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Research article

Individual-based modeling of COVID-19 transmission in college communities

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Abstract: The ongoing COVID-19 pandemic has created major public health and socio-economic challenges across the United States. Among them are challenges to the educational system where college administrators are struggling with the questions of how to mitigate the risk and spread of diseases on their college campus. To help address this challenge, we developed a flexible computational framework to model the spread and control of COVID-19 on a residential college campus. The modeling framework accounts for heterogeneity in social interactions, activities, environmental and behavioral risk factors, disease progression, and control interventions. The contribution of mitigation strategies to disease transmission was explored without and with interventions such as vaccination, quarantine of symptomatic cases, and testing. We show that even with high vaccination coverage (90%) college campuses may still experience sizable outbreaks. The size of the outbreaks varies with the underlying environmental and socio-behavioral risk factors. Complementing vaccination with quarantine and mass testing was shown to be paramount for preventing or mitigating outbreaks. Though our quantitative results are likely provisional on our model assumptions, sensitivity analysis confirms the robustness of their qualitative nature.

Keywords: COVID-19, individual-based model, non-pharmaceutical interventions, vaccine, college

1. Introduction

The ongoing COVID-19 pandemic has created major public health and socio-economic challenges across the United States. Among them are challenges to the educational system. After the 2020 Spring Break, many colleges and universities in the U.S. sent residential students' home and transitioned partially or completely to remote learning as an attempt to reduce the risk of COVID-19 transmission on their campuses. Though such a policy may have contributed to reducing the spread of the disease on college campuses as well as their surrounding communities, it resulted in severe financial and potential academic losses for many colleges. In an attempt to mitigate these losses, college administrators have struggled with the questions of how to open in-person activities while prioritizing student safety. In August, 2020, over a third of US colleges and universities had fully in-person classes and around 20% chose to be hybrid (a mix of in-person and remote classes) [1]. Many of these reopenings were followed by campus outbreaks that led several universities to shut down or impose increased restrictions once again.

Analyses on the relative risk factors involved in the spread of COVID-19 have been conducted [2]. Before the availability of vaccines, control strategies focused on social/behavioral factors and preventive strategies such as facemask, reduced class size, reduced social gatherings/events size, and reduced residence hall (dormitory) occupancy to share the common utilities, bathrooms, and so on. Those strategies were combined with regular testing to rapidly detect and quarantine infected students. After vaccines became widely available, many colleges required or encouraged their students to get vaccinated before returning to campus. But with college reopening, many colleges, including some highly vaccinated colleges, experienced COVID-19 outbreaks [3–5]. Previous modeling studies have investigated different aspects of COVID-19 spread on college campuses [6–10]. For example, Paltiel et al. [11] used a simple homogeneous mixing SEIR compartmental model to evaluate the effectiveness of screening strategies in a college with 5000 students; Weeden and Gornwell [12] designed student contact networks though transcript data and used these networks to studied the effectiveness of small course enrollments on reducing the risk of epidemic spread. Gressman and Peck [13] used a full-scale stochastic agent-based model (ABM) of a reasonably large research university to conclude that testing accuracy is a critical issue and holding large classes greatly increases the risk of a significant outbreak on campus. Goyal et al. [14] also developed an ABM that incorporates important features related to risk at the University of California San Diego to assess the potential impact of strategies to reduce outbreaks. They found that increased frequency of asymptomatic testing from monthly to twice weekly has minimal impact on average outbreak size, but substantially reduces the maximum outbreak size and cumulative number of cases. Inspired by their work, we developed an individual-based model that explicitly accounts for the contribution from class, dorm, and social activities to COVID-19 transmission through complex student interaction pathways on college campuses and use the model to quantitatively assess different control strategies such as vaccination, test screening, and symptomatic quarantine.

