Frequency of Routine Testing for Coronavirus Disease 2019 (COVID-19) in High-risk Healthcare Environments to Reduce Outbreaks

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Routine asymptomatic testing strategies for COVID-19 have been proposed to prevent outbreaks in high-risk healthcare environments. We used simulation modeling to evaluate the optimal frequency of viral testing. We found that routine testing substantially reduces risk of outbreaks, but may need to be as frequent as twice weekly.

Keywords. SARS-CoV-2; infection control; epidemiology; pandemic.

Outbreaks of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of coronavirus disease 2019 (COVID-19), have been commonly documented in high-risk healthcare environments including skilled nursing facilities, hospitals, and homeless shelters [1, 2]. Routine viral testing strategies with polymerase chain reaction (PCR) of asymptomatic persons have been proposed to detect and prevent outbreaks in high-risk healthcare environments, by testing residents and workers at routine intervals in absence of documented cases. Yet it remains unclear how often routine asymptomatic testing would need to be performed, and how effective such a strategy would be to prevent outbreaks of COVID-19. The United States Centers for Disease Control and Prevention has recently issued partial guidance for viral testing during an outbreak, although no preventive testing guidelines exist [3, 4]. In this study, we aimed to estimate the effectiveness of routine testing with PCR to reduce transmission of COVID-19.

METHODS
Overview
We developed a simulation model of SARS-CoV-2 transmission to evaluate the effectiveness of various frequencies of routine PCR testing of all persons in a high-risk healthcare environment (ie, long-term residents or patients admitted to hospitals, daily healthcare workers) to reduce cases of COVID-19. Some examples of representative healthcare environments include nursing facilities, hospitals, clinics, dialysis centers, and substance use treatment centers. The primary study outcome for each strategy was the simulated reduction in the mean effective control reproduction number (Re) in the healthcare environment, corresponding to the average number of secondary infections caused by an infected person averaged over the simulation period, starting with a fully susceptible population, and accounting for the impact of interventions. For interpretation, a mean effective reproduction number below one would ensure decline in the number of cases when averaged over time.

Model Structure
The SARS-CoV-2 transmission model was a stochastic microsimulation, where individuals were simulated and assigned a health state that included being susceptible to infection (nonimmune), early infectious, late infectious, or recovered and immune (Supplementary Figure 1). We simulated transmission in a population of 100 people within a healthcare environment interacting with a community with daily incidence of 0.5%, over 10 months, where people in the healthcare environment were constantly interacting with new community members. We chose a high daily incidence to ensure a sufficient number of new infections for the simulation; this choice should not affect the study results, and was also tested in sensitivity analysis. We used published data on the natural history of SARS-CoV-2, including an estimated 5-day incubation period and a time-varying infectiousness profile. We inferred the probability of infection per day of work based on the estimated infectiousness profile of SARS-CoV-2 (including infectiousness beginning on average 4 days prior to onset of symptoms) (Supplementary Figure 2) [5]. We assumed a 40% subclinical proportion, with
50% relative infectiousness of subclinical infections to clinically apparent cases [1, 6, 7]. More details on the model structure and parameters are available in the Supplementary Material.

Simulation
We modeled transmission occurring within a high-risk healthcare environment that was fully susceptible through introduction from the community. We assumed a basic reproduction number ($R_0$) within the healthcare environment, corresponding to the number of secondary infections caused by an infected person in an entirely susceptible population in absence of intervention [5, 8]. We tested a base case $R_0$ of 2.5 based on published literature, but also varied $R_0$ to test lower values that may represent complementary interventions (eg, universal masking, social distancing).

We evaluated routine asymptomatic PCR testing of various frequencies, from daily to once monthly testing. We modeled the sensitivity of PCR testing as a function of day of infection based on data of time-varying sensitivity of this test modality (50%–80% during first 2 weeks; Supplementary Figure 3) [9], and PCR specificity as 98%–100%. We estimated the effect of testing on $R_e$, with a goal of achieving a $R_e$ below one. We assumed that persons self-isolated upon symptom onset, and persons with PCR-confirmed infection self-isolated 1 day after being tested, while those who were not detected remained in the environment and potentially infected others. We performed Monte Carlo sampling across the uncertainty ranges of each parameter to estimate the range of possible outcomes. We performed sensitivity analysis by varying test result delays and test performance. Additional details are available in the Supplementary Material and data and code are available online (https://github.com/etchin/covid-testing).

