Modeling the effectiveness of healthcare personnel reactive testing and screening for the SARS-CoV-2 Omicron variant within nursing homes

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Running title: Testing strategies for the Omicron variant in nursing homes

Abstract:

The SARS-CoV-2 Omicron variant has been hypothesized to exhibit faster clearance (time from peak viral concentration to clearance of acute infection), decreased sensitivity of antigen tests, and increased immune escape (the ability of the variant to evade immunity conferred by past infection or vaccination) compared to prior variants. These factors necessitate re-evaluation of prevention and control strategies — particularly in high-risk, congregate settings like nursing homes that have been heavily impacted by other COVID-19 variants. We used a simple model representing individual-level viral shedding dynamics to estimate the optimal strategy for testing nursing home healthcare personnel and quantify potential reduction in transmission of COVID-19. This provides a framework for prospectively evaluating testing strategies in emerging variant scenarios when data are limited. We find that case-initiated testing prevents 38% of transmission within a facility if implemented within a day of an index case testing positive, and screening testing strategies could prevent 30-78% of transmission within a facility if implemented daily, depending on test sensitivity.

Keywords: COVID-19, Omicron, outbreak testing, screening testing, nursing homes

Background

The SARS-CoV-2 Omicron variant (B.1.1.529) was first detected in South Africa on November 24, 2021, and this virus has rapidly spread globally [1]. Understanding how the transmissibility and severity of Omicron may impact the effectiveness of targeted infection prevention and control (IPC) measures (e.g., testing, quarantine, and isolation strategies), particularly within high-risk, congregate settings like nursing homes, should facilitate appropriate adaptation of these measures to this new variant. Quantitative analyses using modeling methods can be valuable tools to understand and improve mitigation measures prospectively. Such methods provide a framework for overcoming lack of data and uncertain estimates in scenarios of emerging variants that have the potential to be harmful, especially for populations at higher risk for severe COVID-19 outcomes. Case-initiated testing and testing of asymptomatic healthcare personnel are two current strategies used to identify cases and prevent transmission of SARS-CoV-2 in nursing homes; these interventions have been demonstrated to be effective for prior SARS-CoV-2 strains [2, 3]. Here, we present a modeling framework to prospectively quantify how testing and isolation measures may need to be altered to optimally control the spread of Omicron and other COVID-19 variants with similar characteristics.

The Omicron variant has been hypothesized to either exhibit similar viral shedding dynamics and clearance (time from peak viral concentration to clearance of acute infection) to the Delta variant, or possibly a shorter duration of infection compared to prior strains, although this has been difficult to disentangle from prior immunity [4, 5]. Experience with the Omicron variant has also raised concerns about lower detection by commonly used antigen tests, though more recent findings have demonstrated similar sensitivity ranges to prior variants [6, 7]. Additionally, 87% of nursing home residents and healthcare personnel are fully vaccinated, and 44% of nursing home personnel and 74% of nursing home residents have received a primary or additional booster dose as of March 6, 2022 [8]. Therefore, it may be necessary to re-evaluate the optimal testing strategy (including timing), since

vaccination may affect viral shedding dynamics, with breakthrough infections exhibiting faster clearance (5.5 days) compared to unvaccinated cases (7.5 days) [9]. We also consider the impacts of booster doses on viral shedding dynamics, as more robust immune responses are associated with faster clearance [10]. Here, we model the timing and effectiveness of two testing strategies for healthcare personnel for Omicron: a) case-initiated testing, defined here as broad testing following identification of a COVID-19-positive index case, and b) screening testing, defined here as periodic testing of asymptomatic workers.

Methods

We use a simple model representing individual-level viral shedding dynamics to estimate the optimal time to test nursing home healthcare personnel and quantify the potential reduction in transmission for both case-initiated testing strategies and asymptomatic periodic screening testing strategies [11]. This model prospectively assesses testing strategies in congregate settings, quantifying the impacts on transmission early after the emergence of a novel variant when data are limited, and thus the model is general and makes six assumptions that could be re-parameterized to account for the characteristics of future variants, numbered below. This analysis was conducted in R version 4.1.1.

