Engineering 28 (2023) 234–242

Contents lists available at ScienceDirect

Engineering

journal homepage: www.elsevier.com/locate/eng

Research
Public Health—Article

Quantitative Analysis of the Effectiveness of Antigen- and Polymerase Chain Reaction-Based Combination Strategies for Containing COVID-19 Transmission in a Simulated Community

Qiangru Huang [a,#], Yanxia Sun [a,#], Mengmeng Jia [a], Ting Zhang [a], Fangyuan Chen [a,b], Mingyue Jiang [a], Qing Wang [a], Luzhao Feng [a,*], Weizhong Yang [a,*]

[a] School of Population Medicine and Public Health, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China
[b] School of Arts and Sciences, Beijing Institute of Fashion Technology, Beijing 100105, China

ARTICLE INFO

Article history:
Received 12 October 2022
Revised 9 December 2022
Accepted 15 January 2023
Available online 11 February 2023

Keywords:
COVID-19
Antigen testing
PCR testing
Testing strategies

ABSTRACT

The number of coronavirus disease 2019 (COVID-19) cases continues to surge, overwhelming healthcare systems and causing excess mortality in many countries. Testing of infectious populations remains a key strategy to contain the COVID-19 outbreak, delay the exponential spread of the disease, and flatten the epidemic curve. Using the Omicron variant outbreak as a background, this study aimed to evaluate the effectiveness of testing strategies with different test combinations and frequencies, analyze the factors associated with testing effectiveness, and optimize testing strategies based on these influencing factors. We developed a stochastic, agent-based, discrete-time susceptible–latent–infectious–recovered model simulating a community to estimate the association between three levels of testing strategies and COVID-19 transmission. Antigen testing and its combination strategies were more efficient than polymerase chain reaction (PCR)-related strategies. Antigen testing also showed better performance in reducing the demand for hospital beds and intensive care unit beds. The delay in the turnaround time of test results had a more significant impact on the efficiency of the testing strategy compared to the detection limit of viral load and detection-related contacts. The main advantage of antigen testing strategies is the short turnaround time, which is also a critical factor to be optimized to improve PCR strategies. After modifying the turnaround time, the strategies with less frequent testing were comparable to daily testing. The choice of testing strategy requires consideration of containment goals, test efficacy, community prevalence, and economic factors. This study provides evidence for the selection and optimization of testing strategies in the post-pandemic era and provides guidance for optimizing healthcare resources.

1. Introduction

The coronavirus disease 2019 (COVID-19), which was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1], is still ongoing. The dominant Omicron variant, which is highly transmissible and can evade immune surveillance but causes low mortality, is rapidly replacing the previous variants and has become globally dominant [2–4]. Although vaccination coverage is increasing globally and the number of reported deaths from the virus has reached the lowest level since the pandemic's beginning [5], many new cases are still being reported. In the week of September 5–13, 2022, WHO reported 3.1 million new cases, but the number of infections is grossly underestimated as testing has been scaled down in many countries [6]. In the first five months of 2022, more than 750 000 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections were reported in the mainland of China with the majority in Shanghai [2]. For countries and regions with large population sizes and high population densities, sudden outbreaks of infection in a short time can strain medical resources, including insufficient intensive care unit (ICU) beds, shortage of ventilators, and crowding out of healthcare resources for other diseases, leading to increased mortality [7,8]. Therefore, screening infectious populations remains an essential strategy to

* Corresponding authors.
E-mail addresses: fengluzhao@cams.cn (L. Feng), yangweizhong@cams.cn (W. Yang).
[#] These authors contributed equally to this work.

https://doi.org/10.1016/j.eng.2023.01.004

contain unpredictable outbreaks in the future. Further increasing testing, eliminating testing gaps, and optimizing testing strategies are effective measures to accelerate the end of the COVID-19 pandemic [5].

People suspected of COVID-19 need to know quickly if they are infected to self-isolate, receive treatment, and inform close contacts [9]. WHO and the Centers for Disease Control and Prevention have adopted reverse transcription polymerase chain reaction (PCR) technology as the standard diagnostic assay for SARS-CoV-2 detection [10]. PCR testing has a high sensitivity ranging from 71% to 98% and is 100% specific for SARS-CoV-2 [11,12]. Despite its high sensitivity, PCR testing has disadvantages, including needing professional lab expertise, costly reagents, and centralized equipment, often requiring at least 24 hours for result turnarounds [13]. In 2020, the WHO recommended antigen testing to aid the early diagnosis of COVID-19 [7]. The advantages of antigen testing include relatively low cost, short turnaround time [14], greater accessibility, ease of use, and the ability to scale up testing outside of laboratory settings [15], which facilities prompt identification of infected individuals. Multiple studies have evaluated the sensitivity and specificity of the two tests [9,16]. However, to our knowledge, few studies have examined how the performance of antigen testing varies during the transmission of infection [17]. Whether screening using rapid antigen tests is superior to PCR-based testing strategies remains uncertain, and evidence is lacking to evaluate the effectiveness of these tests and combination strategies.

A community is defined as multiple multi-unit dwellings. Such multi-unit dwellings, living in the same apartment/condominium/dormitory building [18], are the current residential choice for most of China's urban population. In China, screening strategies rely heavily on community- or multi-unit-dwelling-based testing. Communities are at risk of transmission of infections from households and public areas (e.g., elevators) because residents live nearby and are in frequent contact with other residents and staff [18]. Furthermore, understaffing in many communities leads to even higher contact rates between staff and residents, resulting in more severe outbreaks [19].

Therefore, we used an agent-based model simulating a community to estimate the associations between a range of testing strategies and the transmission of SARS-CoV-2 Omicron variants. The objective of this study was to evaluate the containment effect of antigen and PCR testing in the setting of community outbreaks. We examined the effects of different testing frequencies and testing strategies combinations, evaluated the demand for hospital and ICU beds, analyzed the factors associated with testing effectiveness, and modified testing strategies accordingly. In order to achieve tailored measures and scientific and precise prevention and control, this study evaluated the effectiveness of case screening strategies from the perspective of community prevention and control and provided evidence for the formulation of future epidemic prevention and control policies.