Mathematical models are powerful tools to explore disease transmission, and the complex landscape of intervention strategies to quantify and assess different options. One of the key challenges

in modeling the spread of Covid-like pathogens in local communities is an efficient account (parameterization) of human social interactions. Conventional approach (population-based) employs a simplified form of social interactions based on 'mean contact rate/host' [15–18]. To address this limitation, individual-based modeling has been widely used in the study of pathogen spread and infection control, including Pandemic Influenza [19,20] and Covid-19 [21–24] among others [25–27]. Some have used individual-based models (IBM) where a community is viewed as a randomly colliding system of 'host-particles', whereby 'infectives' transmit the pathogen to 'susceptibles' via random collisions. The intensity (rate) of transmission is proportional to mean contact rate. On the opposite side are individual-based models based on social network structure where transmission pathways are rigidly confined to one's 'neighbors' - adjacent nodes on the social network [28]. In real life human social contact mixing combines both random and scheduled (prescribed) contacts/interactions. Our proposed approach differs from previous IBM works in two important aspects: 1) the basic transmission step in our model is 'many-to-many' [29] vs. conventional 'one-to-one'; 2) the model keeps a detailed account of daily social interactions.

Here, we developed a flexible computational framework to model the spread of COVID-19 on a residential college campus. The modeling framework accounts for heterogeneity in social interactions, activities, disease progression, and control interventions. This allows us to generate and simulate more realistic synthetic college communities using a handful of basic inputs that combine scheduled and random contacts, and prescribed patterns of disease progression.

2. Materials and methods

2.1. Basic components of IBM

The two basic components of our college IBM include (i) college community with structured social interaction patterns and (ii) infection transmission and disease progress. College community is made of individual students (other population groups such as faculty and staff could be added). They are engaged in their daily activities (classes, dorm residence, social activities). As a pathogen is introduced into such a community, it could spread via daily interactions.

(i) **Student body and social mixing** combine scheduled and random contacts (See Figure 1). Scheduled contacts include classes with assigned seating and weekly schedule, plus dorm residence. Random social mixing consists of daily aggregation in contact pools of different sizes and frequencies.

(ii) **Disease progression**. In our model, the individual's health states are classified as susceptible (S), infected (I), and recovered (R) stages (See Figure 1). Once infected, each individual undergoes a prescribed infection progress history determined by I-stage duration (L) and variable, time-dependent infectivity (b_max). In our setup, infectivity serves as a proxy for viral load, as well as a predictor for symptoms expression, and diagnostic test sensitivity. We allow two types of disease progression: asymptomatic (mild, A-type) and symptomatic (severe, S-type), which differ in their duration of infection and infectivity levels. Only the infected S-type have symptomatic disease expression, which is used for simulating quarantine isolation strategies. Furthermore, we account for the effect of vaccination (imperfect protection), via a reduced susceptibility and infectivity profiles. Figure 3 shows infectivity patterns for all 3 types (A,S, vaccinated). Each host is assigned its infectivity type.

