Community vaccination can shorten the COVID-19 isolation period: an individual-based modeling approach

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Abstract

Background: Isolation of infected individuals and quarantine of their contacts are usually employed to mitigate the transmission of SARS-CoV-2. While 14-day isolation of infected individuals could effectively reduce the risk of subsequence transmission, it also significantly impacts the patient's financial, psychological, and emotional well-being. It is, therefore, vital to investigate how the isolation duration could be shortened when effective vaccines are available and in what circumstances we can live with COVID-19 without isolation and quarantine.

Methods: An individual-based modeling approach was employed to estimate the likelihood of secondary infections and the likelihood of an outbreak following the isolation of an index case for a range of isolation periods. Our individual-based model integrates the viral load and infectiousness profiles of vaccinated and unvaccinated infected individuals. The effects of waning vaccine-induced immunity against Delta and Omicron variant transmission were also investigated.

Results: In the baseline scenario in which all individuals are unvaccinated, and no nonpharmaceutical interventions are employed, there is a chance of about 3% that an unvaccinated index case will make at least one secondary infection after being isolated for 14 days, and a sustained chain of transmission can occur with a chance of less than 1%. We found that at the outbreak risk equivalent to that of 14-day isolation in the baseline scenario, the isolation duration can be shortened to 7.33 days (95% CI 6.68-7.98) if 75% of people in the community are fully vaccinated during the last three months. In the best-case scenario in which all individuals in the community are fully vaccinated, isolation of infected individuals may no longer be necessary, at least during the first three months after being fully vaccinated, indicating that booster vaccination may be required after being fully vaccinated for three to four months. Finally, our simulations showed that the reduced vaccine effectiveness against Omicron variant transmission does not much affect the risk of an outbreak if the vaccine effectiveness against infection is maintained at a high level via booster vaccination.

Conclusions: The isolation duration of a vaccine breakthrough infector could be safely shortened if a majority of people in the community are immune to SARS-CoV-2 infection. A booster vaccination may be necessary three months after full vaccination to keep the outbreak risk low.

Background

SARS-CoV-2 spreads rapidly throughout the world, causing over 288.23 million infections and 5.48 million deaths by the end of 2021 [1]. During the early phase of transmission, when vaccines were unavailable, nonpharmaceutical interventions have been frontline measures to mitigate the transmission [2, 3]. Isolation, i.e., separation and limitation of mobility of infected people, is a critical strategy widely employed to break the transmission chain. Institution-based isolation of confirmed cases has been shown in a modeling study to delay the epidemic's peak and reduce the epidemic's size by approximately 57% [4]. Isolation, however, will be effective only if it can be promptly employed to prevent presymptomatic and asymptomatic transmission [5]. In addition, the isolation period should also be long enough to ensure that the infected individuals do not spread the disease after the isolation. However, while prolonged confinement may reduce the risk of transmission more effectively, it may have a significant impact on the patient's financial, psychological, and emotional well-being [6-8].

COVID-19 vaccines were first made available in the last month of 2020 [9], and they have been shown to be effective at preventing infection and transmission [10-12]. Despite the fact that infections can occur even after being fully vaccinated, a faster viral clearance was seen in the breakthrough infections, resulting in a shorter duration of infectiousness [13, 14]. As a result, it suggests that those who have been vaccinated may require a shorter period for isolation. It is vital to comprehend how the isolation duration could be reduced based on vaccine effectiveness, particularly when we want to return to normalcy and live with COVID-19 without quarantine and isolation measures.

In this study, we used an individual-based modeling approach to assess the likelihood of secondary infections and the likelihood of an outbreak following isolation of a vaccinated index case for a range of isolation periods. Our individual-based model accounts for transmission heterogeneity, variation in the course of infection, and the disease's infectivity profile. The effects of waning vaccine-induced immunity and the delay in isolating infected individuals in the community were also examined.

Methods

Estimation of infectiousness profiles and vaccine efficiency against transmission

People infected with SARS-CoV-2 can become infectious prior to the onset of symptoms. In the case of unvaccinated individuals, the infectiousness peaks 2.1 days before the start of symptoms and then decreases gradually during the course of the illness [15]. Viral trajectories in proliferation duration are similar in the unvaccinated and vaccinated individuals, but the viral load is cleared faster in vaccine breakthrough infection than in the unvaccinated group [13, 14]. The disease infectiousness (F) prior to the peak of both vaccinated and unvaccinated infectors was therefore assumed to follow a gamma distribution, as described in [15]. After the peak period, data on C_t values collected in Singapore [13] were used to determine the infectiousness profile. The infectiousness was considered to be directly proportional to the viral load (V) that exceeds a threshold of 10^6 copies, i.e., $F \propto Vx10^{-6}$ [16]. C_t values were converted to viral load (V) using the procedures outlined in [14]. Because of the faster viral clearance time, the disease transmissibility of vaccinated infectors could be averted compared to unvaccinated ones. In this work, we estimated the vaccine efficacy against transmission from a percentage of reduction in the area under the curves of the disease infectiousness profiles.

