Clinical Infectious Diseases

BRIEF REPORT

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

Elizabeth T Chin,[1,a] Benjamin Q Huynh,[1,a] Lloyd A. C. Chapman,[2] Matthew Murrill,[2] Sanjay Basu,[3,4,5] and Nathan C Lo[2]

[1]Department of Biomedical Data Science, Stanford University, Stanford, California, USA, [2]Department of Medicine, University of California, San Francisco, San Francisco, California, USA, [3]Center for Primary Care, Harvard Medical School, Boston, Massachusetts, USA, [4]Research and Population Health, Collective Health, San Francisco, California, USA, and [5]School of Public Health, Imperial College, London, United Kingdom

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

Received 18 June 2020; editorial decision 8 September 2020; accepted 6 October 2020; published online October 26, 2020.

[a]Co-first author.

Correspondence: N. C. Lo, Department of Medicine, University of California, San Francisco, San Francisco, CA 94110 (nathan.lo@ucsf.edu).

Clinical Infectious Diseases® 2021;73(9):e3127–9

DOI: 10.1093/cid/ciaa1383

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.

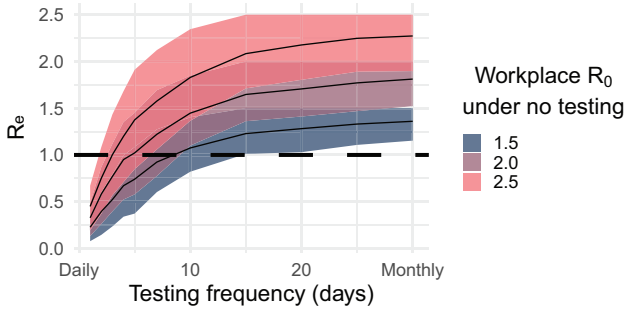

Figure 1. Projected impact of routine PCR testing frequency on the mean effective reproduction number under different testing scenarios. We estimated the effectiveness of increasing frequency of routine PCR testing to reduce the mean effective reproduction number, R_e, under different assumptions on the underlying basic reproduction number, R_0. The x-axis refers to the frequency of PCR testing simulated, from daily (testing frequency of 1 day) to once a month (testing frequency of 30 days). The y-axis represents the mean effective reproduction number (R_e), which is 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. The goal is to reduce R_e to below one to ensure decline in the number of cases when averaged over time. Bands represent the interquartile range accounting for parameter and stochastic uncertainty. Abbreviation: PCR, polymerase chain reaction.

In sensitivity analysis, we observed only small changes in results with variation in test sensitivity, but large changes with variation in test result delays. With $R_0 = 1.5$, reducing test sensitivity by 20% reduced the impact of daily testing (in terms of reduction in R_e) from 85.3% (95% CI: 85.1–85.6) to 80.7% (95% CI: 80.5–81.0). Longer test result delays of 3 and 5 days reduced daily testing impact from 85.3% reduction in R_e to 56.5% (95% CI: 56.2–56.9) and 25.9% (95% CI: 25.4–26.3), respectively. In an ideal case with zero delay and perfect sensitivity, daily testing reduced R_e by 98.9% (95% CI: 98.6–99.1) (Supplementary Figure 4). Varying the background incidence had minimal impact on the study results (Supplementary Figure 5).

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 nonhealthcare 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.

Disclaimer. The views expressed here reflect the opinions of the authors and not necessarily those of affiliated organizations.

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.

References

1. McMichael TM, Currie DW, Clark S, et al; Public Health–Seattle and King County, EvergreenHealth, and CDC COVID-19 Investigation Team. Epidemiology of Covid-19 in a long-term care facility in King County, Washington. N Engl J Med **2020**; 382:2005–11.
2. Tobolowsky FA, Gonzales E, Self JL, et al. COVID-19 outbreak among three affiliated homeless service sites—King County, Washington, 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:523–6.
3. US CDC: testing guidelines for nursing homes. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/nursing-homes-testing.html. Accessed 22 August 2020.
4. US CDC: interim guidance on testing healthcare personnel for SARS-CoV-2.. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-healthcare-personnel.html. Accessed 22 August 2020.
5. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med **2020**; 26:672–5.
6. Li R, Pei S, Chen B, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science **2020**; 368:489–93.
7. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann Intern Med **2020**; 173:362–7.
8. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. Lancet Infect Dis **2020**; 20:678–88.
9. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. Ann Intern Med **2020**; 173:262–7.
10. Grassly NC, Pons-Salort M, Parker EPK, White PJ, Ferguson NM; Imperial College C-RT. Comparison of molecular testing strategies for COVID-19 control: a mathematical modelling study. Lancet Infect Dis **2020**; S1473-3099(20)30630-7. doi:10.1016/S1473-3099(20)30630-7
11. Paltiel AD, Zheng A, Walensky RP. Assessment of SARS-CoV-2 screening strategies to permit the safe reopening of college campuses in the United States. JAMA Netw Open **2020**; 3:e2016818.
12. Lewnard JA, Lo NC. Scientific and ethical basis for social-distancing interventions against COVID-19. Lancet Infect Dis **2020**; 20:631–3.
13. Courtemanche C, Garuccio J, Le A, Pinkston J, Yelowitz A. Strong social distancing measures in the United States reduced the COVID-19 growth rate. Health Aff (Millwood) **2020**. doi:101377hlthaff202000608