2. Methods

2.1. Model structure

This decision analytical modeling study used simulated data and transmission parameters of the SARS-CoV-2 Omicron variant and did not require approval by an ethics committee. We developed a stochastic, agent-based, discrete-time susceptible–latent–infectious (asymptomatic (A)/symptomatic (I))–recovered model to examine SARS-CoV-2 transmission in a simulated community. This study modeled daily time steps over 180 days with different initial numbers of latent or infectious SARS-CoV-2 cases (N = 10, 50, or 100). Once identified, infected residents were transferred to the COVID-19 cohort, which has no interaction with susceptible or undiagnosed residents in the non-COVID-19 cohort (Fig 1). Based on *China's urban residential area planning and design standards* [20], we simulated a five-min pedestrian-scale neighborhood community with 2000 households. According to the *China statistical yearbook 2021*, we set the size distribution of permanent households in the community at an average of 2.6 people per household, and detailed population size ratios for a household are listed in Table S1 in Appendix A [21]. Each resident was assigned a unique identity document (ID) number to a room of 1–5 people and transferred to the COVID-19 cohort if found infected. The infected individuals returned to their original rooms upon recovery.

Individuals infected with SARS-CoV-2 were identified as either asymptomatic (in which case they could only be identified by testing) or symptomatic (in which case they were identified either by symptom onset or testing, whichever came first). Symptom-based testing refers to individuals who developed symptoms that were presumed positive and either quarantined (for residents) or sent home (for staff), regardless of test turnaround time. The staff was divided into COVID-19 and non-COVID-19 cohorts in proportion to the number of residents. Infected staff members were sent home and replaced by temporary workers until they recovered.

Daily contact was modeled between residents, staff, and the two populations. We assumed that transmission occurred through contact only and did not strictly consider the airborne transmission. Except for roommates who were modeled explicitly, we assumed homogeneous (i.e., random) mixing. Each individual's daily risk of infection was binomial, with the probability determined by the mean infectiousness of the population they contacted multiplied by the number of contacts. Despite the restrictions on communities during the pandemic [18], we ensured necessary contact rather than strict stasis. Each resident interacted primarily with their roommates and staff and less with other residents. In contrast, each staff member contacted six residents and two other staff members per day.

Each type of contact (staff–resident, staff–staff, and resident–resident) was weighted to represent different contact intensities. Proximity and duration of contact were not explicitly incorporated, but we aimed to capture the heterogeneity in transmission risk. The lowest intensity was observed between staff, with a baseline transmission probability per contact of 0.0466. The transmission probability was calculated by dividing the primary reproduction number (R_0) for the Omicron variant by the average number of contacts per day [22]. Roommates had the highest risk of transmission, ten times higher (0.466) than the baseline, because of closer contact.

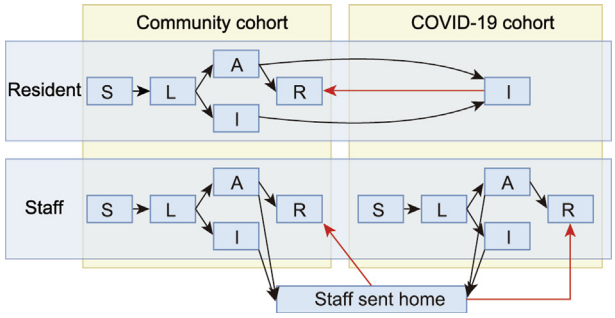

Fig. 1. Flowchart of movement through susceptible–latent–infectious–recovered model. The model uses a cohort framework wherein residents who become infected symptomatically (I) or asymptomatically (A) with SARS-CoV-2 are moved out of the non-COVID-19 cohort and separated into a distinct COVID-19 cohort after showing symptoms or testing positive. S: susceptible individuals; L: latent individuals; R: individuals who have recovered from COVID-19.

2.2. Setting of viral load (VL) and infectiousness

For each infected individual, after a latent period of 2–4 days, VL increased rapidly from 4 to 6 days before peaking and declined after that. For symptomatic individuals, symptom onset occurred after two days of increasing VL [23,24]. We made the conservative assumption of the same VL distribution for asymptomatic and symptomatic infections [25]. The peak VL was determined from a normal distribution on a logarithmic scale [26]. The duration of detectable VL is normally distributed and can be longer than the infectious period [27]. In this model, we categorized infectiousness based on VL as follows: non-infectious ($VL < 1 \times 10^3$ copies·mL^{-1}), moderately infectious (1×10^3 copies·mL$^{-1} \leq VL < 1 \times 10^7$ copies·mL^{-1}), and fully infectious ($VL \geq 1 \times 10^7$ copies·mL^{-1}) [28]. We assumed that the sensitivity of the tests depended only on VL dynamics and did not incorporate other factors, such as variations in sample quality.

2.3. Simulated testing interventions

We evaluated the screening effectiveness of rapid antigen testing and PCR testing interventions for all individuals in the simulated community. Based on the available parameters of these tests, antigen testing was assumed to have a higher limit of detection (LOD) and lower sensitivity relative to PCR. However, antigen tests produced results immediately, whereas PCR had a 1-day delay. In addition, PCR was assumed to have one more test-related contact than a rapid antigen (Table S2 in Appendix A). The sensitivity of the PCR test was 100% because the VL cutoff for infectiousness was higher than the LOD of the PCR test.

We established 11 testing strategies with different antigen testing and PCR testing combinations, and varying test intervals. According to the testing frequency, strategies were divided into three intensity levels. Level 1 strategies referred to daily testing strategies and included daily antigen, daily PCR, PCR–antigen–antigen (P–A–A), and PCR–antigen–PCR (P–A–P). Level 2 strategies were performed at 1- or 2-day intervals and included PCR–none–antigen–none–PCR (P–N–A–N–P), 1-day interval antigen testing (antigen–none–antigen, A–N–A), 1-day interval PCR testing (PCR–none–PCR, P–N–P), 2-day interval antigen testing (antigen–none–none–antigen, A–N–N–A) and 2-day interval PCR testing (PCR–none–none–PCR, P–N–N–P). Level 3 strategies included weekly antigen and PCR testing.

2.4. Simulated population immunity and interventions

We set the vaccination coverage according to the vaccination data released by the Chinese Center for Disease Control and Prevention [29]. As of June 22, 2022, 34.7% of the population have been fully vaccinated, 54.1% have completed booster vaccination, and 11.1% have not been fully vaccinated. Vaccine efficacy (VE) included three parts: against infection, against symptomatic disease, and against onward transmission [30]. Considering the significant effect of the post-vaccination period on VEs, we also set different VEs for receiving the second or booster dose within six months and over six months. The detailed setting of vaccination coverage and VEs were listed in Table S1, considering a low immune escape scenario with the same VEs against hospitalization and deaths between the homologous booster and heterologous booster vaccinations, as observed in Hong Kong [31].

We assumed that contacts in the community were necessary. Our interventions did not reduce contacts but rather changed with whom those contacts were made. Whenever possible, these interventions reduced the proportion of contacts presumed to be susceptible (potentially infected) and replaced them with recovered (immune) contacts. Residents were moved back to the non-COVID-19 cohort after recovery. The immunity-based staffing intervention prioritized placing recovered staff members, who were assumed to be immune, in the non-COVID-19 cohort, leaving susceptible staff members to work in the COVID-19 cohort. Importantly, we assumed adequate personal protective equipment (PPE) for staff and masks for residents to reduce infection risk.

