*Clinical Infectious Diseases*

MAJOR ARTICLE

# Mathematical Modeling to Inform Vaccination Strategies and Testing Approaches for Coronavirus Disease 2019 (COVID-19) in Nursing Homes

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***Background.*** Nursing home residents and staff were included in the first phase of coronavirus disease 2019 vaccination in the United States. Because the primary trial endpoint was vaccine efficacy (VE) against symptomatic disease, there are limited data on the extent to which vaccines protect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the ability to infect others (infectiousness). Assumptions about VE against infection and infectiousness have implications for changes to infection prevention guidance for vaccinated populations, including testing strategies.

***Methods.*** We use a stochastic agent-based Susceptible-Exposed-Infectious (Asymptomatic/Symptomatic)-Recovered model of a nursing home to simulate SARS-CoV-2 transmission. We model 3 scenarios, varying VE against infection, infectiousness, and symptoms, to understand the expected impact of vaccination in nursing homes, increasing staff vaccination coverage, and different screening testing strategies under each scenario.

***Results.*** Increasing vaccination coverage in staff decreases total symptomatic cases in the nursing home (among staff and residents combined) in each VE scenario. In scenarios with 50% and 90% VE against infection and infectiousness, increasing staff coverage reduces symptomatic cases among residents. If vaccination only protects against symptoms, and asymptomatic cases remain infectious, increased staff coverage increases symptomatic cases among residents. However, this is outweighed by the reduction in symptomatic cases among staff. Higher frequency testing—more than once weekly—is needed to reduce total symptomatic cases if the vaccine has lower efficacy against infection and infectiousness, or only protects against symptoms.

***Conclusions.*** Encouraging staff vaccination is not only important for protecting staff, but might also reduce symptomatic cases in residents if a vaccine confers at least some protection against infection or infectiousness.

**Keywords.** COVID-19; nursing homes; vaccine efficacy.

Nursing homes have been devastated by the coronavirus disease 2019 (COVID-19) pandemic in the United States [1]. Nursing home residents are disproportionately affected by severe disease and mortality because of their older age and high prevalence of comorbidities. In addition, congregate living and necessarily close contacts (eg, assistance with activities of daily living) between staff and residents have made controlling outbreaks in these settings challenging. Because of this, residents and staff of nursing homes were included in the Advisory Committee on Immunization Practices' first phase (1a) for vaccination, alongside healthcare personnel [2]. Vaccine rollout began in nursing homes across the country in late December 2020.

Screening testing (ie, testing of asymptomatic individuals, paired with enhanced infection prevention and control (IPC)—such as personal protective equipment and environmental cleaning [3]—has been one of the primary strategies available to control outbreaks in nursing homes, although the extent and frequency of testing has been hampered by resource availability [4]. Current recommendations are to test previously undiagnosed residents and staff every 3–7 days if there is an outbreak in the facility, and to test staff up to twice weekly regardless of outbreak status, depending on community test positivity [5, 6]. Although both polymerase chain reaction (PCR) and antigen tests are used, we found in previous work [7] that point of care testing, such as antigen tests—which are less sensitive to detect any virus RNA but nearly as sensitive for infectious virus—may better reduce transmission when used at the same frequency. This is due largely to the turnaround time for results: as low as 15 minutes for antigen tests vs up to 48 hours for PCR tests [7, 8].

The results of clinical trials of vaccines currently authorized in the United States show high vaccine efficacy (VE) against

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symptomatic disease across all age groups, which is promising for reducing morbidity and mortality among nursing home residents [9, 10]. Although mortality rates will vary by age and other factors, the ability of the vaccine to reduce symptomatic disease, especially severe symptoms, will have a substantial impact on mortality.

The vaccine trials provided limited data on VE against all infection (ie, including asymptomatic infection) or infectiousness (eg, ability to transmit virus to others, such as by blunting or reducing the duration of peak viral load) [11]. The VE against infection and infectiousness have important implications for understanding whether these vaccines can build herd immunity in a population and for identifying when and to what extent other IPC strategies can be lifted. In nursing homes, outbreak control measures take substantial resources and do have important negative consequences—including restricting visitors and drawing on limited staff time.