Model structure

In order to examine the probability of post-isolation infections, the transmissions of the COVID-19 were simulated with individuals categorized as susceptible (S), latent (L), infectious (I), recovered (R), isolated (Q), and fully vaccinated (V) according to their infection and vaccination status. Infectious individuals are further divided into symptomatic (I_S) and asymptomatic (I_A) groups, with the assumption that asymptomatic individuals are less infectious than symptomatic ones. Although COVID-19 vaccines cannot entirely protect people against the infection, they are still beneficial in decreasing the chance of infection and the chance of becoming symptomatic. In addition, even vaccinated individuals do get infected, they will be less likely to transmit the disease to other individuals. In our model, vaccine breakthrough infections are distinguished from infections in susceptible individuals by subscripts *V* and *S*, as shown in **Figure 1(A)**. After being infected, individuals enter a latent state before becoming infectious. Finally, infectious individuals move either to recovered or isolated compartments.

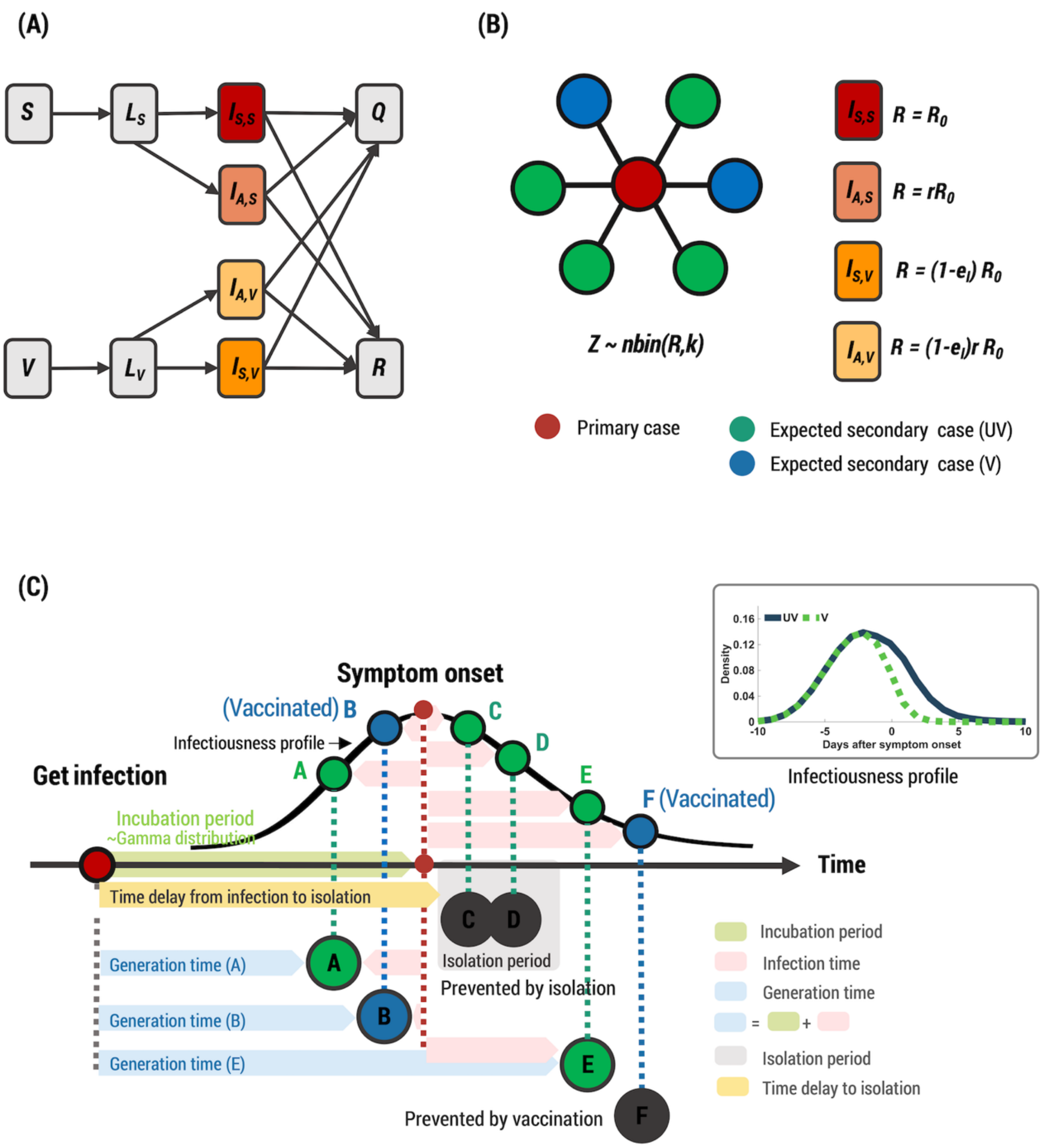

Figure 1: Model structure of the COVID-19 transmission. (A) Schematic of the compartmental model showing progressive of the disease and transition of individuals across different compartments. (B) Example of the expected number of secondary cases made by a single primary case drawn from a negative binomial distribution. (C) An illustration of transmission events due to the primary case (red circle). The generation time is a time duration between a primary case's infection and one of its subsequent secondary cases. The incubation

period is a time duration from exposure to symptom onset. The inset shows the infectiousness profiles of unvaccinated (UV) and vaccinated (V) individuals.

The number of secondary infections caused by a single primary case, Z, for each infected individual is estimated from a negative binomial distribution with a mean equal to the reproduction number (R_0) and dispersion parameter (k) (**Figure 1(B))**. Because of the lower infectivity of asymptomatic infectors, they contribute fewer infections; the mean number of secondary cases made by an asymptomatic individual was reduced by a factor r. For the vaccine breakthrough infectors, the mean of the distribution is also reduced due to the efficiency against transmission (e_I) of vaccines.