Testing strategies

Within our model, case-initiated testing indicates widespread testing of all nursing home healthcare personnel following the identification of a COVID-19 positive individual. Within a nursing home, one positive COVID-19 case qualifies as an outbreak, which triggers testing of other healthcare personnel within the facility [11]. The other strategy evaluated is asymptomatic periodic screening testing. This strategy represents testing of all asymptomatic healthcare personnel in the absence of a known outbreak at predetermined intervals from one to seven days.

Viral shedding dynamics

In our model, infectiousness is directly proportional to viral load (assumption 1). We use the flexibility afforded by the gamma distribution [12] to model both infectiousness and test sensitivity as functions of time, holding the shape parameter constant and calibrating the scale parameter to the pace of viral shedding dynamics based on variant and immune status (i.e., the scale parameter values were selected to make gamma distributions that reach their peak at the time that viral load peak for an individual with a specific immune status). Omicron proliferation is assumed to resemble that of the Delta variant for unvaccinated people in our model (assumption 2), due to lack of available data on the timing of viral shedding dynamics for emerging variants [4, 5]. Unvaccinated people are thus represented by a scale parameter value of 0.53, representing a peak viral load about four days following exposure [13]. Faster clearance rates for fully vaccinated people are quantified with scale parameter values of 0.48, relating to peak viral load, and thus peak infectiousness at 3.5 days post-exposure. People who received a booster are assumed to exhibit a slightly faster clearance rate (assumption 3), with a scale parameter value of 0.44, relating to peak viral load at 3.2 days post-exposure. For the purposes of this evaluation, conclusions about viral load are not varied by vaccine status [9] and instead are based on the timing of the kinetics of viral shedding.

Test sensitivity

Antigen test sensitivity is assumed proportional to viral load (assumption 4), reaching its peak value (20–80%) during peak viral load, but then decreasing. The test sensitivity levels considered are described by their sensitivity at the peak, but they are dynamic; for example, Figure 1A visualizes an 80% sensitive test in the red, solid line. The sensitivity values considered capture a wide range, due to uncertainty of possible sensitivity values when previously approved tests are used for a novel variant.

Model details

For case-initiated testing, we model a hypothetical, flexible, yet plausibly parameterized scenario in which an index individual transmits to a secondary case individual. To represent the plausible timing of this transmission, we use probability distributions; these are visualized in Figure 1A. The index individual has a viral load, and proportional infectiousness, represented by the gamma distributions described above. The day that the index individual tests positive is defined as day zero, and we assume, based on presymptomatic shedding of SARS-CoV-2 [12], that infection of a secondary case occurred three days prior (assumption 5). The probability density of the time of exposure of the index case is modeled proportional to its likelihood — the probability of the positive test given the time of exposure (based on test sensitivity profile and a testing rate). This is used to represent the expected infectiousness of the index case over time —also proportional to the probability density of the time of exposure of the secondary case within the exposure window (assumption 6). In turn, this yields the expected infectiousness of the secondary case as a function of time. We evaluate the impact of decreased test sensitivity as a reduction in the probability of testing positive. We modeled isolation measures as reducing transmissions following positive testing of the secondary case, yielding an estimate of secondary transmissions averted through testing of the contact. The optimal time to test lies where the maximum proportion of secondary transmission would be averted through isolation of those people testing positive. For screening testing, the same approach is used, but with tests implemented at intervals of one to seven days.

Results

Case-initiated testing

Given Omicron immune escape (the ability of the variant to evade immunity conferred by past infection or vaccination), the optimal time to test a secondary case who is fully vaccinated occurs within

a day of the index case testing positive, at day 0.08 following index case testing positive at day zero as the model is parameterized (Figure 1B). Additionally, with the given parameterization, the optimal time to test an individual who received a booster dose occurs at day -0.12 (i.e., before the index case tests positive). This suggests that the best time to test, in order to most effectively reduce transmission to a secondary case, has already passed by the time the index case tests positive. For unvaccinated healthcare personnel, if the Omicron variant's viral shedding dynamics resemble those of the Delta variant, the optimal test time is day 0.4. Testing and isolation prevent more transmission when they are performed closer to the time that the index case tests positive: the estimated percent of transmission averted from fully vaccinated workers is 60%, 38%, and 11% if case-initiated testing starts on days zero, one, or two, respectively, with 80% test sensitivity.