Communities of color comprise a large proportion of nursing home staff [12, 13]. Recent analyses have found lower vaccination uptake among staff compared with residents [14–16]. This may be due in part to hesitancy stemming from historical injustices that have justifiably resulted in reduced trust in medicine and the safety of a novel vaccine [17].

Here, we use mathematical modeling to examine the effects of vaccination in nursing homes, with the understanding that vaccination among the elderly in the general community will lag behind vaccination in nursing homes. Although vaccinating residents is a priority, we focus here on evaluating the effects of increasing vaccination among staff because this is where there have been reported challenges with uptake. Additionally, high resident turnover may make it challenging to maintain high vaccination levels among residents. We also look at testing strategies under different assumptions about the mode of VE to evaluate how, or whether, screening testing recommendations may be changed following vaccine rollout.

## METHODS

### Model Overview

Here, we expand upon a stochastic, agent-based Susceptible-Exposed-Infectious (Asymptomatic/Symptomatic)-Recovered model of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in nursing homes [7]. The nursing home consists of 100 residents, with 2 per room, and 100 staff split evenly across 3 shifts. Although nursing home staff fulfill many roles, involving different types of contact with residents, we simplify this to a single staff population with the same characteristics for generalizability. Resident lengths of stay are drawn from a distribution with a median of 27 days, based on data from the publicly available Centers for Medicare & Medicaid Services Minimum Data Set 3.0 from 2016 [18] (Table S1). We made the simplifying assumption that the nursing home remains at 100% capacity, with new residents replacing those who have died or been discharged. We assume new resident admissions are not vaccinated or immune from previous infection, but vary this in a sensitivity analysis (Table S1).

Individuals have a binomial probability of infection each day based on the total infectiousness of their contacts, the force of infection between each type of population (ie, staff–staff, staff–resident, or resident–resident), and the number of daily contacts with each population. With the exception of roommates, individual contacts are not modeled explicitly. We assume residents do not contact other residents, with the exception of their roommates, and daily contact rates between residents and staff are based on contact rates from nursing homes across the United States (R. Anglo, personal communication; M. Samore, personal communication). Infected individuals are identified either based on symptoms or through screening testing, after which residents are isolated with other COVID-19–infected residents and staff are sent home. We conduct 2 sensitivity analyses of our assumptions regarding transmission dynamics, lowering the probability of infection given contact ($\beta$) and increasing the number of nonroommate resident interactions for each resident.

Staff working with COVID-19–infected residents are assumed to have access to personal protective equipment that reduces their probability of infection (Table S1), reflecting current availability [19]. Infected staff are sent home to recover, resulting in shortages of staff in the nursing home; temporary staff are brought in as replacements once staffing falls below 50%, which is a conservative assumption reflecting continued staffing shortages [20]. We assume that, other than their temporary status, these staff are not different from permanent staff. We assume that there is no turnover among permanent staff.

Viral load (ie, number of RNA copies/mL) is modeled stochastically for each infected individual [7]. The durations of increasing and decreasing viral load are drawn from uniform distributions, and each individual's peak viral load is drawn from a normal distribution (Table S1). Importantly, we assume that viral load trajectories for asymptomatic and symptomatic infections are drawn from the same distributions [21, 22]. We model infectiousness categorically, making the assumption that it depends on viral load: not infectious ($<10^4$ copies/mL), moderately infectious (ie, 50% of full infectiousness), and fully infectious ($>10^7$ copies/mL). Although the relationship between infectiousness and viral load is not fully understood, these assumed values fall within the range used in other models [22]. This is likely conservative as peak viral loads routinely exceed $10^{10}$ copies/mL, and full infectiousness may not be reached until viral loads are closer to this range. More details on the model structure can be found elsewhere [7] and online at https://github.com/rek160/NursingHomeVaccineModel.