An example of the transmission events is illustrated in **Figure 1(C)**. The incubation period, time from exposure to symptom onset, is assumed to follow the Gamma distribution with a mean of 5.8 days [15]. The time of each new infection is drawn from a random number distribution that is distributed according to the infectiousness profile of the infectors. Transmission can take place before symptoms start. As a result of the vaccine's effectiveness against infection, vaccinated persons are less likely to become infected. The effective infectious period was determined by whether or not they were isolated. If infectors are isolated, they will be contagious until they are isolated. Although transmission can be prevented during the isolation period, post-isolation infections are still possible. The generation time between infection of a primary case and one of its subsequent secondary cases is dependent on both the incubation period and the infection time. In our study, the primary index case is assumed to be isolated immediately after becoming infected, whereas other subsequent infected individuals in the community are isolated with a delay of 6.8 days.

Table 1: Model parameters and their default values

Parameter	Default value	Source
Basic reproduction number (R_0)	5.08	[17]
Overdispersion parameter (k)	0.08	[18]
Incubation period distribution (Gamma distribution)		
- Mean	5.8 days	[15]
- Shape parameter	3.64	
- Scale parameter	1.59	
Probability of being symptomatic		
- Unvaccinated individuals	0.573	[19]
- Vaccinated individuals	0.431	[19]
Reduction in infectiousness of asymptomatic individual (r)	0.58	[20]
Vaccine efficiency against infection (e_S)	0.79	[12]
Vaccine efficiency against transmission (e_I)	0.25	Estimation
Probability that symptomatic individuals will be isolated	0.8	Assumption
Probability that asymptomatic individuals will be isolated	0.1	Assumption
Time delay from infection to isolation		
- Index case	0 days	Assumption
- Infected individuals in community	6.8 days	Assumption

Results

Impact of vaccination on post-isolation transmission

We explored the probability of a primary infected individual making at least one secondary infection and the probability of a successful outbreak, i.e., having a sustained chain of transmission, after being released from isolation. In the baseline scenario in which the primary case and all other individuals in the community are unvaccinated, we found that there is a chance of about 3% that the unvaccinated index case will make at least one secondary infection after being isolated for 14 days, and a sustained chain of transmission can occur with a chance of less than 1% (left bars in

Figure 2(A)-(B)). However, if the index case has already been vaccinated, we found that although all other individuals in the community are unvaccinated, only about 10 days of isolation is equivalent to 14-day isolation of unvaccinated index case (red lines and red symbols in **Figure 2**).

