and subsequent transmission in a congregate settings. We use the model to explore via simulation the impact of aligning testing schedules with staffing schedules across testing frequencies, background community infection rates, and within-facility transmission rates.

## Staff work and testing schedules

[Nick describes CDCR data, staffing and testing schedules, maybe reference to figure]

## Model framework and parameterization for SARS-CoV2 (672 words)

Building on previous work investigating the effects of non-pharmaceutical interventions (14) and testing (15) on the transmission of infectious diseases, individual contributions to SARS-CoV2 transmission through time are modeled from an infectiousness profile, , generated from key biological parameters of the virus that determine the distribution of infectiousness over time. A triangle distribution is used to model , with infectiousness beginning after the latent period, ending after the duration of the infectious period, and peaking at some point in between (, , , and a<c<b ; Fig 1a).

The viral dynamics of SARS-CoV2 make control efforts challenging, as asymptomatic and presymptomatic transmission caused by high infectiousness in the absence of symptoms are common (16,17). In terms of the infectiousness profile for SARS-CoV2, this means that peak infectiousness tends to coincide with the onset of symptoms (for cases that are symptomatic), but occurs after completion of the latent period (i.e. >). The expected number of new cases generated at time is thus , where is the effective reproduction number interpreted as the expected number of cases generated by a new case over the duration of the infectious period. The model therefore assumes that new cases are most likely to be generated around the time of peak infectiousness, . Table 1 lists the distributions of , , and used here.

In the presence of interventions that isolate infectious individuals prior to , e.g. through contact tracing, self-isolation following the onset of symptoms, or testing, the effect of isolation on can be directly estimated from the time to isolation as , where is the time at which isolation occurs. Reducing via improved contact tracing or more frequent testing can thus be envisioned as removing a larger slice from the overall infectiousness triangle by reducing (Fig 1a). The size of the slice removed is dependent on the shape of the overall triangle distribution, which is primarily determined by and , and the location of in relation to . For instance, if , then the proportional reduction in can be estimated as .

Figure 1b shows the relationship between and is sigmoidal, implying earlier isolation is incrementally more effective and the benefits of isolation level off later in the infectious period. Other interventions that reduce across all levels of infectiousness such as wearing a mask or reducing the contact rate between infectious and susceptible individuals can also be accommodated simply by multiplying by a constant.

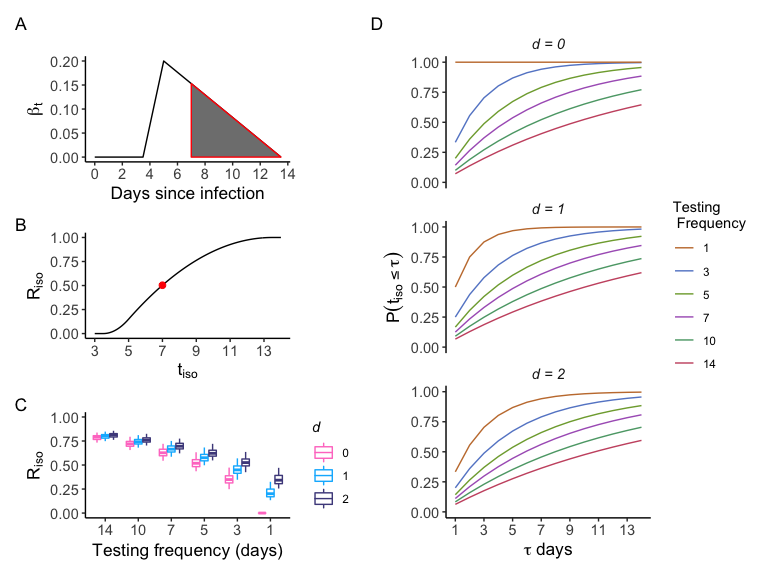
**Table 1**: Distributions and parameter values used in analytic framework and model simulations

|  |  |  |
| --- | --- | --- |
| **Parameter** | **Distribution** | **Source** |
| **Incubation Period ()** | *Lognormal*(1.63, 0.5) | CITE |
| **Latent Period ()** | + *Uniform*(-2, 0) | CITE |
| **Infectious Period ()** | (-) + *Uniform*(6.5, 9.5) | CITE |
| **Community Prevalence** | [0.1%, 0.5%, 1%] | CITE |
|  | [0.5, 1.0, 1.5] | CITE |