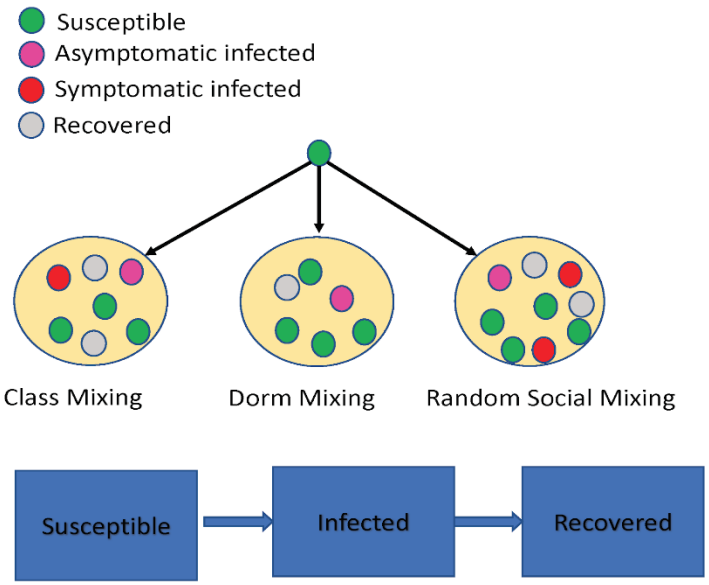

Figure 1. An abstract flowchart of social mixing and disease progress. Social mixing is implemented via contact pools where students aggregate on a daily basis. Two types of contacts are considered: Scheduled (class and dorm mixing) and random (dining and/or other random social mixing). The infection stages are classified as susceptible (S), infected (I), and recovered (R) stages.

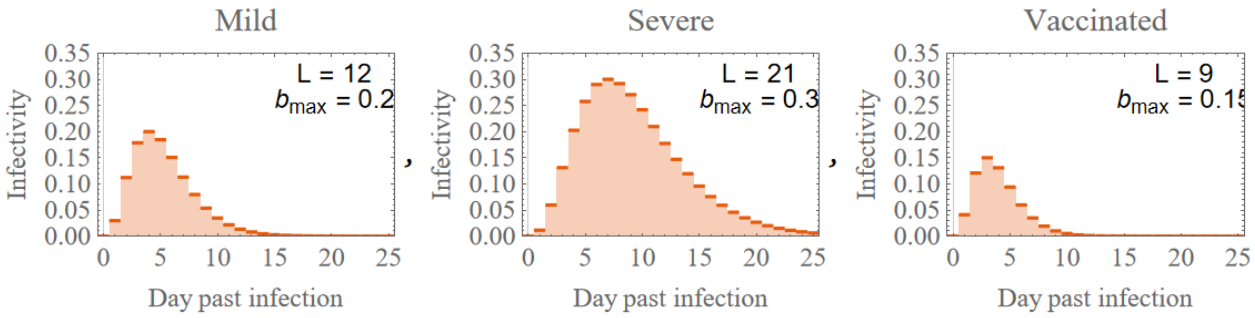

Figure 2. Time-dependent infectivity levels for Mild (Asymptomatic), Severe (Symptomatic), and Vaccinated individuals, respectively.

(iii)**Transmission environment:** Student mixing pools (scheduled and random) aggregate on a daily basis, and provide the key transmission mechanism of disease from infected to susceptible individuals. Furthermore, a student could partake in several daily activities, and thereby accumulate his/her exposure, or contribution to disease spread. We assume each type of activity (class, dorm, and social) takes place in a suitable environment, and each environment has an associated mean risk factor (a_c, a_d, a_s). These factors $(0 < a_i < 1)$ represent the individuals' risk of exposure to the virus in a given environment. They account for physical conditions (e.g. seat density in classrooms, specifics of dorm units), and behavioral practices (e.g. adherence to face mask or other protective means during contacts). They also account for factors of the indoor environment such as ventilation systems and contaminated surfaces that have been

associated with a risk of airborne, aerosol, and fomites transmission of the COVID-19 virus [30]. Their values vary from 0 (full protection) to 1 (full exposure). More generally, risk factors could be made site-specific (varying between classrooms and/or other places of activity). Combined with individual infectivity, environmental risk factors determine the probability of disease transmission from infected to susceptible individuals as elaborated in the next subsection.