### Testing Strategies

We evaluate 2 types of screening tests: (1) rapid antigen and (2) PCR, simulating either weekly testing or testing every 3 days (2.3 times per week) of both staff and residents. These testing scenarios are compared with a scenario in which testing is only symptom-based (ie, there is no testing of individuals without symptoms). PCR and antigen tests vary in their sensitivity (modeled as viral limit of detection) and turnaround time. Based on the data available on these tests, antigen testing has a higher limit of detection than PCR (Table S1) but returns results immediately, whereas PCR here has a 2-day delay. For symptomatic individuals, isolation in the nursing home (for residents) or at home (for staff) begins immediately on symptom onset. For asymptomatic individuals, isolation is not implemented until positive results are returned. Although not explicitly modeled, we assume high specificity of antigen tests would be achieved through rapid confirmatory tests.

### Vaccine Efficacy Scenarios

We incorporate 3 types of VE into the model: VE against progression to symptoms among those infected ($VE_P$), VE against susceptibility to infection ($VE_S$), and VE against infectiousness ($VE_I$) among those infected (Table 1) [11]. In all simulations, we assume VE against symptoms—a combination of $VE_S$ and $VE_P$—is 90%, which is similar to the findings from the Pfizer and Moderna vaccine trials [9, 10]. Because these trials only provided data on VE against disease (ie, symptomatic infection), we compare 3 different scenarios (Table 1) that would all result in a total VE against symptoms of 90% but vary in their efficacy against susceptibility to infection and infectiousness. In scenario 1, we assume that VE against symptoms comes entirely from efficacy against susceptibility to infection ($VE_S$ = 90%) and that efficacy against infectiousness is also high ($VE_I$ = 90%). In scenario 2, we assume a lower efficacy against susceptibility to infection and infectiousness and therefore a higher $VE_P$ than in scenario 1. In scenario 3, we assume the only protection the vaccine confers is against progression to symptoms ($VE_P$ = 90%).

**Table 1. Parametrization of VE Scenarios With Varying Levels of Protection Against Infection and Infectiousness[a]**

| | VE Parameters for Given Scenario | | |
|---|---|---|---|
| VE Scenario | Vaccine Efficacy Against Progression to Symptoms ($VE_P$)[b] | Vaccine Efficacy Against Susceptibility to Infection ($VE_S$)[b] | Vaccine Efficacy Against Infectiousness ($VE_I$)[b] |
| 1: VE against symptoms, infection, infectiousness (high) | 0%, 0% | 45%, 90% | 45%, 90% |
| 2: VE against symptoms, infection, infectiousness, (low) | 27%, 80% | 25%, 50% | 25%, 50% |
| 3: VE against symptoms only | 45%, 90% | 0%, 0% | 0%, 0% |

Abbreviation: VE, vaccine efficacy.

[a]To reflect results of vaccine trials, each scenario has a final VE against symptoms of 90% after 2 doses, which is a combination of $VE_S$ and $VE_P$.

[b]First value is the efficacy of the first dose, and second value is the efficacy after the second dose.

$VE_P$ is implemented as an increase in the probability of an infected individual being asymptomatic. $VE_S$ is implemented as a reduction in the probability of becoming infected per contact. $VE_I$ is implemented as a reduction in the infectiousness of each infected individual, based on their viral load. In all scenarios, partial efficacy is conferred 7 days after the first dose, and full protection is conferred 7 days after the second dose. The efficacy from a single dose is set to 50% of the efficacy after the second dose—this is lower than initial studies of first dose effectiveness [23], making this a conservative assumption. Doses are administered on 2 days only, 21 days apart.

To isolate the effects of the different vaccine scenarios in our analysis, everyone is susceptible to infection (ie, no immunity from previous infections) at the beginning of each simulation. Beginning 8 days after the second dose, when the second dose has taken full effect, staff have a daily probability of infection from the community. Our primary endpoint for comparison is cumulative symptomatic infections over the 6 weeks after community infections are allowed, using the mean across 100 simulations (Figure S1). In a sensitivity analysis, we examine the impact of allowing community infections 8 days after the first dose. We conduct an additional sensitivity analysis of a single-dose, lower efficacy vaccine, to reflect potential use of the Johnson & Johnson Janssen vaccine (Table S1) [24]. To identify the effects of vaccination among staff, 90% of residents are vaccinated with 2 doses at baseline, and we only vary coverage among staff.

