Proactive testing in a partially vaccinated population

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Introduction

In the United States, public health authorities have promised that everyone over the age of 16 will be eligible for COVID-19 vaccination by 2021. A return to in-person workplace activity and university education is expected shortly thereafter. For many institutions, this raises important questions about the utility of SARS-CoV-2 proactive testing as more individuals become vaccinated.

Here we aim to address two such questions.

1. **At what level of vaccination and/or naturally-acquired immunity are proactive testing programs no longer necessary?**
2. **As we transition from present conditions to that point, what are best practices for tapering off testing efforts?**

Model description

To address the questions above, we use two distinct modeling approaches. First, we adapt a simple analytic approximation developed by Bergstrom et al. to examine how testing and vaccination interact to reduce transmission. We illustrate these interactions as isoclines, or indifference curves, that indicate how increased vaccination coverage can compensate for reduced testing in a population.

Second, we deploy the SEIRS+ modeling framework used in our workplace testing and return-to-school models to consider workplaces or other groups in which vaccination efforts are underway. Developed by Ryan McGee and Carl Bergstrom at the University of Washington, SEIRS+ is a stochastic, network-based epidemiological simulation model that accounts for the specific details of SARS-CoV-2 transmission and for the structure of social contact networks along which most infections are spread. We use the SEIRS+ model to simulate the dynamics of COVID spread through a workplace or other group of 1000 individuals, following a single introduction from the community. We consider how the fraction of the population vaccinated and the extent of pre-existing natural immunity play into COVID transmission dynamics.

Model parameters

In modeling the effects of testing and vaccination, we face multiple sources of uncertainty. Two of the largest sources involve the effectiveness of vaccines, and the value of the basic reproduction number R_0. In an epidemiological model, R_0 is the mean number of secondary infections generated by an index case in a wholly susceptible population. For our purposes, the relevant value of R_0 is the expected number of transmissions that occur within the institutional setting we are modeling — the number of transmissions that occur at work, for example.

This value will depend on numerous factors such as the level of mitigations — masking, ventilation, basic hygiene, and distancing procedures — that are in place; interaction patterns within the workplace; and the strains of SARS-CoV-2 circulating in the community. Because all of these factors vary from workplace to workplace and from week to week, obtaining a precise estimate of R_0 is often infeasible. As such, the results of this model are more useful for understanding general trends than for making precise quantitative predictions.

The vaccines currently available in the US have demonstrated efficacy against symptomatic COVID-19 cases in the range of 70-95%, with the most widely-distributed vaccines — the mRNA-based ones — at the high end of that efficacy range. While we lack precise estimates of how effectively these vaccines prevent asymptomatic carriage and transmission, available evidence suggests that they block SARS-CoV-2 symptoms and transmission at similar rates. For the purposes of our model, we assume an average effectiveness of 90% for the mixture of vaccines available to the populations we are modeling.

Results

Analytic approximation

To better understand the benefit of proactive SARS-CoV-2 testing in a partially vaccinated workplace or university setting, we adapt the Bergstrom et al. (2020) analytic model to explore how vaccines and testing interact to reduce opportunities for COVID transmission.

The model estimates how much the *effective reproduction number* R_e , the average number of secondary cases generated by each primary case under current conditions, is reduced by a given level of vaccine uptake and cadence of proactive testing. Chance plays an important role in the dynamics of an outbreak — but as a rule of thumb, an index case has a chance of seeding a sizable outbreak when $R_e > 1$, but is unlikely to do so when $R_e < 1$.

To understand how testing cadence and vaccine coverage affect the likelihood of an outbreak, in Figure 1 we examine contour plots of the effective reproduction number R_e. The horizontal axis represents the fraction of the population that have been vaccinated against COVID-19. The vertical axis indicates the cadence of proactive testing across the same population. Along each of the isoclines (solid black lines), the combined effect of proactive testing and vaccination is constant, i.e., each isocline corresponds to a fixed R_e value. Once R_e falls below unity, as indicated by the dashed line, substantial outbreaks are unlikely.