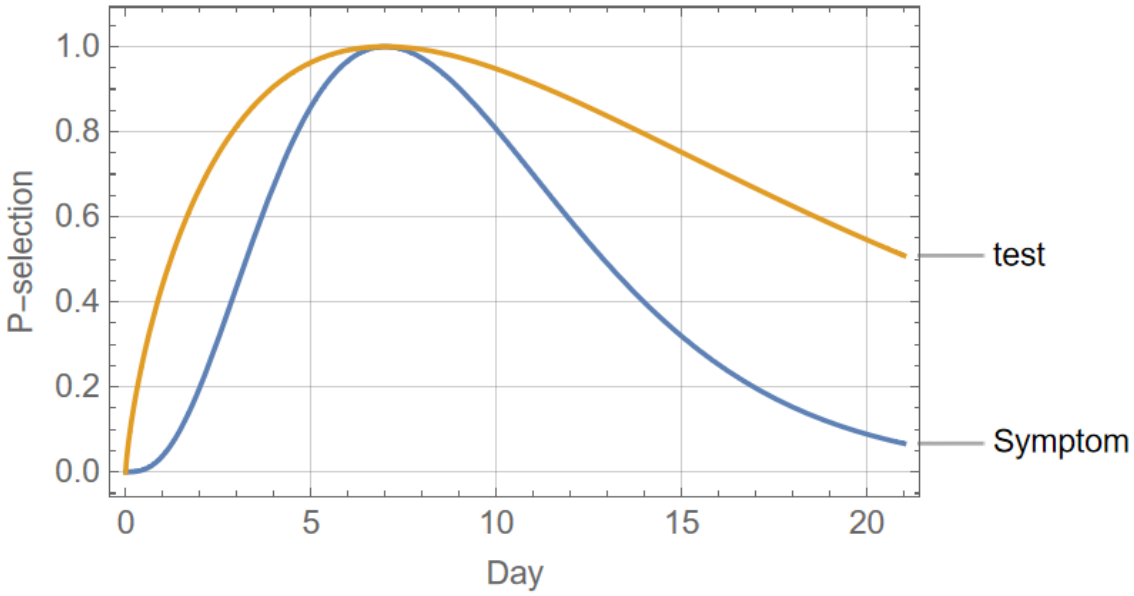

Figure 3. Time-dependent probability of a positive test (yellow) and time-dependent probability of symptomatic expression for Severe infective pathway (See Figure 2) used for likelihood of symptomatic quarantine (blue).

Note that the risk factors (a_c, a_d, a_s) associated with three transmission environments (class, dorm, and social) are highly uncertain and could vary in different colleges. Hence, we explore a range of choices (low, moderate, high) for the three environmental risk factors. Other parameters of disease progression are reasonably chosen based on literature (See Table S3).

Social mixing is implemented in our IBM via contact pools (social groups) with which students aggregate on a daily basis. Two types of contacts are considered: Scheduled and random contacts.

S**cheduled contacts** include classes and housing/dorms.

(i) **Classes**. Our model is capable of utilizing real college class schedules if the data is available. This includes the days and times of classes, each students' attendance in the class, and student seat assignment. If this data is not available, the model can generate synthetic class schedules from a few basic inputs described in Supplement. Specifically, we generate a class weekly schedule, including a seat assignment, for every student in our college. We assume that each student has three randomly selected non-overlapping classes, meeting on a Monday, Wednesday, and Friday (MWF) schedule or on a Tuesday and Thursday (TuTh) schedule. Each class has a prescribed student seating in the classroom and weekly schedule. Based on their seating pattern, an infected individual can spread the pathogen to his/her neighbors within a prescribed radius (Figure 4). Probability of transmission drops with the distance between seats.

(ii) **Housing/dorm.** A particular form of scheduled contact whereby students aggregate in shared units, halls, utilities etc. This can again be initialized with real data if available. If not, synthetic housing assignment is generated by randomly dividing all students into non-overlapping groups of a specified number (unit occupancy).

Random social contacts are simulated using a specified pool size distribution. Specifically, students randomly aggregate on a daily basis in contact pools of prescribed sizes $m_1; m_2; \ldots$, and frequencies $f_1; f_2; \ldots$. The latter accounts for an average number of mixing pools of a given type (per host per day), a proxy for their social-contact preferences. More refined contact pools can be generated from the social network makeup of the host community.