Vaccinating people in the community can further reduce the likelihood of secondary infection and the probability of a successful outbreak. It was found that higher community vaccine coverages decrease the chance of secondary infection following the isolation of the vaccinated index case more, especially when the isolation periods are short. In addition, when the isolation period is longer than 12 days, there is no apparent difference between different vaccination coverages. At the outbreak risk equivalent to that of 14-day isolation in the baseline scenario, the isolation duration of the primary vaccinated infector can be shortened to 9.33 days (95% CI 8.68-9.98) if 50% of people in the community are vaccinated. When 75% of people in the community are vaccinated, the isolation period can be further shortened to 7.33 days (95% CI 6.68-7.98). Finally, we found that in the extreme limit in which all individuals are vaccinated, although post-isolation infections are still possible for the isolation period of shorter than 6 days, the chance of sustained chain of transmission to occur is extremely rare. In this case, isolation may no longer be necessary (**Figure 2** (**D**)).

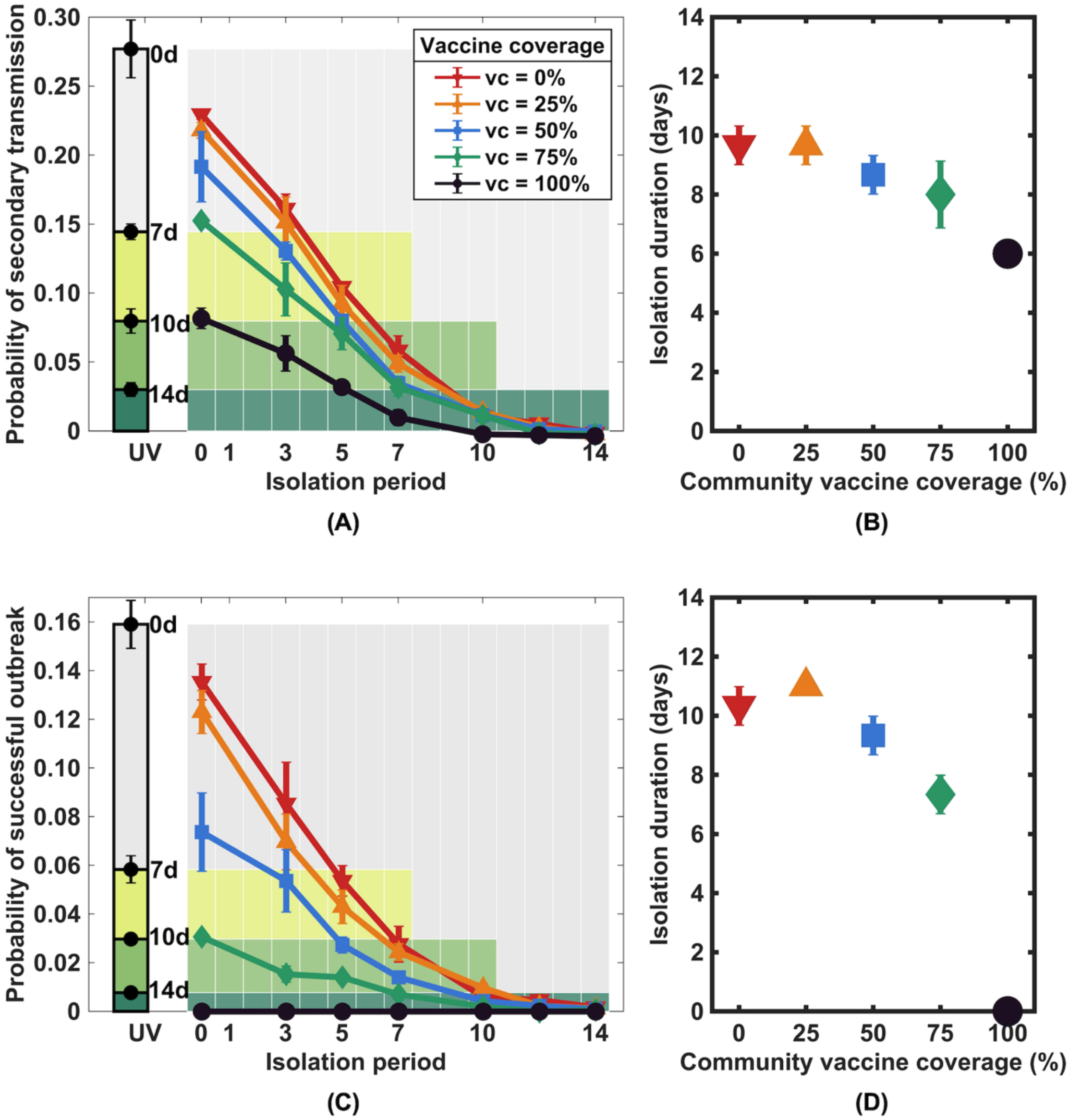

Figure 2: Impacts of isolating a primary vaccinated infector on post-isolation transmission. Probability of secondary transmission (A) and probability of successful outbreak in which a chain of transmission can be sustained (C) after a range of isolation periods and vaccination levels in the community. The corresponding probabilities in the baseline scenario where the index case and all other individuals in the community are unvaccinated are shown as bar graphs on the left side of both subfigures. (B) and (D) show the isolation period equivalent to the 14-day isolation period in the baseline scenarios regarding the probability of secondary transmission and the probability of a successful outbreak, respectively. Error bars indicate 95% CI.