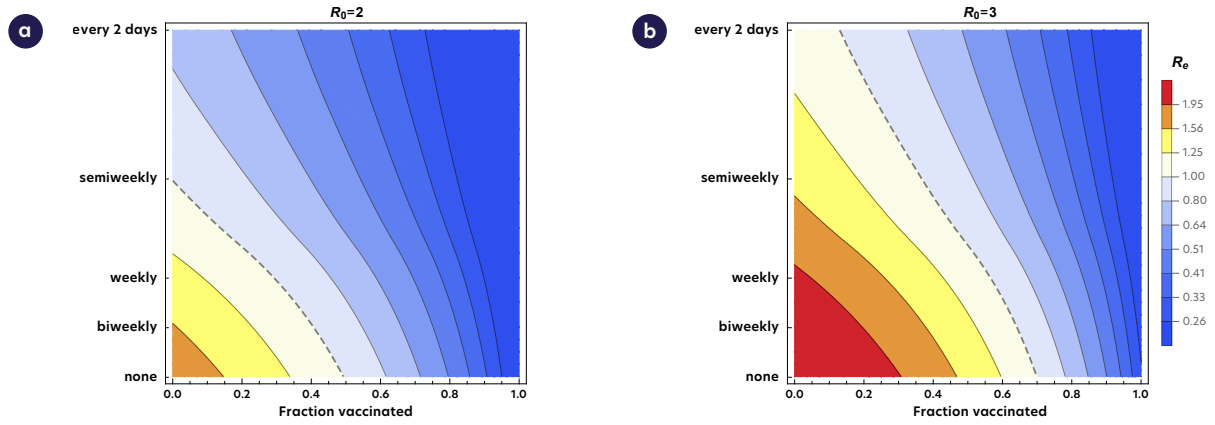


Figure 1. Testing augments vaccination until vaccine coverage is high. Contour plots of the effective reproduction number R_e show how mitigation efforts depend on vaccination coverage and testing cadence. The dashed line in each panel shows the combinations of vaccination and testing that are sufficient to drop R_e to unity. (a) When R_0=2.0, as we might expect with continued masking, distancing, etc., the effective reproduction number can be brought below unity with semiweekly testing, by vaccinating half of the population, or some combination of those interventions. (b) If non-pharmaceutical interventions are relaxed so that R_0 rises to 3.0, higher vaccination coverage and/or testing rates are required. In both panels, we illustrate a situation in which 10% of the population has been previously infected and the vaccines average 90% effectiveness.

Panel 1a illustrates an R_0 value of 2.0, reflecting a situation in which safety measures such as masks and distancing remain in place. Panel 1b illustrates an R_0 value of 3.0, as might be the case in a workplace where safety measures are relaxed to near-2019 levels.

In both panels, we see that frequent testing and broad vaccination coverage reduce the effective reproduction number R_e. The higher the initial level of transmission R_0, the greater the amount of testing and vaccination required to mitigate the risk of outbreaks.

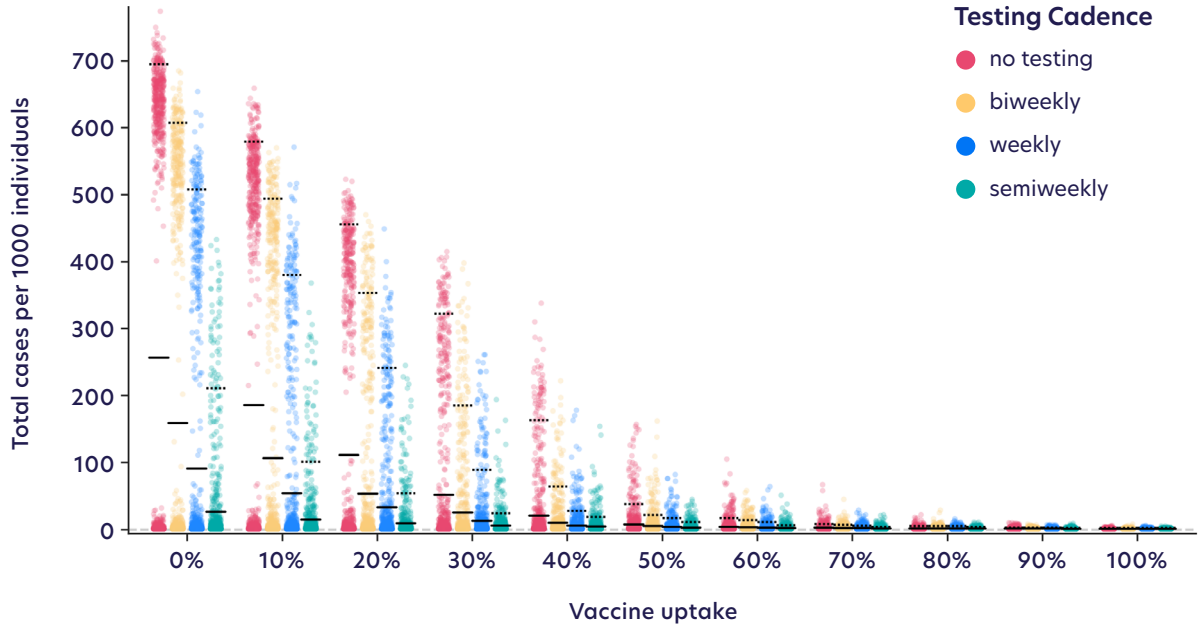
The model reveals that testing is an effective way to reduce R_e — and mitigate outbreak risk — when vaccine coverage is insufficient to do so on its own. For example, we see in Figure 1a that semiweekly testing has a comparable impact to vaccinating half the population. As vaccine coverage becomes more extensive, the effect of testing on R_e declines and eventually testing becomes unnecessary.