## RESULTS

As expected, we find that in each of the VE scenarios, with 90% baseline resident coverage and symptom-based testing only, increasing vaccination coverage among staff reduces total symptomatic cases in the nursing home (Figure 1, S2). Scenario 1, with high VE against infection and infectiousness, is most effective: increasing staff coverage from 0% to 90% reduces total symptomatic cases by 81%. In scenario 2, with lower VE against infection and infectiousness, increasing staff coverage from 0% to 90% reduces total symptomatic cases by 63%. When the vaccine only protects against symptoms (scenario 3), total symptomatic cases are highest within each level of staff coverage, and increasing staff coverage from 0% to 90% reduces total symptomatic cases by only 33%. In a sensitivity analysis examining the impact of a vaccine with lower efficacy against symptoms and moderate efficacy against infection and infectiousness, the

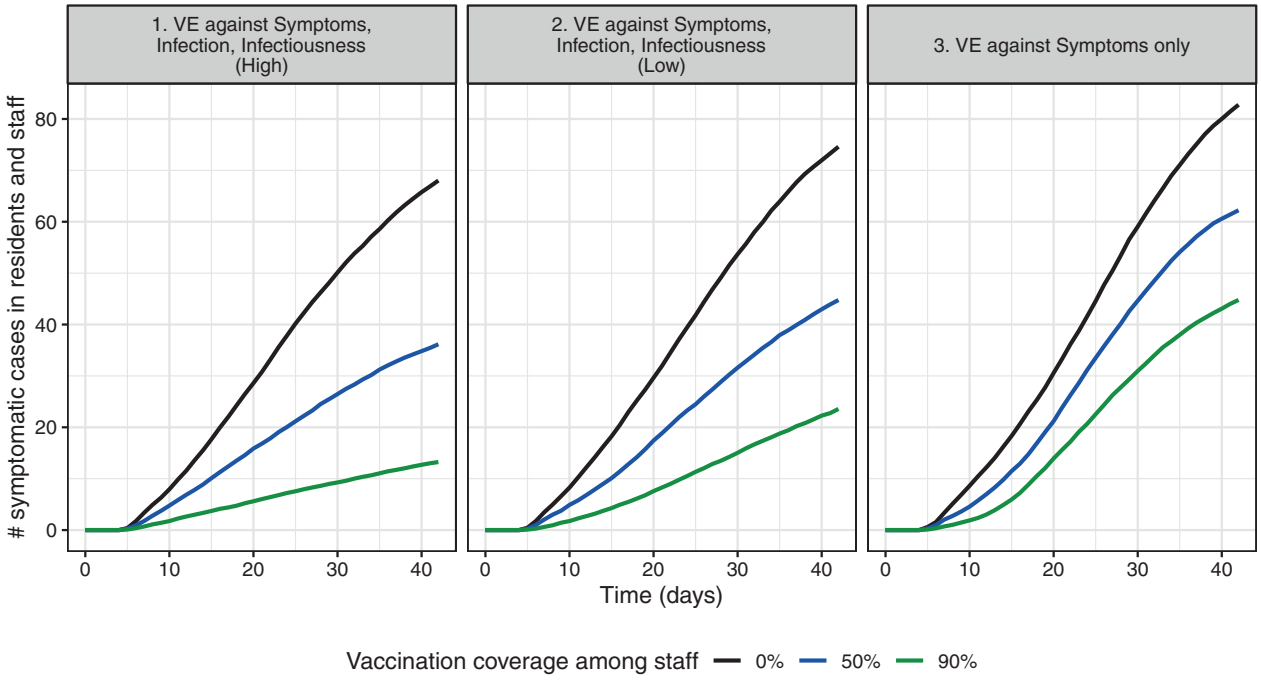


**Figure 1.** Cumulative number of symptomatic cases in residents and staff combined over 6 weeks after full vaccine immunity, under 3 different VE scenarios and varying levels of staff coverage (0%, 50%, and 90%), with symptom-based testing only. Baseline resident coverage is 90%. VE, vaccine efficacy.

cumulative symptomatic incidence falls between our scenarios 1 and 2 (Figure S3).