Effect of waning vaccine-induced immunity

As the vaccine effectiveness decreases over time [21], we evaluated its effect on the probability of secondary infection and the probability of a successful outbreak following isolation. We found that for a low level of immunization (< 25% coverage), both the post-isolation transmission probability and the successful outbreak probability are not significantly affected by the waning of vaccine effectiveness (**even** there is no isolation.

We also investigated how the change in vaccine effectiveness against transmission would influence the likelihood of secondary infection and the probability of a successful outbreak. In this part, we considered the vaccine effectiveness against transmission (e_I) ranges from 0% to 40%, and the vaccine effectiveness against infection (e_S) of 0.9 and 0.5, corresponding to the effectiveness against infection after being fully vaccinated for one month and four months, respectively. We found that during the first four months after complete vaccination, when the vaccine effectiveness against infection is high, the vaccine effectiveness against transmission had only a minor effect on the transmission, especially when the isolation period is long (**Figure 4**).

Figure 3 A and **D**). However, for higher vaccine coverage, the effect of the decline in the vaccine effectiveness is more pronounced, especially when the isolation durations are short. Note, however, that although at high vaccination coverage (> 75% coverage), there is a more significant effect of immunity waning across a range of isolation periods, the probability of an outbreak is still lower than that in the case when 25% of the population are vaccinated. With the vaccine coverage of 75%, for example, after 4 months of vaccination, the outbreak risk climbs from 0.9% to 4.2% for 3-day isolation and increases from 1.3% to 7.7% for no isolation. When all individuals in the community are vaccinated, despite a substantial decrease in vaccine effectiveness after four months, the chance of a successful outbreak is still lower than 4% even there is no isolation.

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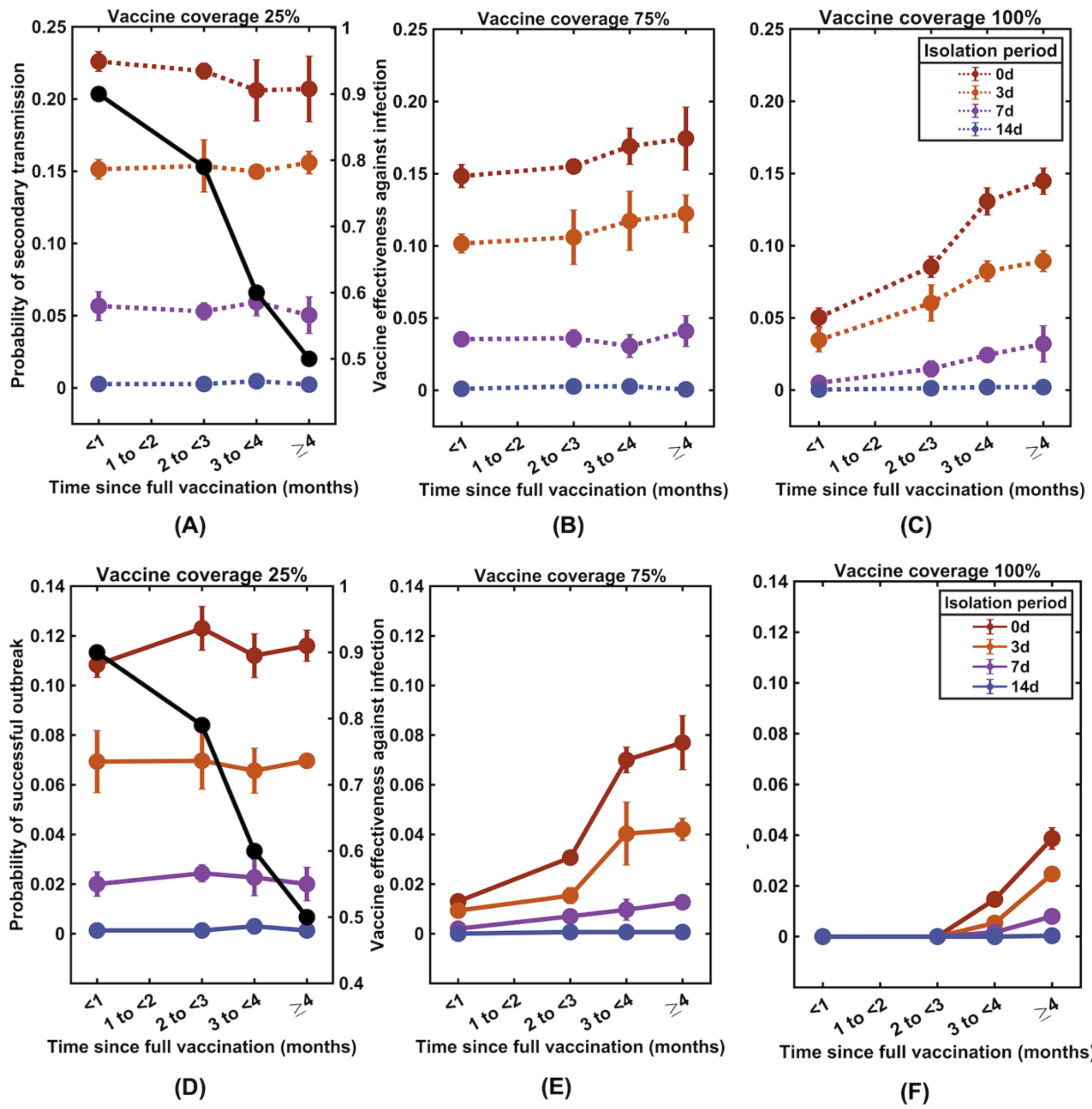