Stochastic network-based simulation

The analytical model above relies on a highly simplified picture of disease dynamics. To account for many of the complexities of the real world — superspreading, social contact networks, variation from person to person in disease progression, and the role of chance in an outbreak — we turn to the SEIRS+ simulation model.

Using this model, we consider the consequences of a single introduction into a workplace or other congregate setting. Figure 2 illustrates the distribution of outbreak sizes resulting directly from this single introduction, at various testing cadences, as vaccine adoption increases. For each combination of parameters, we run 1,000 replicate simulations and plot the outbreak sizes in each as a jitter plot — each dot represents the outcome of a single simulation run. The mean and 95th percentile outbreak size are indicated by the solid and dashed bars, respectively.

Figure 2. Outbreak sizes in the SEIRS+ simulation model. Here we illustrate the outcome of 1000 simulations for each combination of testing cadence and vaccination uptake, when 10% of the population have previously been infected, vaccines are on average 90% effective at preventing infection and transmission, and R_0=3.0. Solid black lines mark the mean outbreak sizes and dashed black lines mark the 95th percentile outbreak sizes for each parameter combination.



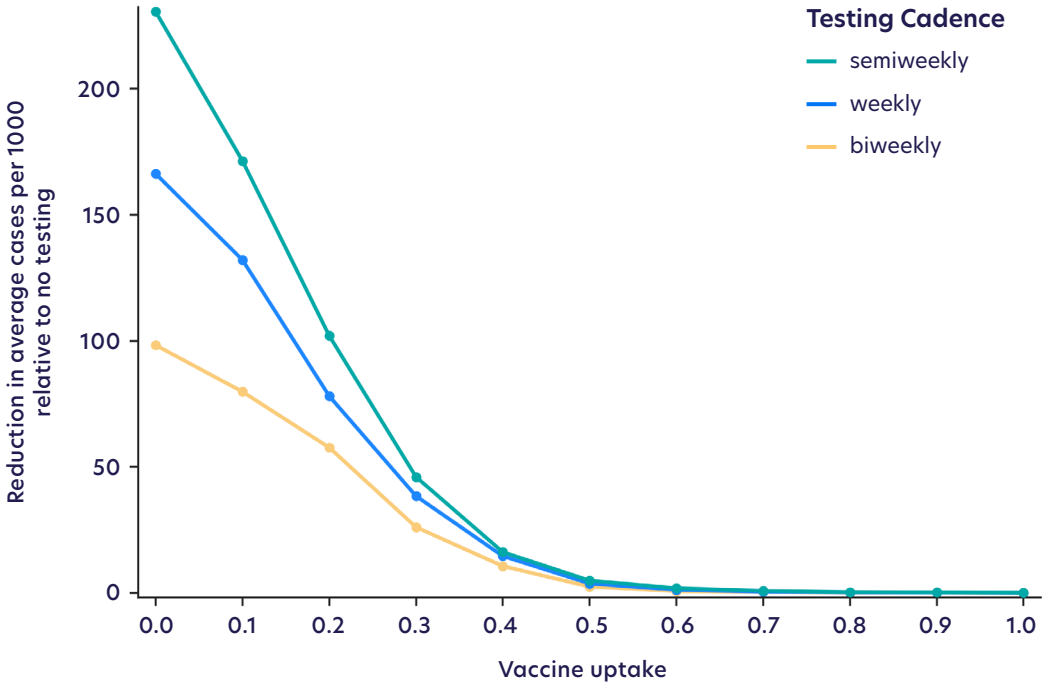
At lower levels of vaccination and testing, we see a bimodal distribution of outcomes. In some simulation runs, large outbreaks occur, while in other runs with the same parameter settings, no outbreak arises at all. This is the consequence of chance events that contribute to the trajectory of disease spread. We also see that when less than half of the population has been vaccinated, testing is a powerful tool for reducing both the mean number of cases and the 95th percentile outbreak size.