2.5. Effectiveness assessments

The effectiveness of testing strategies was assessed based on the mean ± standard deviation (SD) cumulative incidence and the number of days required to detect 90% of total infections, which is an indicator to evaluate the speed of containment of different testing strategies. We calculated the ratio of demand to available beds for inpatient care and the ratio of demand to available beds for ICU beds. The available inpatient and ICU beds-level are shown in Table S1. We further evaluated the cumulative and peak quarantine resources for infectious cases. All analyses were conducted using *R* statistical software version 3.6.3 (R Foundation for Statistical Computing, Austria). The codes used for this study are available at https://github.com/hqraiwxy/Testing-Strategy-in-Community.

3. Results

3.1. Scenario construction with different testing strategies

To compare the effectiveness of the testing strategies, we simulated a community of 2000 households with 5083 residents and 200 staff members with various numbers of initial infections and latent cases. Table S1 presents the estimated parameters for the different testing strategies based on the effectiveness of PPE measures and population vaccine immunization for residents and staff. The testing strategies were categorized into three levels according to the detection interval.

The total number of infections and the speed of detecting infections varied with the different testing strategies (Fig 2 and Table S3 in Appendix A). In the scenario with an initial infection number of 10 ($N = 10$) and no testing strategy, the estimated mean cumulative infection number after 180 days was 796 (15.7%). For Level 1 testing strategies, this number decreased to 41 (0.8%), 46 (0.9%), 50 (1.0%), and 74 (1.5%) with daily antigen, daily PCR, P–A–A, and P–A–P testing, respectively. Compared to the baseline (none-testing), daily antigen and PCR testing reduced infections by 94.9% and 94.3%. Weekly antigen and PCR testing reduced the number of infections by 86.8% and 78.3%, respectively. In general, the cumulative infections with Level 1 testing strategies were fewer than those with Levels 2 and 3 strategies (Fig 2(a)).

In the scenario of $N = 50$, compared with baseline (none-testing), daily antigen and PCR testing reduced infections to 87.0% and 85.1%, respectively, while weekly antigen and PCR testing reduced infections to 64.5% and 60.3%. In the scenario of $N = 100$, the reduction in infection was 79.3% for daily antigen, 75.5% for daily PCR, 53.5% for weekly antigen, and 49.4% for weekly PCR testing. These findings suggest that screening can be effective in reducing the number of infectious cases. Weekly testing strategies can reduce infectious cases by 50%–85%, but the effectiveness decreases as the number of initial infections increases.

We examined the number of days required to detect 90% of the infected cases and used it as an indicator to assess the speed of prevention and control for different testing strategies (Fig 2(b)). Among the Level 1 testing strategies, daily antigen, daily PCR, P–A–A, and P–A–P strategies took 33, 36, 34, and 33 days, respectively, to detect > 90% of infections. The Level 2 strategies were relatively slower than Level 1 strategies, with > 90% of infections being detected within 60 days. However, Level 3 strategies

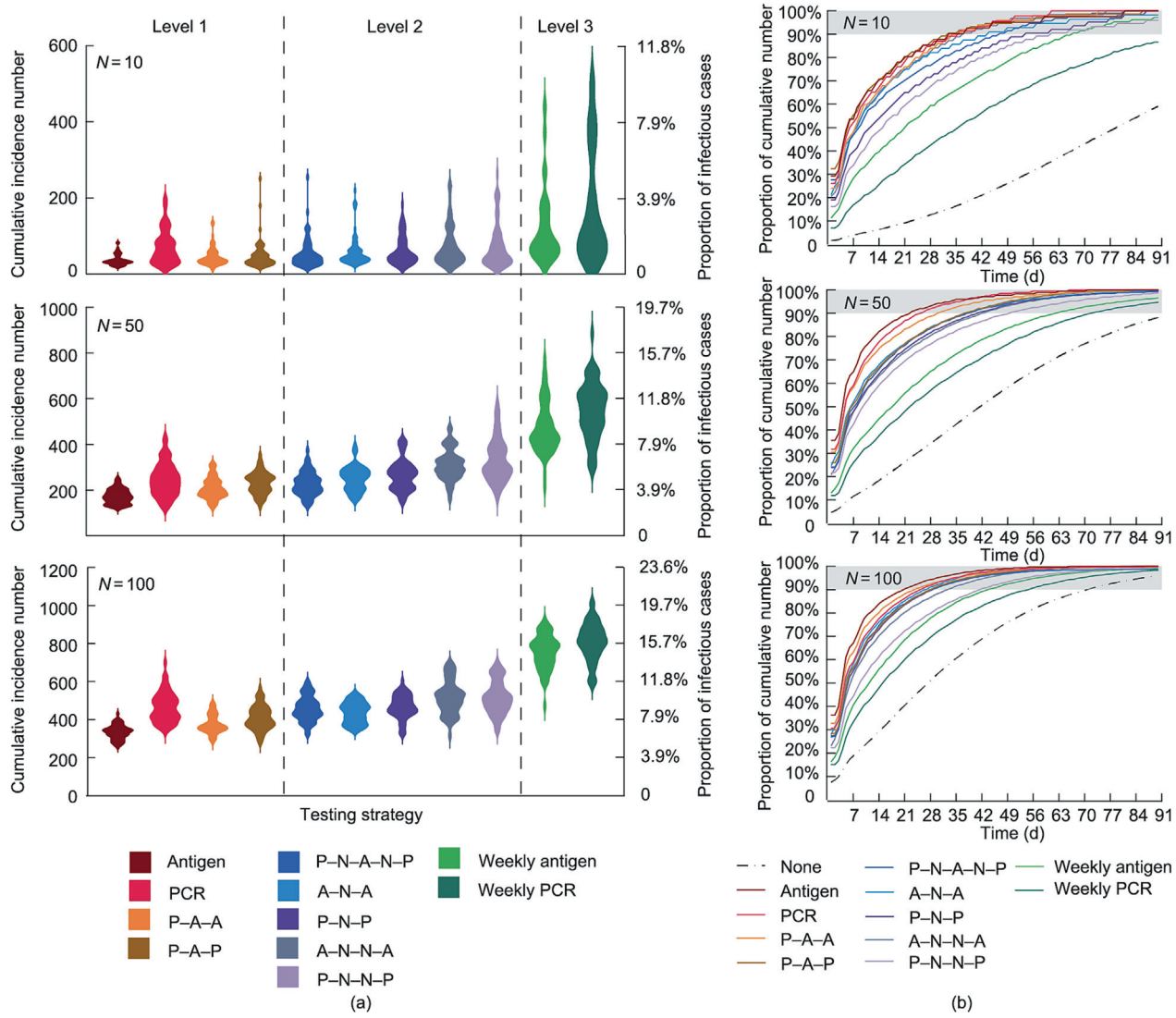

Fig. 2. Comparison of intervention effectiveness under different testing strategies. (a) Violin plots indicate the cumulative incidence number in a simulated community under different testing strategies with various initial infection numbers (*N*). The proportion of infectious cases by the total number of people is shown in the right vertical axis. According to testing frequency, strategies are divided into three levels (Levels 1–3). (b) Line chart indicates the proportion of cumulative incidence numbers by total simulated infections under different testing strategies with various initial infection numbers, showing the speed of containment within three months.