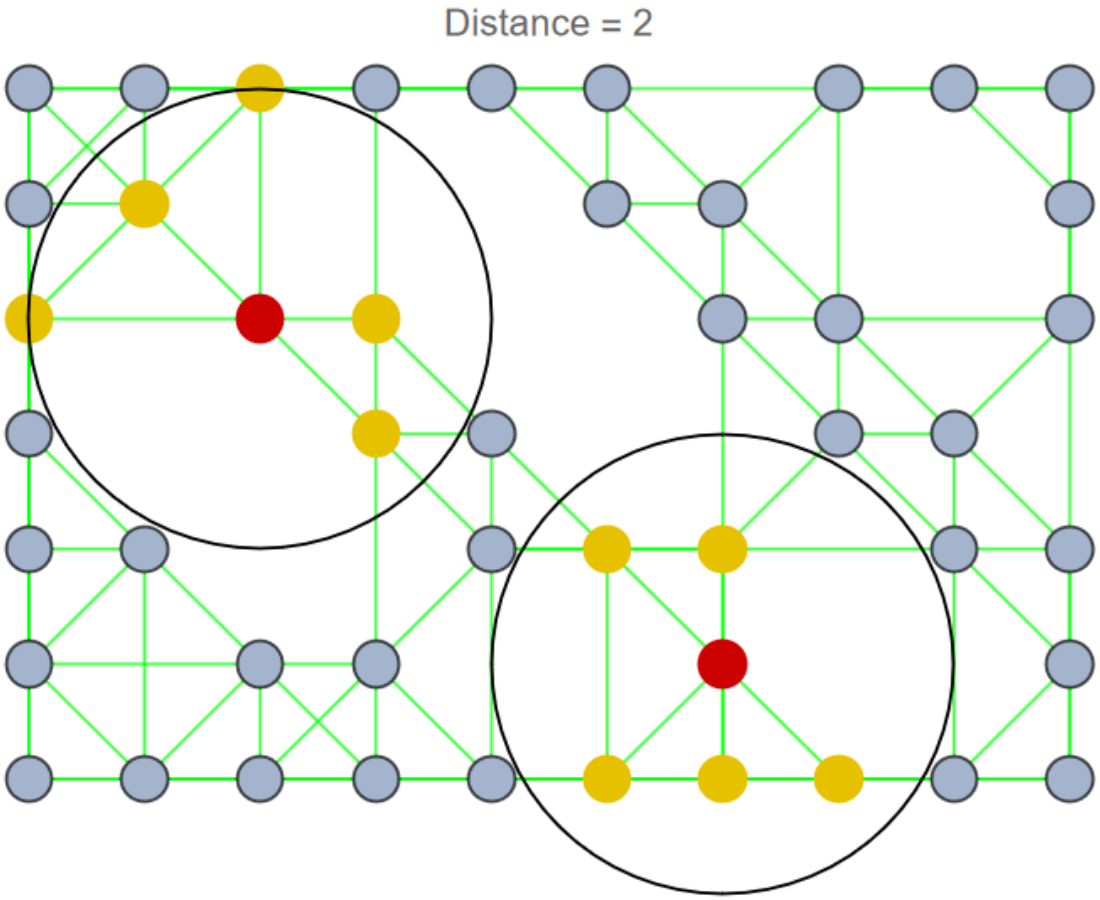

Figure 4. A typical classroom with 2 infected hosts (red) spreading pathogens to nearby susceptible students (yellow) within prescribed areas. Graph links indicate nearest neighbors within distance < r, for all occupied seats (gray).

2.2. Infection and disease progression

Different infected individuals can undergo different disease processes. Here for simplicity, we partition the population into three groups: asymptomatic (A-type), symptomatic (S-type) and vaccinated. The key difference between the three is the stage duration and the infectivity function profile. Vaccinated individuals are assumed to have lower susceptibility factor $(0 < s < 1)$. Asymptomatic individuals have shorter duration and lower infectivity [31,32]; they do not exhibit

symptoms over the duration of infection, but are still capable of transmitting the pathogen. In contrast, symptomatic (S-types) could exhibit disease symptoms over their infection period. Vaccinated individuals similarly do not exhibit symptoms and have a reduced duration of infection and lower infectivity.