Although increasing vaccination coverage among staff reduces overall symptomatic cases among both staff and residents in all 3 scenarios, the impact of staff coverage on total symptomatic cases in residents only is highly dependent on the VE scenario (Figure 2). When the vaccine protects against infection and infectiousness, increasing coverage from 0% to 90% among staff reduces symptomatic cases among residents by 86% in scenario 1 and 45% in scenario 2. Although initial resident coverage is 90%, this coverage falls quickly because of high resident turnover and low assumed community coverage (Figure S4). In a sensitivity analysis, in which 50% of incoming residents are vaccinated, the total number of symptomatic cases is lower, but staff coverage remains important for reducing cases among residents, and we see the same trends across VE scenarios (Figures S5–S7).

However, if the vaccine only protects against symptoms, higher coverage among staff may increase the proportion of cases that are asymptomatic, leading to more undetected transmission. In scenario 3, increasing staff coverage from 0% to 90% leads to 22% more symptomatic cases among residents (Figure 2).

The importance of screening testing also varies by type of VE (Figure 3). When baseline coverage in staff and residents is 90% and the vaccine has partial efficacy against infections and infectiousness (scenario 2), screening testing conducted 2.3 times per week reduces total symptomatic cases in residents by 63% for antigen testing and 45% for PCR testing compared with symptom-based testing only. When the vaccine has no efficacy against infections and infectiousness (scenario 3), this same change in testing reduces total symptomatic cases in residents by 52% for antigen testing and 27% for PCR testing. Because of faster turnaround time, antigen testing always results in lower symptomatic incidence than PCR testing done at the same frequency. If the vaccine has high efficacy against infection and infectiousness (scenario 1), screening testing has little added benefit over symptom-based testing. In a sensitivity analysis in which cases are allowed to be introduced 8 days after the first dose (compared with 8 days after the second dose in our baseline scenario), screening testing is important for reducing cumulative symptomatic cases under all VE scenarios (Figure S8). In sensitivity analyses of $R_0$, varying either β or the number of daily contacts between residents (Table S1), the cumulative symptomatic incidence changes, but the shape of the epidemic curves and the relative trends remain the same (Figures S9–S12).

## DISCUSSION

As vaccination continues in nursing homes and across the country, understanding how well vaccines are able to reduce infection and infectiousness is critical for informing strategies to control COVID-19 outbreaks. By modeling outbreaks within a single nursing home, we look at the impact of vaccination coverage among staff and multiple testing strategies under different