required more time to contain the outbreak, failing to detect 90% of infections within 90 days with the weekly PCR strategy. In scenarios of N = 50 and N = 100, the estimated mean cumulative infection numbers were much higher than at N = 10. The test strategies showed similar effectiveness, with Level 1 strategies showing a lower cumulative infection number and detecting > 90% of the infected people in fewer days. Notably, antigen testing strategies and combinations were more effective than PCR-related strategies at all levels.

We turned R_0 up to simulate the increased transmissibility caused by SARS-CoV-2 variants, using N = 10 as an example (Table S4 in Appendix A). The results show antigen testing and their combination strategies were more efficient than PCR-related strategies, indicating model results are relatively stable. In addition, there was similar effectiveness between daily antigen and PCR testing for prevention and control at R_0 = 7.5, while antigen testing was significantly faster than PCR testing at R_0 = 9.5. Daily antigen testing took the least days to detect 90% of the infected cases (28 days), while daily PCR testing took approximately 60 days, suggesting that antigen testing is more advantageous in scenarios of increased transmission.

By comparing the number of daily infectious cases, we could directly assess the effectiveness of the different testing strategies for community control. Fig. 3 shows the residents' daily symptomatic and asymptomatic cases. We found that daily PCR or antigen testing was quick and effective in reducing community infections, whereas mixed testing strategies showed saw-tooth fluctuations in the number of infections. As for Level 2 strategies, there was no significant difference in the control efficacy of different testing strategies, regardless of the 1-day or 2-day intervals.

Our results also show that implementing testing helps reduce the number of severe and critical cases, thereby reducing the demand for hospital beds and ICU beds and alleviating the bed shortage. When N = 10, as a baseline, none-testing required at least 36.0% of the available beds, while for daily antigen, daily PCR, P–A–A, and P–A–P testing strategies, the proportion decreased to 1.6%, 1.9%, 2.0%, and 3.0%, respectively (Fig. 4 and Table S3). For none-testing cases, the shortage of ICU beds was more severe at higher prevalence (N = 50 and N = 100), exceeding the available ICU beds. We also assessed quarantine resource requirements for infectious cases (Table S3). In the scenario of N = 10, the cumulative quarantine resource of the daily antigen strategy was the lowest, totaling

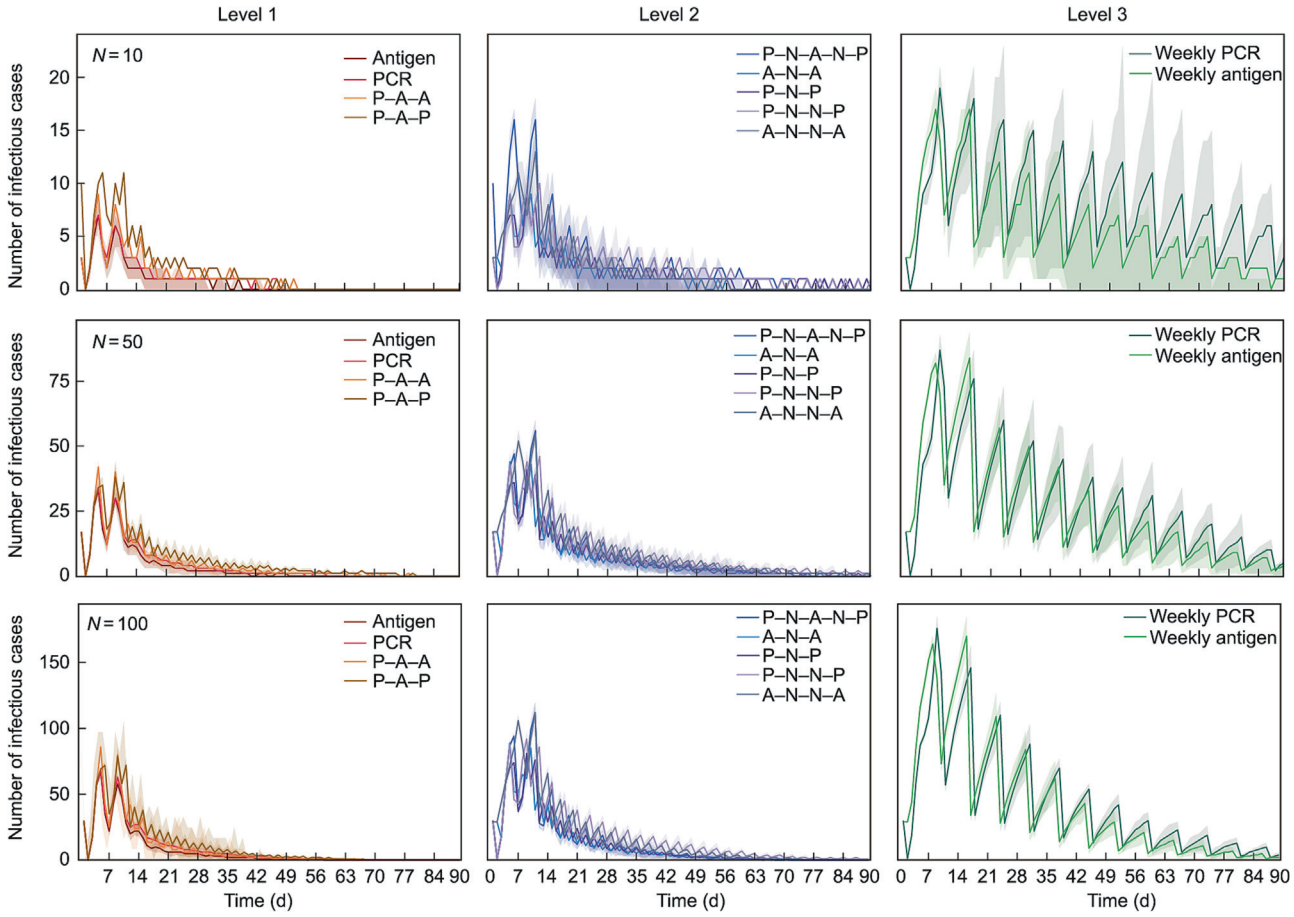

Fig. 3. Infection number containment effectiveness of different testing strategies. The line chart shows the number of infectious cases under Levels 1–3 testing strategies within 90 days. All data are presented as median with 2.5% and 97.5% quantiles of 50 simulations.