Assuming testing is independent of symptoms, known contacts, and other reasons for explicitly seeking testing, the probability of going days without being tested from the testing frequency, , can be estimated as and the probability that as , assuming isolation occurs immediately after testing. Given substantial turnaround times between testing and isolation, particularly when relying on PCR-based tests, the delay between testing and isolation, , can also be incorporated as: , where is simply the average number of days between tests. Figure 1d shows that such delays have a detrimental effect that is greater than additive on the probability of achieving prompt isolation. For example, with a daily testing frequency and no delay, . However, increasing the delay to 1 or 2 days leads to 0.875 and 0.704, respectively.

Testing frequency and delay can also be incorporated into estimation of , essentially as the infectiousness on day weighted by the probability of remaining un-isolated on day :

Figure 1c shows distributions of derived from 100 random draws sampling from uncertainty in the SARS-CoV2 latent, peak, and total infectious periods, across test frequencies ranging from daily () to biweekly () and test delays from 0 to 2 days. These results again reiterate the importance of reducing test delays, as is approximately the same when testing every day () with a two-day turnaround time for test results () vs testing every three days () with immediate test results () (fig 1c, median 0.35 and 0.34, respectively).

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**Figure 1. Model framework and analytic results**. A) Example infectiousness profile for , , , , with shaded area demonstrating infectiousness slice removed if , leading to . B) as a function of with same parameters as in A and point indicating scenario depicted in A. C) Boxplots showing distributions of as a function of testing frequency, , and test delay, , incorporating uncertainty in , , and by drawing parameter sets for each, with baseline . Boxplots indicate median, interquartile range, and full range of values of . D) Relationship between testing frequency, , test delay, , and probability isolation occurs by day , i.e. , demonstrating that delays in testing substantially reduce the probability of prompt isolation, particularly in more frequent testing scenarios.

## Individual-based model simulations (631 words)

### Model setup (can probably move a lot of this to a supplement?)

To incorporate staff schedules and expand the modeling framework above to a facility-level setting, we next describe the development and simulation of individual based microsimulations. In a modeled facility, staff are assigned a work schedule that determines time frames when they are in the facility and interacting with facility residents and other staff working at the same time. We denote as an indicator function for whether staff member is working at the facility on day . In addition to their work schedule, all staff are assigned a testing schedule, encoded by function , with different testing schedules discussed further below. The model is simulated at an 8-hour time step, with each time step corresponding to a work shift as described further below.

Staff move through susceptible (S), exposed (E), infected (I), and recovered (R) states, with the infected state corresponding to time when . Parameters for newly exposed staff are drawn to determine , , and , from which an infectiousness profile, is generated. Tested staff produce a positive result if and , at which time they enter a quarantined (Q) state immediately if , or first enter a tested (T) state before Q if there is a delay between test administration and the test result. Staff in state Q have for 10 days and have for 90 days following a positive result.

Assuming constant across all individuals, the expected number of cases produced in the facility on day by individual is . Staff may acquire infection from the community or workplace, therefore we denote two separate forces of infection, and . Infection for each individual is simulated at each time step by subjecting each staff member to a bernoulli trial with . The expected number of infections in the facility generated by staff is estimated from each simulation as: .

### Staffing and testing strategies

[Nick: Oneish sentence summary of test/staffing strategies observed in CDCR data]. Generation of work schedules in simulations was informed by observed CDCR schedules by sampling one of the consecutive 4-day sequences of work days shown in Fig 1 and a regular shift (morning, evening, night) for each worker. A fifth shift was then added to each worker’s weekly schedule by randomly sampling from all other potential shifts. Two testing strategies were considered. Under a random testing strategy, testing for each worker occurs at random during their five shifts depending on the frequency (i.e. with , workers would be tested during two of their five shifts, chosen at random each week). Under a systematic testing strategy, each worker is always tested on the same day(s) of their shift each week. For , systematic testing always occurs on the first day of the regular 4-day work schedule; for , systematic testing always occurs on the first and third days; and for , testing occurs on each of the regular 4-day work days.