Screening testing

Screening testing and IPC measures could prevent between 5%–78% of transmission, depending on testing periodicity and sensitivity (Figure 1C). Daily testing could prevent up to 78% of onward transmission if tests had 80% sensitivity, but daily testing prevents only about 30% of transmission if tests had 20% sensitivity. The testing strategy of screening every three days and IPC measures could prevent 43% of onward transmission with 80% testing sensitivity. Less frequent screening testing is even less effective, with screening every seven days and IPC measures only preventing 19% of onward transmission even with 80% test sensitivity. Faster clearance due to vaccination reduces the effectiveness of periodic testing, but only marginally. With daily test frequency and 40% test sensitivity, maximum avertible transmission ranges between 44% for individuals that have received a booster dose and 46% for fully vaccinated people.

Discussion

This work provides a simple characterization of viral shedding dynamics, infectiousness, and testing sensitivity specific to SARS-CoV-2 for use when complete data are unavailable (i.e., lack of epidemiological estimates, lab studies of viral shedding dynamics, etc.). The likely individual-level viral shedding dynamics, potential decrease in sensitivity of antigen testing, and probability of immune escape make effective testing-based mitigation strategies challenging, even in highly vaccinated populations. Reactive mitigation (i.e., case-initiated testing) will only effectively reduce transmission of the Omicron variant if conducted quickly (i.e., within one day of the index individual testing positive). If the timescale of viral shedding dynamics is faster, due to characteristics of the Omicron variant or immune status of the individual, reactive mitigation will be even less effective. Onward transmission to a secondary case from an imported case is likely to have already occurred by the time that the index case tests positive. Testing could be further escalated following identification of the index case or specific facility structures or cohorting could reduce further generations of transmission, however with high rates of presymptomatic and asymptomatic transmission and dense contact with nursing home facilities, it is valuable to consider additional mitigation strategies in tandem with testing strategies. Screening testing may be an effective strategy for reducing onward transmission when tests are administered very frequently (i.e., daily) and have high sensitivity. However, frequent widespread testing is likely to be logistically challenging for nursing homes. Indeed, while this model is prospective, spread of the Omicron variant was very high in nursing homes, reaching peaks of more than 40,000 weekly cases in residents and more than 60,000 weekly cases in staff at the peak in the US [14, 15]. We highlight that this work only evaluates the specific testing strategies described in the methods. This work is a hypothetical, but plausible framework that quantifies the effects of only these strategies in the case of an emerging variant. One limitation of this work is that it does not account for the additional impact of

the other measures in the recommended package of interventions that are triggered following a positive test in a nursing home. Thus, these estimates cannot capture the net decreases in transmission that a full package of interventions could have due to the prospective, simple, and flexible nature of this analysis. An additional limitation is that this work focuses on the timing of testing and viral shedding dynamics for nursing home healthcare personnel only, since there are no available estimates of the viral shedding dynamics of COVID-19 among adults ≥65 years old with comorbid health conditions. Collection of these estimates for nursing home residents is further complicated by consent issues for residents with cognitive impairment. There are likely to be differences in the immune response of nursing home resident populations that make this model not generalizable for them, and we thus focus on healthcare personnel.

These findings highlight that testing and isolation alone may not be an effective mitigation strategy for Omicron and other variants with similar characteristics and timing. Testing and isolation strategies are highly valuable, especially when deployed strategically, but continued use of source control in healthcare settings, rapid outbreak investigation with broad testing of those potentially exposed, and promotion of being up to date with all recommended COVID-19 vaccinations, including booster doses once eligible, will be needed to mitigate transmission in populations at higher risk for severe COVID-19 outcomes. These other mitigation measures supplement identifying and isolating infectious individuals by reducing potential transmission pathways, screening the susceptible population, and reducing the susceptible pool. Further, these findings may be translatable to other congregate settings, such as assisted living communities, homeless shelters, jails, and prisons.