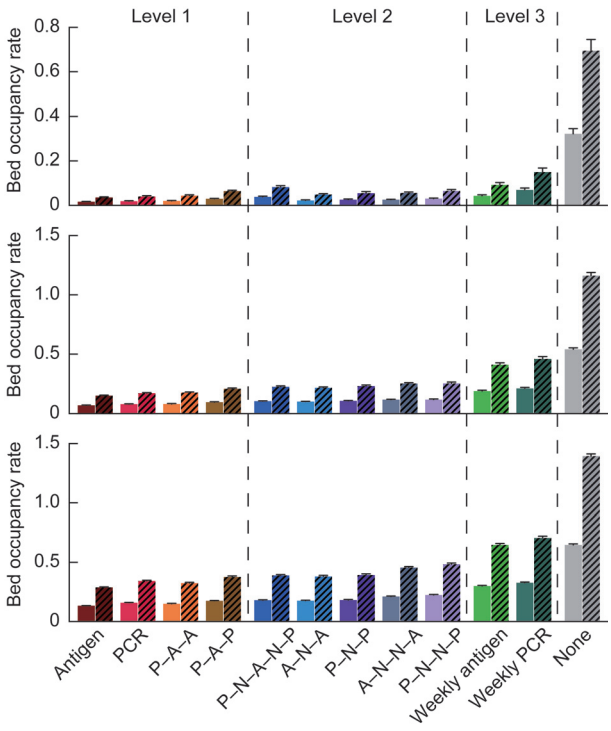

Fig. 4. Demands in hospital and ICU beds under various testing strategies. For each testing strategy, the left bar represents hospital bed occupancy, and the right bar with a slash represents ICU bed occupancy.

279 person-day, with a peak of 16 people in a day. The cumulative quarantine resource of the weekly PCR strategy was the highest, totaling 681 person-day. In addition, the P–N–A–N–P strategy had the highest peak quarantine resource at 28 people in a day. The higher the frequency of testing, the less the demand for beds and quarantine resources. Overall, antigen testing performed better than PCR testing in reducing the demand for medical beds and quarantine resources.

3.2. Factors affecting testing strategy efficiency

Based on the above results, we assumed that the factors affecting the efficiency of the testing strategy might be ① delays in results turnaround time, ② detection limits of VL, and ③ testing-related contact. Therefore, we explored the contribution of each factor by varying the combination of VL, delay time, and testing-related contact (Table 1). Of these, we consider a testing intervention with VL = 1×10^3 copies·mL^{-1} (VL3), no delay, and no testing-related contact to be an ideal strategy. In the N = 10 scenario, the estimated mean cumulative infection number detected with ideal strategy testing was 22 (0.4%), with more than 90% of infected individuals detected within 28 days, compared with 39 (0.8%) when the testing intervention included a 1-day delay. We further explored the impact of testing cutoffs for VL and testing-related contact on the testing strategies. With VL = 1×10^5 copies·mL^{-1} (VL5) and increasing testing-related contact, the cumulative infection numbers were 41 (0.8%) and 23 (0.5%), respectively. Similar trends were observed in other scenarios. For example, when N = 100, the cumulative infection number for the VL3 testing

strategy (VL-3) was 198 (3.9%), requiring only 14 days to detect more than 90% of infected cases.

In summary, a 1-day delay in delivering results had the most significant impact on testing effectiveness, followed by the VL5 testing strategy (VL-5), and the least impact of reducing one testing-related contact. Despite the relatively low sensitivity, the reduction in transmission was more pronounced for antigen testing compared to that for PCR testing of the same frequency because of the faster turnaround time. For PCR testing, the 1-day delay in obtaining results had the most significant effect on testing effectiveness.

3.3. Efficiency of modified testing strategies

To optimize PCR testing, we eliminated the delay in obtaining results. The testing efficacy of modified PCR and its combination strategies was significantly improved (Fig. 5). In the scenario of N = 10, the estimated mean cumulative infection number with the modified daily PCR was 23 (0.5%), showing a 49.4% reduction. The infection numbers with the modified P–A–A and P–A–P strategies were 26 (0.5%) (down 47.7%) and 24 (0.5%) (down 67.5%), respectively. Scenarios of N = 50 and N = 100 also showed similar trends with a decrease in the mean cumulative infection numbers compared to those in the original strategies (Table S5 in Appendix A).

In addition, the modified daily PCR was superior to the original daily PCR strategy and significantly better than the original daily antigen, P–A–A, and P–A–P strategies. Compared to the original daily antigen strategy, the modified P–A–A and P–A–P strategies reduced cumulative infection and took fewer days to detect > 90% of the infected people (Table S5).

4. Discussion

The community is the basic unit of society, the frontline and main battlefield of public health emergency response, and the last mile of health emergency management. The community is closely connected with the public and has played an active role in epidemic prevention and control, mapping the situation of residents, organizing PCR testing, and providing basic services for quarantine people. In order to achieve tailored measures and scientific and precise prevention and control, this study evaluated the effectiveness of current-available testing strategies and combinations from the perspective of community prevention and control. This method of investigation can propose optimal testing strategies that consider population health and economy and provide information for adjusting future screening strategies in case of policy adjustments.

The findings of this analytical modeling study suggest that antigen testing strategies and their combinations were more efficient than PCR-related strategies at all levels. In higher transmissible scenarios, antigen testing is more advantageous, which can effectively accelerate the speed of prevention and control. Our study found that the delay in obtaining the results, VL detection limit, and detection-related contacts all impact testing efficiency and that modified PCR testing strategies with shorter turnaround times and earlier response performed better than the original daily PCR strategy and daily antigen testing strategy. This is consistent with previous findings showing the benefits of frequent and rapid testing [32], suggesting that faster results should take precedence over high sensitivity [33,34].

Our study also highlights that we should consider replacing daily PCR testing with other more cost-effective test strategies, such as daily antigen or P–A–A combination testing strategies. PCR testing has been widely used as a screening method and played a key role in COVID-19 outbreak control during the COVID-19 pandemic in China [35]. However, it takes a lot of resources and time. In the setting of PCR tests with short turnaround time, the modified PCR tests (including P–A–A and P–A–P combination strategies) showed significant effectiveness. The modified PCR and its combination strategies were even superior to daily antigen testing, demonstrating the advantage of the higher sensitivity of PCR detection. In addition, the modified P–N–N–P testing strategy showed similar effectiveness to the modified daily PCR test. Therefore, if the turnaround time can be shortened or contact before returned results can be limited, it is economically advantageous to consider the P–N–N–P testing strategy as an alternative to the modified daily PCR test.