Figure 3: The effect of reduction in vaccine effectiveness against SARS-CoV-2 infection. The time evolution of the probability of at least one secondary infection (A-C) and probability of successful outbreak (D-F) following the release of a breakthrough infector from isolation as the vaccine effectiveness against infection wanes (black lines, right y-axis) [21].

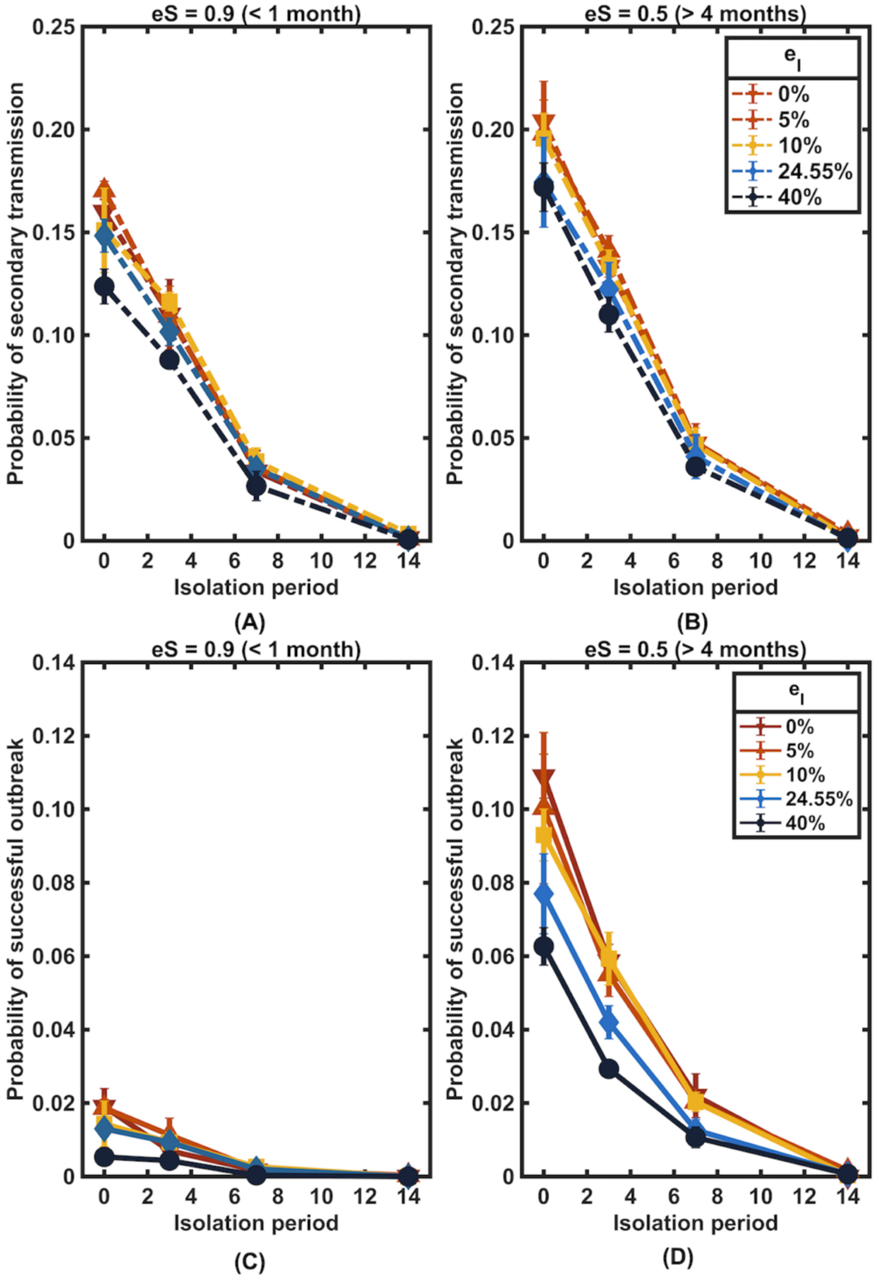

Figure 4: The influence of vaccine effectiveness against SARS-CoV-2 transmission. The probability of at least one secondary infection (A and B) and a successful outbreak (C and D) after being released from isolation into a community with a vaccination level of 75%. The vaccine effectiveness against transmission (e_I) was varied from 0% to 40%, and the vaccine effectiveness against infection (e_S) was fixed at 0.9 (left column) and 0.5 (right column).

Impact of community case-isolation and other control measures

We next evaluated the impact of time delay from infection to the isolation of infected individuals in the community on the spread of SARS-CoV-2. Our results indicated that the outbreak would be less likely to occur if case isolation is performed with a shorter delay (

Figure 5). For example, under the vaccine coverage of 75%, the outbreak risk could be suppressed to low than 1% if the isolation can be performed within 3 days after infections. To maintain the same level of an outbreak risk, a longer