We made several assumptions to overcome limitations due to lack of data and necessity to simplify complexities for this modeling work. First, the timescales of viral shedding dynamics and infectiousness were assumed to be directly proportional, and they are characterized as probability distributions. However, these represent reasonable timeframes based on limited available data for the

Omicron variant [4, 9]. We assume there is dense contact and high probability of onward transmission following transmission to a secondary case individual. Person-to-person contacts within a nursing home are dense, thus we represent contacts with a homogenous mixing process with residents sharing meals, social activities, and roommates. Additionally, there are contacts with nursing home healthcare personnel providing resident care. Also, the timeline for testing the index case (3 days following exposure to the secondary case) is somewhat arbitrary. We chose this timeframe to be a reasonable timeframe for symptom presentation and time between HCP tests. Delayed testing of the index case or a false negative test early in the timeframe of viral shedding kinetics would further increase transmission. We assumed that durations of infectiousness among individuals that received boosters would be shorter than durations among fully vaccinated individuals. The shifts in these timelines are quite small (from 3.5 days to 3.2 days to peak infectiousness), yet our analysis demonstrates that these small shifts have substantial impact on optimal timing of case-initiated testing. Thus, we find this difference important to consider as boosters appear to increase antibody response in people, which could possibly shorten the duration of infectiousness [15]. Usefully, we believe this model would be relevant to other variants with similar viral shedding dynamics, and thus provides a framework that could inform the timing of testing for future strains. Prior work quantifying the impacts of testing strategies for nursing home personnel based on individual-level viral shedding dynamics for emerging SARS-CoV-2 variants was not available, thus this provides a potentially useful tool for future scenarios.

We considered various levels of antigen test sensitivity, which affects the effectiveness of screening testing. We considered this wide range (20-80% sensitivity) for the possibility that previously approved tests could be less sensitive for a novel variant. Indeed, there was concern about reduced sensitivity of antigen tests for the Omicron variant, although findings are varied [6, 15]. Understanding the sensitivity of viral tests for any emerging variant is necessary to assess how testing strategies need

to be modified to protect populations. We focused on antigen tests because these are widely used in U.S. nursing homes [3] and make rapid detection and isolation possible.

Testing and IPC measures must be evaluated and updated as the COVID-19 pandemic evolves. We find that case-initiated healthcare personnel testing and IPC measures will have limited effectiveness as a sole mitigation strategy for nursing homes, preventing only 38% of transmission if testing is conducted one day after an index case is identified with the slowest estimated viral shedding dynamics (i.e., unvaccinated). Periodic testing could substantially reduce transmission, preventing up to 78% of transmission with daily testing with 80% test sensitivity. Thus, periodic testing would need to be implemented with high frequency and sensitivity. We highlight that testing and isolation are still valuable and necessary strategies, but other mitigation measures, such as use of source control in healthcare settings, rapid outbreak investigation with broad testing of those potentially exposed, and promotion of being up to date with all recommended COVID-19 vaccinations, will likely be needed to curb outbreaks of the Omicron variant.

NOTES

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Conflict of Interest:

KMJS reports attending NADONA, participating in the AMDA infection advisory board, and serving as a federal member of the Advancing Excellence in Long-term care Collaborative. NDS reports receiving financial support to attend the American Healthcare Association meeting, the Society for Healthcare Epidemiologists of America meeting, and the Infectious Diseases Society of America meeting. CG, CZ, PP, RS, and SR have no conflicts to report.

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Figure Legend:

Figure 1. Visualization of case-initiated testing model for unvaccinated persons (A) and potential impact of COVID-19 antigen testing for case-initiated (B) and screening testing (C). (A) The index case viral shedding dynamics and proportional infectiousness are represented in the blue solid line. The secondary case is exposed to the index case during the exposure window (gray) and the secondary case exhibits viral shedding dynamics (blue dashed line). The area under the viral shedding curves remains constant, but the secondary case has a narrower window of exposure, increasing the likelihood of the timing of viral shedding, and thus narrowing the distribution. The index case tests positive at day zero (black dashed line). Based on the secondary case viral shedding dynamics (blue dashed line) and the secondary case test sensitivity (red), the potential impact of a test is estimated (red dashed line), and the peak of this curve is the optimal time to test to achieve maximum avertable transmission (black solid line). (B) The optimal time to test a secondary case measured in terms of maximum possible avertible transmissions (%) compared to the days since an index individual tested positive, considering different infectiousness profiles of unvaccinated persons with a Delta-like timing of infection (black), fully vaccinated (orange), and persons who have received a booster dose (blue). The optimal day to test is highlighted with a dashed line in the respective color. (C) For screening testing, less frequent testing (i.e., a longer period between tests) yields lower maximum avertible transmissions (%), but this depends on test sensitivity. Less sensitive tests (light blue and dark blue) prevent less transmission compared to more sensitive tests (light green and dark green).