Furthermore, reducing the frequency of testing in low-prevalence settings is similarly effective in detecting infection, reducing the strain on healthcare resources, and improving the economics of surveillance. The choice of testing strategy should

Table 1
Mean cumulative incidence of cases and speed of containment within three months under various testing-related factors.

Number	Testing strategy	Incidence cases	Proportion of incidence cases	Containment time	Efficiency of the testing strategy					
					7 d	14 d	21 d	28 d	60 d	90 d
10	VL-3	22	0.4%	7	72.7%	81.8%	86.4%	90.9%	100.0%	100.0%
	VL-5	41	0.8%	12	53.7%	70.7%	80.5%	85.4%	97.6%	100.0%
	Delay = 1	39	0.8%	11	56.4%	71.8%	76.9%	84.6%	97.4%	100.0%
	Contact + 1	23	0.5%	7	69.6%	82.6%	87.0%	87.0%	100.0%	100.0%
	PCR	46	0.9%	13	52.2%	67.4%	78.3%	84.8%	97.8%	100.0%
	Antigen	41	0.8%	12	53.7%	70.7%	80.5%	85.4%	97.6%	100.0%
50	VL-3	96	1.9%	16	79.2%	90.6%	93.8%	96.9%	100.0%	100.0%
	VL-5	173	3.4%	27	64.9%	82.2%	89.1%	93.1%	98.9%	100.0%
	Delay = 1	182	3.6%	43	61.5%	76.9%	84.1%	89.0%	98.9%	100.0%
	Contact + 1	101	2.0%	19	79.2%	91.1%	95.0%	97.0%	100.0%	100.0%
	PCR	198	3.9%	33	59.1%	77.8%	86.9%	91.9%	99.5%	100.0%
	Antigen	173	3.4%	27	64.9%	82.2%	89.1%	93.1%	98.9%	100.0%
100	VL-3	198	3.9%	27	79.8%	91.4%	94.9%	97.0%	99.5%	100.0%
	VL-5	333	6.6%	41	69.1%	85.6%	91.6%	95.2%	99.7%	100.0%
	Delay = 1	362	7.1%	50	62.7%	77.9%	85.1%	89.8%	98.6%	100.0%
	Contact + 1	211	4.2%	29	76.8%	88.6%	92.9%	95.7%	99.5%	100.0%
	PCR	393	7.7%	43	59.0%	77.6%	86.3%	91.9%	99.2%	100.0%
	Antigen	331	6.5%	39	67.1%	84.0%	90.3%	94.3%	99.7%	100.0%

VL-3 refers to tests with a LOD of 1×10^3 copies·mL^{-1}, no delay in turnaround time, and no testing-related contact; VL-5 refers to tests with an LOD of 1×10^5 copies·mL^{-1}, no delay in the turnaround time, and no testing-related contact; Delay = 1 refers to tests with an LOD of 1×10^3 copies·mL^{-1}, a 1-day delay turnaround time, and no testing-related contact; Contact + 1 refers to tests with an LOD of 1×10^3 copies·mL^{-1}, no delay in turnaround time, but with an additional contact directly related to testing. The containment time refers to the time required for the number of new cases to reach zero for the first time.

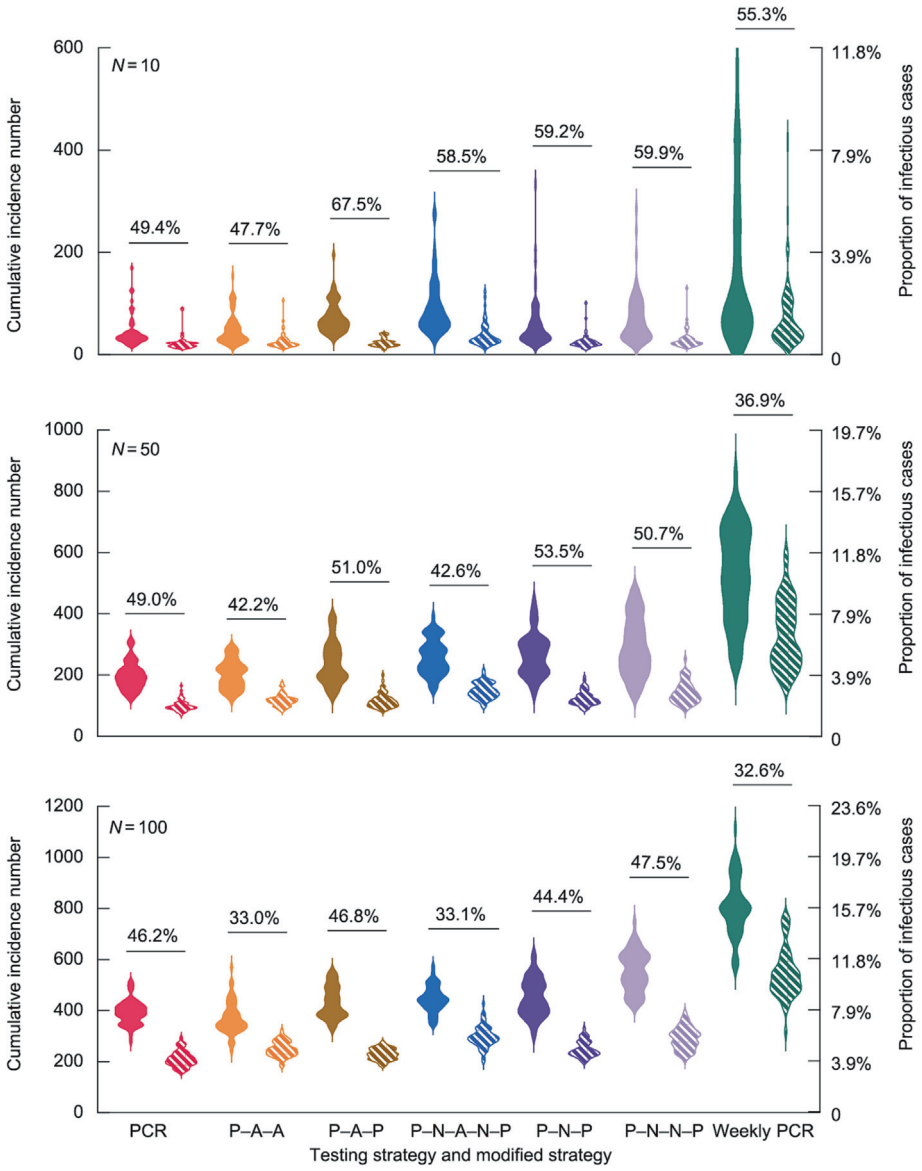

Fig. 5. Comparison of intervention effectiveness of different testing strategies with modified PCR-related testing strategies. Violin plots indicate the cumulative incidence number in a simulated community under different testing strategies with various initial infection numbers (*N*). For each testing strategy, the left violin represents the original interventions, and the right violin with a slash represents modified interventions. The numbers above violin plots show the ratio of reduction in cumulative incidence after modified PCR-related testing strategies. The proportion of infectious cases by the total number of people is shown in the right vertical axis.