duration of the isolation is needed for the isolation with longer delays. For instance, for a 5-day delay, at least 5 days of isolation may be required, and for a 7-day delay, at least 7 days of isolation may be needed. When only 25% of individuals are vaccinated, isolation may be required for at least 10 days, regardless of how quickly infected individuals are isolated.

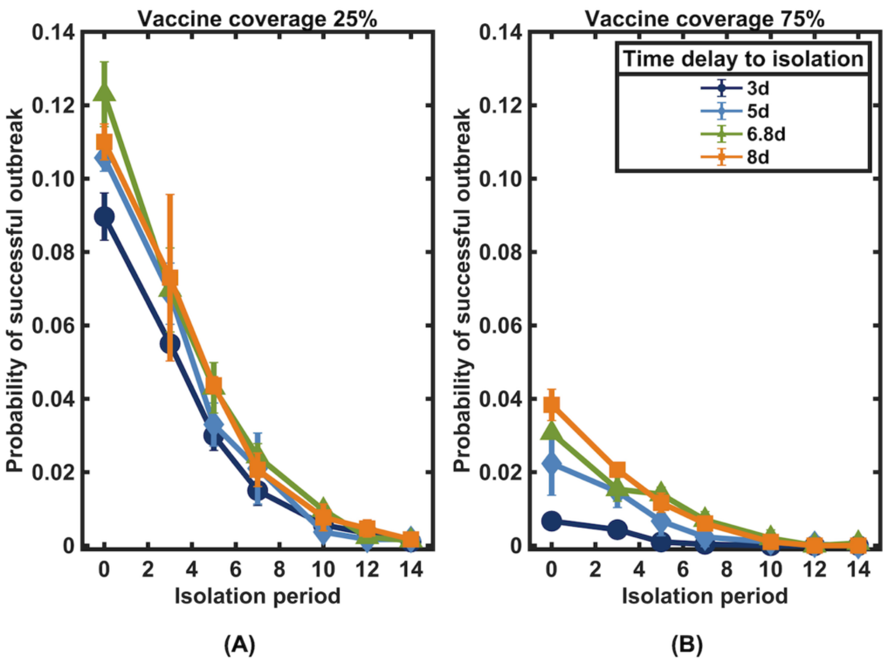

Figure 5: Impact of time delay from infection to isolation under vaccination coverages of (A) 25% and (B) 75%.

The effective reproduction number (R) is commonly used to measure the disease transmissivity under different control measures. To consider the effects of other control measures, a sensitivity analysis on the effective reproduction number has been performed. In combination with other non-pharmaceutical interventions, we found that community vaccination could further shorten the isolation period (**Figure 6**). For instance, in the absence of any non-pharmaceutical interventions and the vaccine coverage is only 25%, case isolation may be required for at least 12 days to reduce the outbreak risk to 1%. However, if other control measures are concurrently implemented at a level that could reduce the effective reproduction number to 3.2, only one week of isolation is sufficient. Importantly, in this case, isolation will be no longer necessary if the community vaccination level reaches 75%.