RESULTS
In this microsimulation, with daily testing in high-risk environments by PCR and an assumed basic reproduction number $R_0$ of 2.5, we estimated an 82.2% (95% CI: 82.0–82.5) reduction in $R_e$, corresponding to $R_e = 0.44$. When testing persons every 3 days, we observed a 61.4% (95% CI: 61.2–61.7) reduction, corresponding to $R_e = 0.97$. When testing weekly, we observed an 36.9% (95% CI: 36.5–37.2) reduction, corresponding to $R_e = 1.58$; and when testing monthly, we observed a 8.9% (95% CI: 8.7–9.2) reduction, corresponding to $R_e = 2.28$ (Supplementary Table 3).

The optimal testing frequency to bring $R_e$ below one was dependent on baseline $R_0$ (Figure 1). In an environment with $R_0 = 2.5$ [5, 8], testing would have to occur almost every other day to bring $R_e$ below one. If $R_0 = 2$ [5, 8], testing would need to occur at least twice weekly (every 3–4 days), unless other measures were added to testing and self-isolation. If assuming $R_0 = 1.5$, testing weekly would suffice.

DISCUSSION
This simulation study finds that in high-risk settings with ongoing community-based transmission, frequent (twice-weekly) routine asymptomatic viral testing may be required to prevent outbreaks and reduce case counts of COVID-19. Due to the imperfect sensitivity of PCR testing and infectiousness early in the natural history, even with frequent testing, a meaningful proportion of infected persons may be missed. We find that strategies with less frequent testing—such as once-a-week testing—may be sufficient in settings with low community incidence, especially when implemented with additional infection control measures. Furthermore, we find that delays in returning test results would severely impact the effectiveness of routine testing strategies.

The study conclusions are most applicable to high-risk healthcare environments, with long-term residents and daily workers. These settings include nursing facilities, hospitals,
prisons, homeless shelters, dialysis centers, and other healthcare and non-healthcare environments. The assumptions in the model are most applicable in a setting with ongoing community transmission of SARS-CoV-2, as evidenced by ongoing new infections. In settings with higher community incidence, testing multiple times per week would be required to prevent an outbreak and control case counts, and require the addition of other control strategies (eg, universal masking, social distancing). Our study conclusions are similar to recently published model-based analyses on PCR testing strategies [10, 11], which support the finding that very frequent testing (every 2–3 days) is required to have a meaningful impact on transmission, despite modeling different environments.

The study has limitations in the model assumptions and available data. Transmission of SARS-CoV-2 is documented to have high degree of heterogeneity across settings, whereas we used a transmission rate that considered an average among high-incidence settings such as nursing facilities. Our analysis focused on outbreaks and transmission in high-risk environments, rather than the population at large. Furthermore, routine PCR testing would require substantial resources, logistical support, and high participation from the population, with consideration of cost-effectiveness [12]. We assumed that results of testing would be available after one day, which may only be possible in higher resource settings, but we also tested the impact of slower turnaround time, which reduced the overall effectiveness of this strategy.

In conclusion, our findings support that routine testing strategies can provide benefit to reduce transmission in high-risk environments with frequent testing, but may require complementary strategies to reliably prevent outbreaks of COVID-19. Further evidence should be generated on the use of strategies in combination with testing, including masking, ventilation changes, disinfection, and physical distancing [8, 13].

**Supplementary Data**

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

**Notes**

*Author contributions.* E.T.C, B.Q.H, L.A.C.C., and N.C.L developed the transmission model. E.T.C, N.C.L, and B.Q.H coded the simulation and analysis. S.B. and N.C.L supervised the study. All authors contributed to study design, interpretation of results, and writing of the manuscript.

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**Financial support.** E. T. C. acknowledges support by the National Science Foundation Graduate Research Fellowship under Grant No. DGE 1656518. N. C. L. is supported by the University of California, San Francisco. B. Q. H. acknowledges support by the National Science Foundation Graduate Research Fellowship under Grant No. DGE 1656518 and the National Library of Medicine under Training Grant T15 LM 007033. Funding sources had no role in the writing of this correspondence or the decision to submit for publication.

**Potential conflicts of interest.** S. B. serves on the City of San Francisco's Department of Public Health street outreach team for homeless adults affected by COVID-19, as a provider at the HealthRight360 Integrated Care Center, and as an employee of Collective Health, all of which provide COVID-19 testing. S. B. reports grants from National Institutes of Health and Centers for Disease Control and Prevention; and personal fees from PLOS Medicine and The New England Journal of Medicine, outside the submitted work. N. C. L. reports grants and personal fees from World Health Organization, and grants from California Department of Public Health, outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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