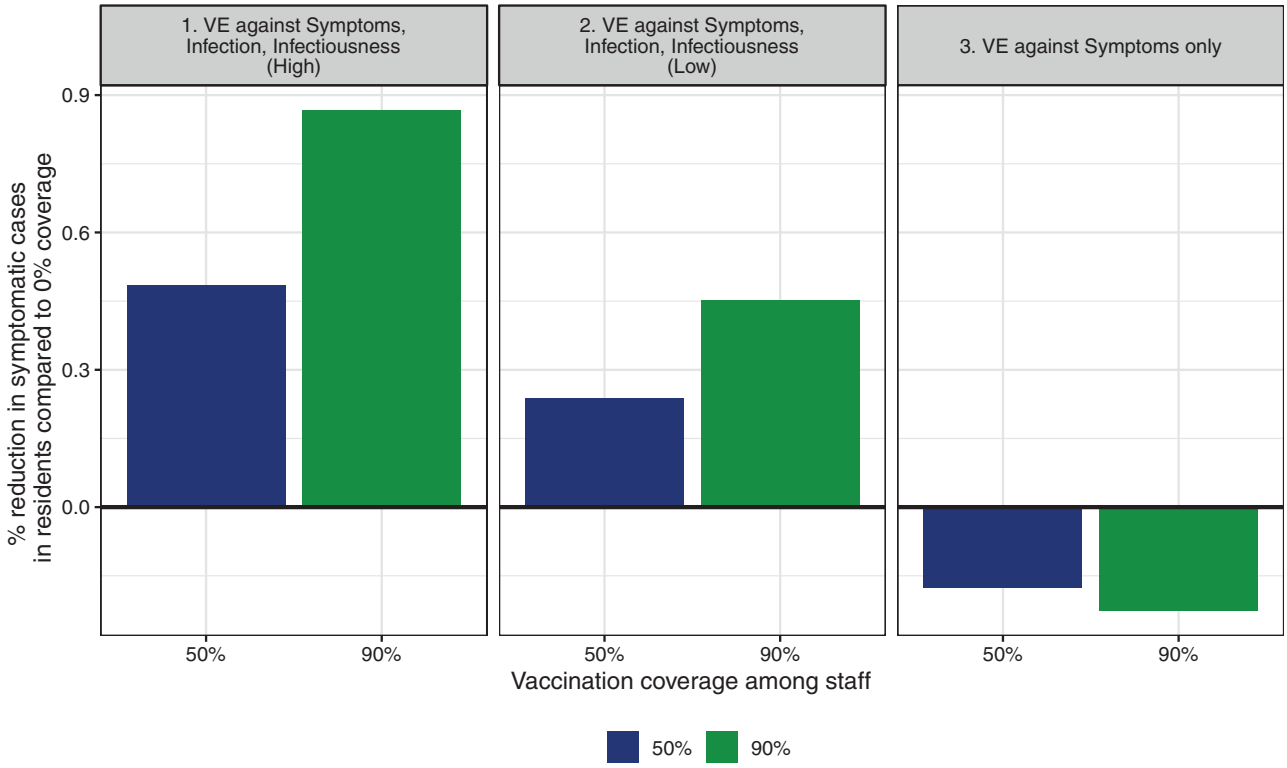


**Figure 2.** Percent reduction in cumulative number of symptomatic cases in residents over 6 weeks after full vaccine immunity, under 3 different VE scenarios and varying levels of staff coverage (50% and 90% compared with 0%). Baseline resident coverage is 90%. VE, vaccine efficacy.

assumptions about VE. We find that, given high resident turnover in nursing homes, staff vaccination coverage is a critical factor driving symptomatic incidence. Because of limited vaccine supply, vaccine program implementation will likely continue to be targeted based on risk for some period; in this paper, we focus on the period in which vaccines are available to specific risk groups but are not yet offered to the community at large [2].

As expected, increasing vaccination coverage among staff can have a protective effect for residents if the vaccine provides at least some protection against infection and infectiousness. These results highlight the importance of encouraging vaccination among staff—both for their protection because they have been 1 of the groups most severely affected, and also to protect residents, who are among those at highest risk of mortality. Efforts to increase staff vaccination should include culturally competent messaging and support to address concerns. Reaching higher vaccine coverage among staff could allow for less screening testing, as we see that increased frequency of testing has little benefit when efficacy against infection is high.

If the vaccine does not protect against infection and infectiousness, but only against symptoms, our analysis indicates that increasing staff coverage could lead to higher numbers of symptomatic cases among residents. These results underscore the importance of continuing frequent screening testing in nursing homes, particularly during outbreaks, until more data are available on the types of protection the vaccines provide. Given the importance of rapid results, we see that point-of-care tests, such as antigen tests, may be more effective than PCR tests in reducing symptomatic incidence, particularly when rapid PCR turnaround is not feasible.

We have made simplifying assumptions about the logistics of vaccine rollout, with only 2 days for vaccination (1 for each dose); many nursing homes conducted vaccinations across 3 days. Offering vaccination upon nursing home admission would help maintain higher levels of resident vaccination coverage; however, given the 2-dose schedule, many residents will not stay long enough to get a second dose, even if opportunities for vaccination are provided during their stay (Table S1). This underscores the importance of vaccination among community-dwelling individuals (eg, older adults, those with multiple comorbidities) before they become nursing home residents to ensure that short-stay residents are protected.