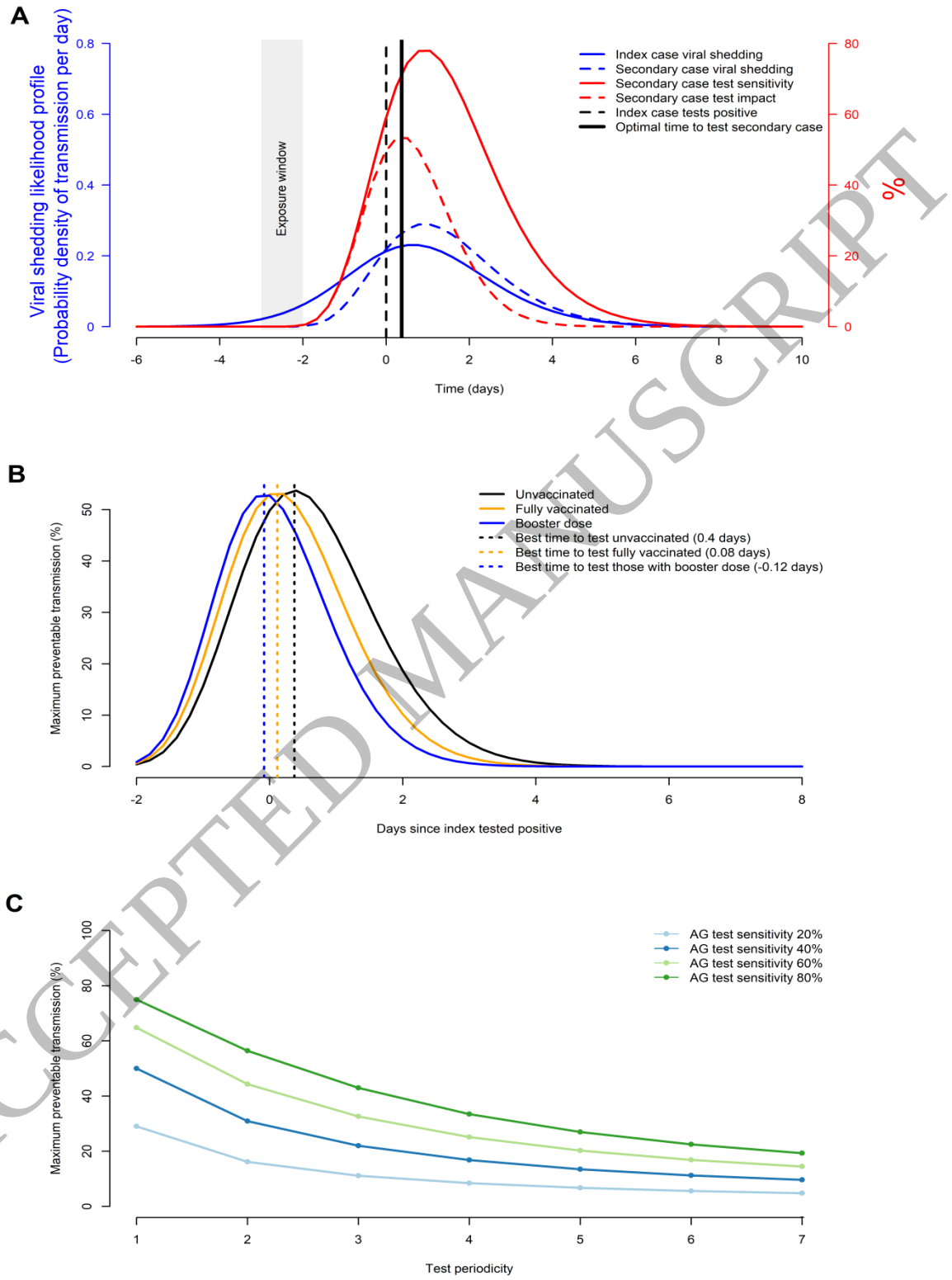

Figure 1
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