Figure 3 illustrates how the average benefit of testing declines as more of the population becomes vaccinated. The benefit of testing is measured as the reduction in the mean number of individuals infected after a single introduction due to testing. In the absence of vaccination and with R_0=3.0, for example, weekly testing prevents an average of 170 cases after a single introduction into a population of 1000 people. By the time 70% of the population is vaccinated, weekly testing prevents only a few cases. In general, we see that (1) when vaccination is limited, more frequent testing confers greater benefits, and (2) once vaccination becomes very common, the benefits of testing become diminished.

Interpretation

The two models — the analytic approximation and the SEIRS+ simulation — generate concordant results. Both demonstrate that testing is valuable when vaccination is limited, but testing becomes unnecessary — quite abruptly — once vaccination coverage expands. Specifically, once the effective reproduction number R_e drops below 1 without testing, proactive testing offers little additional value and can be suspended if preventing outbreaks is the sole objective. Note that even when R_e < 1 and an outbreak is unlikely, high-cadence testing can help prevent one-off transmissions and thereby provide additional security and peace of mind for unvaccinated workers. Individual employers will have to decide whether this is cost- and time-effective.

Figure 3. Value of testing in the SEIRS+ simulation model, as more of the population becomes vaccinated. Here we show how many cases per 1000 individuals are prevented on average when using a given testing cadence relative to not testing, where R_0=3.0, 10% of the population have previously been infected, and vaccines are on average 90% effective at preventing infection and transmission.



Testing generally offers a high return-on-investment in an unvaccinated workplace population (see our previous workplace testing model), and these benefits persist in a partially vaccinated cohort. Given the uncertainties surrounding the exact value of R_e, and the logistical complexities of adjusting testing cadence in real time, most employers will not find it practical to try to scale down the testing cadance gradually as vaccination rates increase. Moreover, the range of vaccine adoption in which it may be beneficial to reduce testing cadence is so short-lived, it is logistically much simpler to continue at the original pre-vaccination testing cadance until there is good reason to believe that $R_e < 1$ in the workplace, at which point the proactive testing program can be halted entirely.

The challenge, of course, is knowing when this point has been reached. Workplaces may wish to conduct surveillance testing to be certain that they have not misjudged the point at which it is safe to end a proactive testing program.

For reasons of both logistics and morale, we strongly encourage that when testing in the workplace, employers test all employees irrespective of vaccination status and past infection status.

Interactive model demonstrates robustness

In the figure and discussion above, we focused on a single set of parameters: R_0=3.0 and incidence 10%. There is nothing special about these parameter values; we selected them as reasonable estimates of the situation on the ground in many settings. The important thing about the models in question is that the precise parameter values do not matter a great deal, because our results are robust to changes in these parameters.

To illustrate the general robustness of our results to differences in parameters, we have developed an interactive web application that displays results from the SEIRS+ model across a wide range of parameters.

Conclusion

Both an analytic approximation and a SEIRS+ simulation model demonstrate that proactive testing is a valuable tool for preventing or mitigating outbreaks, when vaccination is limited. Proactive testing becomes unnecessary once vaccination is widespread. Specifically, once the effective reproduction number R_e drops below 1 without testing, proactive testing offers little additional value and can be suspended.

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About Color

Color, a health technology and services company based in Burlingame, CA, provides distributed clinical healthcare services anchored in technology. We've built our programs to ensure the health and safety of large populations and provide individuals with a simple, efficient, and high-quality testing experience. Color works with hundreds of organizations and since April 2020, Color has returned over 3.5 million COVID-19 testing results.