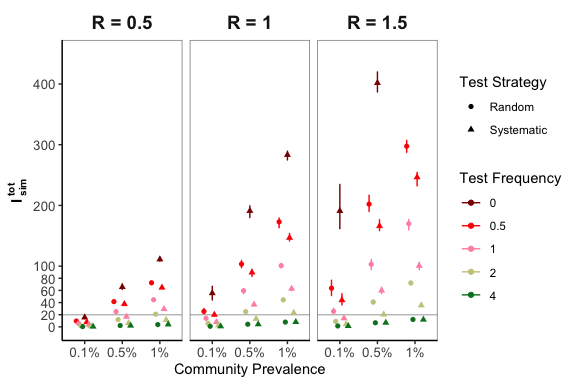
We assume rapid tests in which the test result is known immediately after the test is conducted () are used and further assume that all tests conducted when return a positive result. The total number of tests conducted in each simulation is recorded as: . Combined with the expected number of cases in the simulation, we estimate the incremental test effectiveness ratio (ITER) as: , where is the number of infections in a reference scenario with no testing. The ITER can be interpreted as the number of tests needed to prevent one infection in the simulation scenario being evaluated.

All simulations and analyses were conducted in R software version 4.0.4 (18) with aid from the tidyverse (19), triangle (20), and patchwork (21) packages. Code is made available freely online at <https://github.com/cmhoove14/CDCR-Staff-Testing>.

## Simulation Results (324 words)

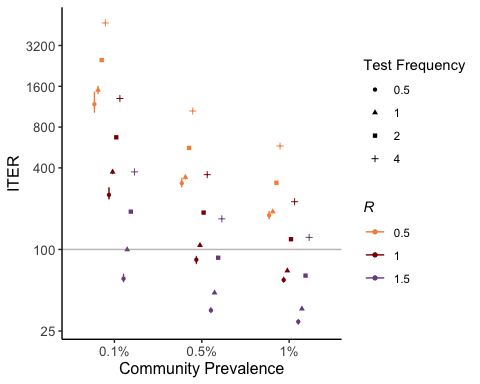
Systematic testing strategies were found to consistently outperform random testing strategies in terms of preventing infections within simulated facilities. Figure 2 shows a comparison of the number of infections generated () when implementing a random vs systematic testing strategy across testing frequencies, community prevalences, and within-facility . In the highest transmission scenario (), testing randomly once per week resulted in a median 169.92 (IQR 159.07 - 177.43), whereas testing systematically on the first day of the work week resulted in 100.6 (IQR 93.41 - 106.93; Fig 2, right panel in pink).

The horizontal gray line in figure 2 demonstrates a potential threshold number of infections to avoid exceeding at . Implementing a systematic–rather than random–testing strategy can be sufficient to prevent from exceeding such a threshold without changing the frequency in many transmission scenarios, though in the highest transmission scenarios, greater than twice-weekly testing may be needed.

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**Figure 2. Number of expected infections in a facility from model simulations comparing random and systematic testing strategies across transmission scenarios and test frequencies**. Systematic testing strategies ([triangles]) prevent more infections than random strategies ([circles]) across all transmission scenarios and test frequencies. The horizontal gray line serves as a reference to assess the testing frequency needed to maintain across different transmission scenarios. Error bars represent the interquartile range of derived from 100 simulations per scenario.

An alternative threshold approach to aid decision-making, particularly in resource-constrained settings, is the ITER. Figure 3 shows estimates of the ITER across transmission scenarios only for systematic testing strategies since they were found to substantially outperform random strategies. In the highest transmission scenario (, community prevalence), testing on the first day of every other work week (, fig 3 circles) leads to 29.31 (IQR 28.08 - 30.35), while increasing test frequency to weekly, , results in 36.49 (IQR 36.02 - 36.9), to : 64.12 (IQR 63.67 - 64.49), and to : 122.73 (IQR 121.86 - 123.49). These values approximately correspond to test positivity rates of 3.41%, 2.74%, 1.56%, and 0.81% due to the interpretation of the ITER as the number of tests per positive result. Figure 3 also provides an example reference line at , corresponding to an approximate test positivity, to demonstrate how testing frequency may be determined from the transmission scenario and target ITER, which may be influenced by the number of tests available.

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**Figure 3. Incremental test effectiveness ratio (ITER) from simulations implementing systematic testing across transmission scenarios and testing frequencies**. The ITER remains relatively low in higher transmission scenarios even at high () testing frequencies, potentially favoring such high-frequency testing strategies when within-facility transmission () and/or community prevalence are high. The y-axis is log-transformed and the horizontal line at is provided to aid visual comparison across scenarios. Error bars represent the interquartile range of expected infections derived from 100 simulations per scenario.