The key quantifier of disease progression is the host infectivity function $b(d)$ on day d post infection. We view it as a proxy for variable viral load in the course of infection. It follows a prescribed dynamic pattern (shown in Figure 2); specifically, we use function $B(t) = t^k e^{-kt}$ [33–35] with steepness k and define $b(d) = b_M B(d/L)$, where b_M is the peak infectivity and L is the mean duration. Each infected individual would progress according to his/her *b(d)*. Specific choices $(b_M; k; L)$ for asymptomatic, symptomatic, and vaccinated hosts are given in Supplement Table S3.

The infectivity function *b(d)* determines the probability of transmission per contact from an infected individual to a fully susceptible individual. Hence, we employ it to estimate transmission rates within contact pools. We also use its value *b(d)* (or timing *d*) as a predictor for symptomatic expression and isolation, as well as a predictor of positive test diagnostics (See Figure 3).

Host infection ($S \to I$) is modeled as a Bernoulli random process with the success probability determined by cumulative daily contacts of a given susceptible-host. In each contact pool, scheduled or random (class, dorm, social mixing), we estimate the survival probability (staying uninfected) depending on the pool's makeup and the associated-environmental risk factor. Specifically, for an individual with susceptibility level *s*, a contact pool with m infectives with infectivity levels $\{b_1; \ldots; b_m\}$, and environmental risk factor a gives a survival probability $p_S = \prod_i (1 - a b_i s)$. Note that the classroom setting is somewhat different from other contact pools, as the probability of survival depends not on the entire body of infected classmates, but only on the 'nearest infected neighbors' determined by classroom seating (see Supplement for details). All contact mixing pools for a given S-host accumulate over a daily period; they determine the final probability of infection $p_I = 1 - p_{sc} \cdot p_{sd} \cdot p_{ss}$, where p_{sc}, p_{sd}, p_{ss} are survival probabilities in class, dorm and random social mixing.

2.3. IBM community

Each host in the IBM community is described by her/his attributes (id + disease type), and her/his current infectious state: (S-I-R); for I-hosts it also includes the day on infection *d*. The details are provided in Supplement. Hosts aggregate on a daily basis, determined by their scheduled and random activities, and the resulting change of infection status is recorded. The recorded IBM history keeps track of all individual histories, and the community outputs can be extracted from those. As our IBM is stochastic, such histories and outputs could vary in different simulations under identical conditions. So, in each case we simulate an ensemble of random histories.

2.4. Model initializations

We make suitable choices for model parameters mentioned in previous subsections. Important ones include (i) the population fractions of A-, S-, vaccinated types with pathways of Figure 2 (the peak infectivity, duration, and steepness); (ii) the environmental risk factors; (iii) social mixing parameters.

All inputs, social, environmental, disease, are freely adjustable, including A-S-vaccinated pathways (the duration and peak infectivity). For instance, should vaccinated individuals be fully immune, the peak infectivity simply needs to be set to zero.

2.5. *Control interventions*

Our IBM setup allows us to investigate a wide range of interventions, including (i) vaccination, (ii) symptomatic isolation, (iii) test screening.

(i) Vaccination is not fully protective, therefore vaccinated individuals can still undergo infectious processes and contribute to transmission. We assume that vaccination reduces the susceptibility of vaccinated individuals by a given factor (s = ½), and the host's infectious pathway as shown in Figure 2. Symptomatic isolation depends on symptom expression defined by a probability function shown in Figure 3. Only S-type individuals can express symptoms depending on their infectivity level and be isolated. So, on a daily basis the infected S-pool is selected, and some of them are sent to the quarantine via Bernoulli toss, determined by their probability of symptomatic expression. The quarantined individuals are excluded from social mixing, and no longer contribute to disease spread.