consider not only the testing efficacy but also the containment targets, community prevalence, and the impact on social order and economics. In the scenario of a small number of initial infections, such as N = 10, daily testing can reduce the number of infections by approximately 95% compared with no testing. Hence, daily testing can contain a cluster outbreak with the fastest speed and the lowest number of cumulative infection cases, while weekly testing can also reduce the number of infections by 85%. In addition, when combination strategies with detection intervals were implemented, saw-tooth fluctuations in the number of infection cases were observed, which may partially explain the slower containment speed than daily testing. As the intervals increased, the fluctuations became increasingly evident. For example, weekly testing showed significant fluctuations in detection. Although weekly testing strategies took longer to end the outbreak, the number of infected cases can be controlled at a relatively low level within two months (approximately 45 days).

In addition, antigen tests are most likely to perform well in patients with high VLs (cycle threshold (Ct) values < 35), which is typically seen in the pre-symptomatic and early symptomatic phases of COVID-19. Our study illustrates the prospective value of antigen testing in outbreak containment. Although antigen testing has lower sensitivity than PCR testing with a risk of diagnostic failure, our results suggest that the advantage of a rapid return of results can partially compensate for the low sensitivity. In addition, antigen testing could theoretically reduce the risk of public area transmission, such as test-related contacts. However, several practical challenges remain. First, it is necessary to improve the sensitivity of the antigen detection method and reduce the detection limit further [36]. Second, user operation methods should be promoted and standardized to achieve optimal detection quality [37]. Third, further standardization of the verification test results and the isolation of positive persons is warranted.

5. Limitations

This study has some limitations. To facilitate model building and analysis, we made several conservative simplified assumptions. First, we assumed no difference in VL dynamics between symptomatic and asymptomatic individuals and ignored the persistent low VLs after individuals are no longer infectious [26]. We do not expect the dynamics of VL to affect our results as we are looking at frequent detection strategies. Second, although we incorporated varying transmission risks based on the type of contact (resident–staff, resident–resident, and staff–staff), we did not explicitly model different staff roles that may have different levels of risk. This simplification makes the model results more generalizable, as the community staff structure varies widely. Finally, it is difficult for us to consider all the influencing factors and evolutionary mechanisms or even simulate the complete outbreak situation in the real world. This study did not consider the importation or spillover of cases, age structure, and exposure patterns. In future research, it is important to expand the range of scenarios to include ones consistent with the actual situation, which will help provide more reference decision-making evidence for future epidemics and pandemics of respiratory infectious diseases.

6. Conclusions

In conclusion, the choice of testing strategy depends on the available resources and the scenarios in which antigen testing and combination testing strategies would serve as suitable and beneficial alternatives to PCR testing. A crucial role of testing in the post-pandemic era is to identify individuals not infected with SARS-CoV-2 so they can travel, return to school or work, and participate in mass gatherings. The wide availability of antigen testing and its rapid turnaround time promise to efficiently test large numbers of people in the community. Utility analyses of the strategy implementation of testing-related factors (such as the VL detection limit, delay in returned results, and the number of contacts) provide important insights into the possible trade-offs in decision-making processes regarding the type of tests used for both congregate and community settings. Health systems and healthcare resources are overburdened, and we need to optimize our strategies to fully support our healthcare systems in combating COVID-19 while mitigating socio–economic losses in the national interest.

Acknowledgments

This study was supported by grants from the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (2020-I2M-1-001 and 2021-I2M-1-044). The co-authors would extend their heartfelt thanks to all the individuals who generously shared their time and materials for this study.

Compliance with ethical standards

Qiangru Huang, Yanxia Sun, Mengmeng Jia, Ting Zhang, Fangyuan Chen, Mingyue Jiang, Qing Wang, Luzhao Feng, and Weizhong Yang declare that they have no conflict of interest or financial conflicts to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eng.2023.01.004.