We have also made several assumptions regarding contact patterns, including modeling staff as 1 population; in reality, staff have many different responsibilities and levels of interaction with residents that affect risk of transmission. We made the conservative assumption of equal infectiousness given vaccination status for asymptomatic and symptomatic infections. We also did not assess the potential benefits of outbreak vs nonoutbreak

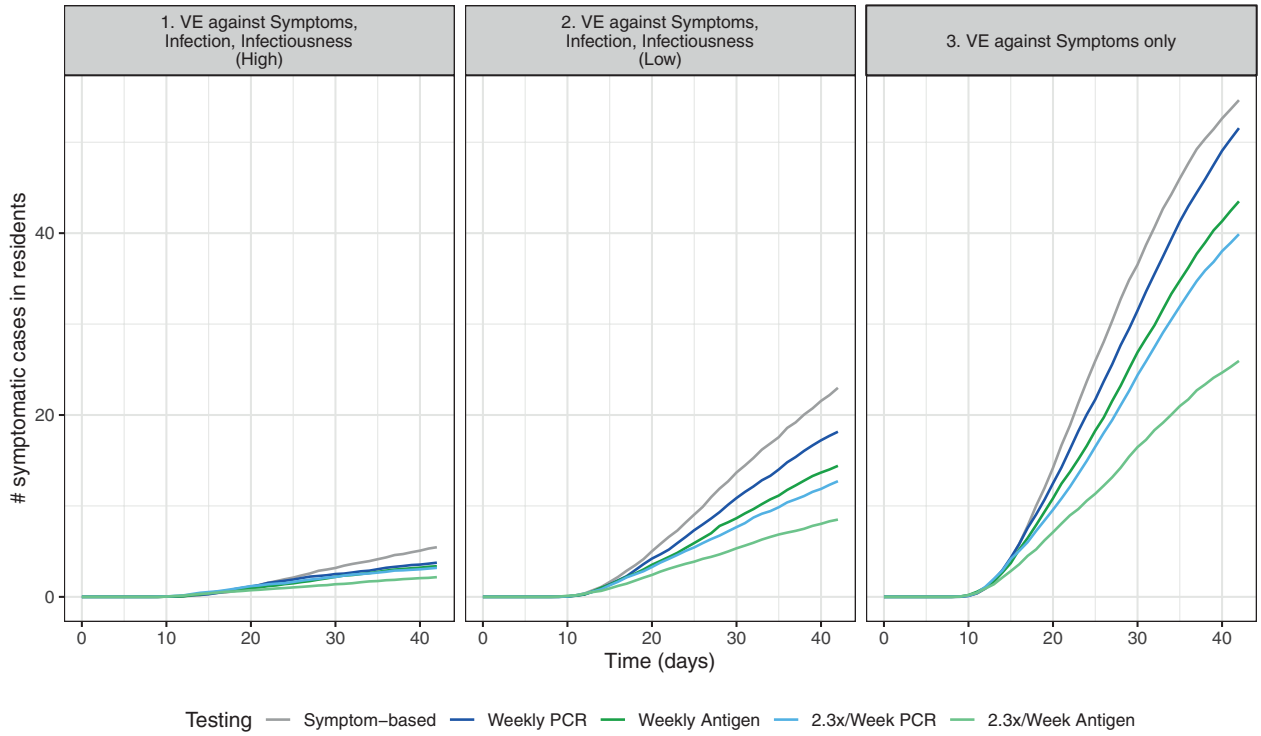


**Figure 3.** Cumulative number of symptomatic cases in residents over 6 weeks after full vaccine immunity, under 3 different VE scenarios and 5 different testing strategies. Baseline resident and staff coverage is 90%. VE, vaccine efficacy.

testing [8] in a vaccinated population, which may have important implications for prioritizing limited testing resources (because of time, cost, or both); we focus on screening testing in this analysis. We further assumed nursing homes would maintain strict policies limiting visitation over the simulation's time horizon. These policies have important implications for quality of life. Future research is needed to explore the impact of VE, testing practices, and community incidence rates on the ability to safely relax these and other IPC policies.

Data from vaccine rollout in nursing homes and other settings prioritized for early vaccination have the potential to improve our understanding of the mode(s) and level of VE. These data may also provide insight into the efficacy of these vaccines against new variants of concern. Until there is sufficient evidence indicating the extent of VE against infection or infectiousness, screening testing remains a key tool for reducing symptomatic incidence in these high-risk settings, and frequent screening testing in addition to symptom-based testing should continue to be conducted to prevent nursing home outbreaks [25].

## 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

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