(ii) Test screening is implemented via a preset number of tests per day to be randomly conducted on non-quarantined individuals. The test results will depend on their infectivity levels (the stage of infection), via probability function (Figure 3). A Bernoulli toss with this probability will determine individuals with a positive test, sent to the quarantined state similar to symptomatic isolation.

Different control strategies can be compared in terms of their efficacy in mitigating an outbreak. For quantitative assessment of control interventions and their impact we use is the outbreak size (the cumulative infection by the end of a given time period, e.g. 15-weeks semester, relative to total population) as the primary measurement. This is estimated and compared with baseline cases to assess the efficacy of control.

2.6. *Model outputs*

Infection outbreaks in college communities were run over the 15-week (semester) period. However, under low transmission intensity, such outbreaks could last much longer and won't be terminated by the end of semester. To have an outbreak run its full course, we extended the simulation beyond the 15-week academic semester. All results presented below were simulated over such extended (if necessary) time periods.

The basic outputs used in our analysis below are outbreak size and duration, determined by daily SIR-counts. Many additional outputs however, could be derived on a daily or cumulative basis, including quarantine counts and infection severity.

2.7. *Numeric implementations*

All numeric codes were implemented in the Wolfram Mathematica platform, and used a variety of Wolfram tools for setting up and manipulating annotated objects, data structures and associations. Mathematica codes are provided in Github (https://github.com/qimin-h/College-IBM-of-covid-19).

3. Results

We generated a synthetic college community (class schedule and dorm residence), with no pre-

existing immunity, and no external source of infection. We first explored the effect of college size (student body) on outbreak patterns, by simulating a range of colleges from small (1000) to medium-large (6000-12,000), under similar social/environmental conditions. Within our setup, contact rates and patterns are independent of total student body and are limited by dorm occupancy, class seating distributions, and social interactions (see Figure S2). As such, the overall effect of size was marginal; more significant factors were social interactions (patterns and rates), and disease inputs.

Therefore, all simulations below were run with a N = 3000 size synthetic community.

3.1. Outbreak in naïve host community

The students' infectious pathways are split 60% Mild (A-type) and 40% Severe (S-type) as consistent with empirical COVID-19 data among young adults/college students [36-38]. A naive host population is initialized with a few infected individuals.

3.1.1. Typical outbreak patterns and parameter sensitivity: baseline cases

The most uncertain parameters of our model are the environmental risk factors. These can vary widely depending on the college and setting of student interactions. Influences such as quality of air ventilation and prevalence of mask wearing can alter the environment's ability to spread pathogens. These influences can lead to disparate environmental risk factors even among neighboring classrooms on college campuses.

To combat this uncertainty, it would be useful to explore a range of values for the environmental risk factors. We do not, however, perform an exhaustive analysis of the parameter-space, but explore a few scenarios to show how a range of risk factors can be useful in interpreting various strategies to combat outbreaks. Specifically, we focused on environmental risk factors $\{a_c, a_d, a_s\}$, assigned 3 values, low, medium, high, (See Table 1), along with the classroom distance scale for three values (d = {1.5, 2, 2.5}). So, most simulations below have varying a-factors, and some include d-factors.

A typical outbreak pattern and duration depends strongly on the environmental risk factors. Under high values for the risk factors (see Table 1**)**, we observe strong outbreaks over a relatively short time duration (usually less than a 15-week academic semester).

An ensemble of 50 simulations were run for each combination of parameters with results presented in Figure 5(a). For the naïve cases, variation in the distance scale and environmental risk factors had a relatively minimal effect, but lower values for each did reduce the overall outbreak size.

Table 1. Environmental risk factors for three different scenarios (Low, Moderate, and High).