References

[1] World Health Organization. WHO Timeline: WHO's COVID-19 response [Internet]. Geneva: WHO; [updated 2022 Mar 25, cited 2022 Oct 5]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline.
[2] Gozzi N, Chinazzi M, Davis JT, Mu K, Piontti AP, Vespignani A, et al. Preliminary modeling estimates of the relative transmissibility and immune escape of the Omicron SARS-CoV-2 variant of concern in South Africa. medRxiv 2022.
[3] Muik A, Lui BG, Wallisch AK, Bacher M, Mühl J, Reinholz J, et al. Neutralization of SARS-CoV-2 Omicron by BNT162b2 mRNA vaccine-elicited human sera. Science 2022;375(6581):678–80.
[4] Zhang L, Li Q, Liang Z, Li T, Liu S, Cui Q, et al. The significant immune escape of pseudotyped SARS-CoV-2 variant Omicron. Emerg Microbes Infect 2022;11(1):1–5.
[5] United Nations. Coronavirus global health emergency [Internet]. New York City: UN; [updated 2022 Sep 24, cited 2022 Oct 5]. Available from: https://www.un.org/en/coronavirus.
[6] World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. Geneva: WHO; [updated 2022 Sep 13, cited 2022 Sep 13]. Available from: https://covid19.who.int.
[7] Chen Z, Deng X, Fang L, Sun K, Wu Y, Che T, et al. Epidemiological characteristics and transmission dynamics of the outbreak caused by the SARS-CoV-2 Omicron variant in Shanghai, China: a descriptive study. Lancet Reg Health West Pac 2022;29:100592.
[8] Zhang T, Wang Q, Leng Z, Yang Y, Yang J, Chen F, et al. A scenario-based evaluation of COVID-19-related essential clinical resource demands in China. Engineering 2021;7(7):948–57.
[9] Dinnes J, Deeks JJ, Adriano A, Berhane S, Davenport C, Dittrich S, et al.; Cochrane COVID-19 Diagnostic Test Accuracy Group. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. Cochrane Database Syst Rev 2020;8(8):CD013705.
[10] Safiabadi Tali SH, LeBlanc JJ, Sadiq Z, Oyewunmi OD, Camargo C, Nikpour B, et al. Tools and techniques for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID-19 detection. Clin Microbiol Rev 2021;34(3):e00228-20.
[11] Lieberman JA, Pepper G, Naccache SN, Huang ML, Jerome KR, Greninger AL. Comparison of commercially available and laboratory-developed assays for *in vitro* detection of SARS-CoV-2 in clinical laboratories. J Clin Microbiol 2020;58(8):e00821-20.
[12] Watson J, Whiting PF, Brush JE. Interpreting a COVID-19 test result. BMJ 2020;369:m1808.
[13] Chen CC, Lu SC, Bai CH, Wang PY, Lee KY, Wang YH. Diagnostic accuracy of SARS-CoV-2 antigen tests for community transmission screening: a systematic review and meta-analysis. Int J Environ Res Public Health 2021;18(21):11451.
[14] Pray IW, Ford L, Cole D, Lee C, Bigouette JP, Abedi GR, et al.; CDC COVID-19 Surge Laboratory Group. Performance of an antigen-based test for asymptomatic and symptomatic SARS-CoV-2 testing at two university campuses—Wisconsin, September–October 2020. MMWR Morb Mortal Wkly Rep 2021;69(5152):1642–7.
[15] Peeling RW, Olliaro PL, Boeras DI, Fongwen N. Scaling up COVID-19 rapid antigen tests: promises and challenges. Lancet Infect Dis 2021;21(9):e290–5.
[16] Hanson KE, Caliendo AM, Arias CA, Hayden MK, Englund JA, Lee MJ, et al. The infectious diseases society of America guidelines on the diagnosis of COVID-19: molecular diagnostic testing. Clin Infect Dis 2021:ciab048.
[17] Smith RL, Gibson LL, Martinez PP, Ke R, Mirza A, Conte M, et al. Longitudinal assessment of diagnostic test performance over the course of acute SARS-CoV-2 infection. J Infect Dis 2021;224(6):976–82.
[18] Santé Publique Ottawa. Community COVID-19 outbreak definitions [Internet]. Ottawa: Santé Publique Ottawa; [updated 2022 Sep 13, cited 2022 Sep 13]. Available from: https://www.ottawapublichealth.ca/en/reports-research-and-statistics/resources/Documents/covid-19/community-outbreak_definitions_en.pdf.
[19] Dean A, Venkataramani A, Kimmel S. Mortality rates from COVID-19 are lower in unionized nursing homes. Health Aff 2020;39(11):1993–2001.
[20] Ministry of Housing and Urban–Rural Development of the People's Republic of China. China's urban residential area planning and design standards [Internet]. Beijing: MOHURD; [cited 2022 Sep 13]. Available from: https://www.mohurd.gov.cn/gongkai/fdzdgknr/tzgg/201811/20181130_238590.html. Chinese.
[21] National Bureau of Statistics of China, editor. China statistical yearbook 2021 [Internet]. Beijing: China Statistics Press; [update 2021 Sep 15, cited 2022 Sep 11]. Available from: http://www.stats.gov.cn/tjsj/ndsj/2021/indexeh.htm.
[22] Mossong J, Hens N, Jit M, Beutels P, Auranen K, Mikolajczyk R, et al. Social contacts and mixing patterns relevant to the spread of infectious diseases. PLoS Med 2008;5(3):e74.
[23] Bar-On YM, Flamholz A, Phillips R, Milo R. SARS-CoV-2 (COVID-19) by the numbers. eLife 2020;9(9).
[24] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382(13):1199–207.
[25] Lennon NJ, Bhattacharyya RP, Mina MJ, Rehm HL, Hung DT, Smole S, et al. Comparison of viral levels in individuals with or without symptoms at time of

COVID-19 testing among 32,480 residents and staff of nursing homes and assisted living facilities in Massachusetts. medRxiv 2020.
[26] Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581(7809):465–9.
[27] Mina MAO, Parker R, Larremore DAO. Rethinking COVID-19 test sensitivity—a strategy for containment. N Engl J Med 2020;383(22):e120.
[28] Baker JM, Nakayama JY, O'Hegarty M, McGowan A, Teran RA, Bart SM, et al. SARS-CoV-2 B.1.1.529 (Omicron) variant transmission within households—four U.S. jurisdictions, November 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71(9):341–6.
[29] Chinese Center for Disease Control and Prevention. COVID-19 infection [Internet]. Beijing: CDC; 2022 [cited 2022 Jun 22]. Available from: https://www.chinacdc.cn/jkzt/crb/zl/szkb_11803/. Chinese.
[30] Chinese Center for Disease Control and Prevention. The latest situation of COVID-19 [Internet]. Beijing: CDC; [updated 2022 May 28, cited 2022 Jun 22]. Available from: https://www.chinacdc.cn/jkzt/crb/zl/szkb_11803/. Chinese.
[31] McMenamin ME, Nealon J, Lin Y, Wong JY, Cheung JK, Lau EHY, et al. Vaccine effectiveness of one, two, and three doses of BNT162b2 and CoronaVac against COVID-19 in Hong Kong: a population-based observational study. Lancet Infect Dis 2022;22(10):1435–43.
[32] See I, Paul P, Slayton RB, Steele MK, Stuckey MJ, Duca L, et al. Modeling effectiveness of testing strategies to prevent coronavirus disease 2019 (COVID-19) in nursing homes—United States, 2020. Clin Infect Dis 2021;73(3):e792–8.
[33] Bergstrom T, Bergstrom CT, Li H. Frequency and accuracy of proactive testing for COVID-19. medRxiv 2020.
[34] Larremore DB, Wilder B, Lester E, Shehata S, Burke JM, Hay JA, et al. Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening. Sci Adv 2021;7(1):eabd5393.
[35] Li Z, Chen Q, Feng L, Rodewald L, Xia Y, Yu H, et al.; China CDC COVID-19 Emergency Response Strategy Team. Active case finding with case management: the key to tackling the COVID-19 pandemic. Lancet 2020;396(10243):63–70.
[36] Pilarowski G, Lebel P, Sunshine S, Liu J, Crawford E, Marquez C, et al. Performance characteristics of a rapid severe acute respiratory syndrome coronavirus 2 antigen detection assay at a public plaza testing site in San Francisco. J Infect Dis 2021;223(7):1139–44.
[37] Pollock NR, Jacobs JR, Tran K, Cranston AE, Smith S, O'Kane CY, et al. Performance and implementation evaluation of the Abbott BinaxNOW rapid antigen test in a high-throughput drive-through community testing site in Massachusetts. J Clin Microbiol 2021;59(5):e00083–121.