## Discussion

Here we have built on previous modeling and simulation analyses to demonstrate that systematic testing strategies with fast turnaround that align testing schedules with working schedules prevent more transmission events than non-systematic testing strategies or those with a delay between testing and disclosure of a test result. A major benefit of such strategies is that they do not require higher testing frequency, nor large additional logistical investments. As such, we believe that there is substantial value in implementing systematic rapid testing at the beginning of the work week for staff working in high-risk COVID-19 facilities such as carceral facilities, skilled nursing facilities, and homeless shelters.

Even as systematic testing strategies reduce within-facility transmission, they are not capable of preventing all transmission events. Systematic testing represents one tool of many that should be implemented to prevent SAS-CoV2 introductions into congregate facilities. Universal masking, self-isolation following symptom onset or known exposure, and widespread vaccination all play an important role in preventing introductions into high risk populations [CITEs]. [Rena/Nick Politically tact sentence(s) here on how some of these policies/strategies suffer from low-adherence and therefore testing strategies remain very important.]

The exclusion of these additional interventions is a potential limitation, however, we expect additional interventions to lead to simple proportional reductions in the simulated number of transmission events in a facility. We therefore expect consistent relative findings between testing strategies and frequencies across different transmission scenarios. An additional limitation is that we do not distinguish between staff-to-staff and staff-to-resident transmission events within a simulated facility, but rather record the total number of transmission events. Estimation of staff-staff and staff-resident contact rates or reproduction numbers would enable more precise accounting and simulation of importation events and subsequent transmission within a facility.

[@Seth could you add a couple sentences here about probability of an outbreak given X introductions?]

The modeling and simulation framework presented here is applicable beyond COVID-19 in congregate settings in which outbreaks sparked by staff introductions are a hazard. Other applicable settings may include the introduction of hospital acquired infections from newly admitted patients or from hospital staff, introduction of other respiratory pathogens such as influenza or pertussis into congregate settings, or [3rd example or stick with 2?]. Accurate parameterization of key natural history traits of the pathogen in question such as the latent, incubation, and infectious periods is essential to estimate the impact of nonpharmaceutical interventions such as asymptomatic screening (14). Pathogens that cause symptoms prior to infectiousness (), for instance, may be more effectively controlled at lower cost via symptom screening and subsequent isolation.

For SARS-CoV2, pre- and asymptomatic transmission make viral testing a key component of prevention strategies. Preventing delays between testing and the test result is also found to be an essential component to any testing strategy. Increasing the frequency of testing may also be necessary in settings with high community prevalence or the opportunity for rapid spread within a facility. Testing all four days of a regular work week was necessary to prevent more than 20 transmission events within a facility over the 6-month simulation period considered here when community prevalence was 1.5% and . In the lowest transmission setting with 0.5% community prevalence and , the same threshold of 20 transmission events was met without any systematic testing. For intermediate transmissions scenarios or lower transmission event thresholds, testing frequencies ranging from biweekly to weekly to twice per week may be required.

We also present the incremental test effectiveness ratio (ITER) as a per-test measure of effectiveness for systematic testing across a range of frequencies and transmission scenarios. In resource-constrained environments in which tests are difficult to acquire or limited funds are available to purchase tests, the ITER and its relationship to test positivity may be used to guide decisions on test frequency.

In conclusion, we have shown that aligning the timing of testing with regular working schedules for staff in congregate settings can substantially improve the efficacy of asymptomatic screening. Two metrics, the number of expected within-facility transmission events and the ITER, derived from simulated facilities are presented to inform decisions on the frequency of systematic testing needed in different transmission scenarios to limit transmission under key thresholds. We conclude that systematic testing of staff working with high risk populations in congregate settings should continue until community transmission or within-facility transmission potential are sufficiently reduced to prevent outbreaks.

## Acknowledgements

## Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the U.S. Department of Health and Human Services, the Centers for Disease Control and Prevention, or the authors' affiliated institutions.

## Biographical sketch

Dr. Hoover is a postdoctoral scholar at the Francis I. Proctor foundation at the University of California, San Francisco. He is interested in using quantitative methods to inform intervention strategies to reduce the global burden of infectious diseases.

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