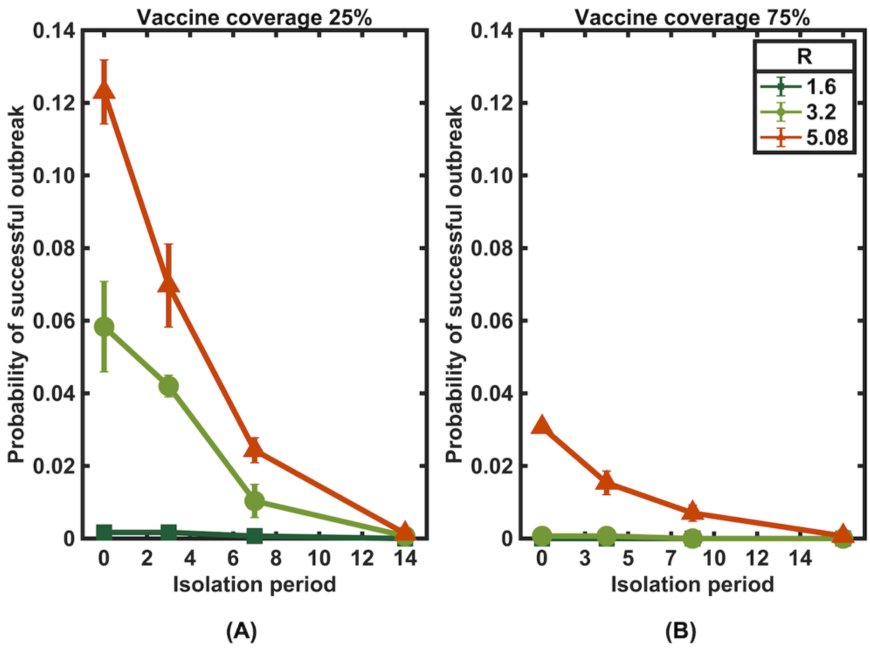

Figure 6: A sensitivity analysis on the effective reproduction number. The probability of successful outbreak under the community vaccination coverages of (A) 25% and (B) 75% with the time delay to the isolation of 6.8 days.

Discussion

In this work, we evaluated the likelihood of at least one secondary infection and the likelihood of an outbreak following the isolation of a vaccine breakthrough infector for a specified period of time. Our modeling results indicated that vaccines play a critical role in reducing the likelihood of post-isolation transmission. We discovered that the duration of isolation for an infected individual who has already been vaccinated could be reduced as opposed to the 14-day duration of isolation for unvaccinated individuals. Additionally, the duration of isolation can be reduced further if the majority of the community members are immune to the disease.

In the best case in which all individuals in the community are fully vaccinated, isolation of infected vaccinated individuals may no longer be required, at least during the first three months after being fully vaccinated, if no other non-pharmaceutical interventions are implemented. After four months, however, as the vaccine effectiveness against infection drops to around 53% [21], the probability of post-isolation transmission increases rapidly after this time, especially in the cases of short isolation periods. This result indicates that booster vaccination may be needed after being fully vaccinated for three to four months; otherwise, more extended isolation periods or other non-pharmaceutical control measures may be necessary to compensate for the increased transmission risk.

With a faster viral clearance time in vaccinated individuals, vaccines have been hypothesized to reduce onward transmission from infected vaccinated individuals. According to our estimations, the vaccine effectiveness against transmission of 24.6% is comparable to the effectiveness against transmission with the Delta variant after getting two doses of the Pfizer vaccine [22]. However, the emergence of the Omicron variant has raised serious concerns about its capability to evade vaccine protection. After receiving two doses of mRNA vaccines, the vaccine effectiveness in preventing Omicron-variant transmission drops to less than 5% [22]. Nevertheless, our simulations showed that the reduced vaccine effectiveness against Omicron-variant transmission does not much affect the risk of secondary infection if the vaccine effectiveness against infection is maintained at a high level, possibly via booster vaccination [23].

When considering the effect of delay in isolation of infected individuals in the community, we found that a shorter delay to isolation can further shorten the isolation period, especially in the high vaccine coverage settings. In addition, we found that while an outbreak may still occur in the absence of isolation in the community with low vaccination coverage, the risk could be minimized when additional control measures such as contact tracing and quarantine of their contacts, as well as testing, are implemented (**Figure 6**).

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