Scenario: Environment	Low	Moderate	High
Classroom	0.15	0.2	0.25
Dorm	0.2	0.25	0.3
Social	0.1	0.15	0.2

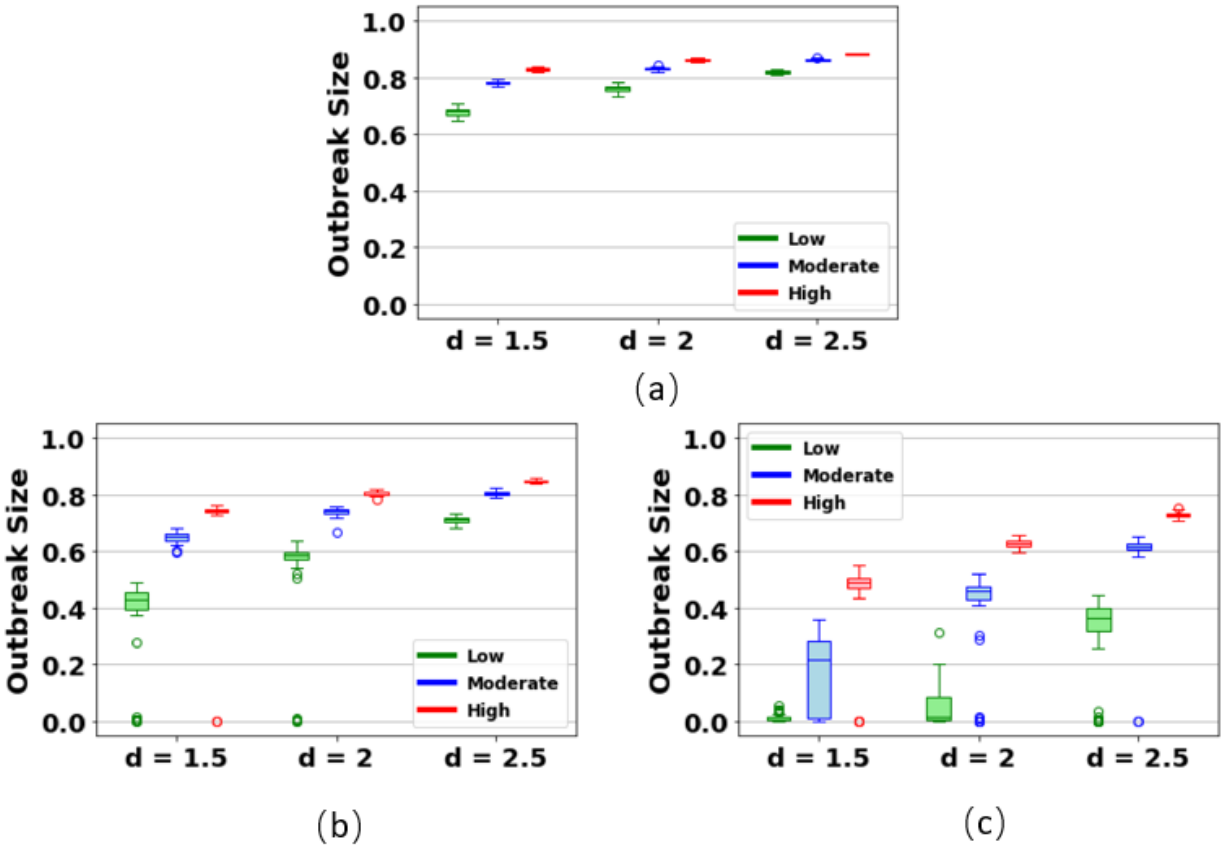

Figure 5: Relative outbreak-size distribution for (a) Naïve host community; (b) 50% vaccination; (c) 90% vaccination, for 3 environmental risk factor scenarios (low in green, moderate in blue, and high in red) and three distance scales for pathogen spread in classrooms (d = {1.5, 2, 2.5}). The environmental risk factor values are given in Table 1.

3.2. Analysis of intervention

3.2.1. Vaccination

We now investigate the effects of vaccination on outbreak size. The two scenarios we look at are a 50% vaccination coverage and a 90% vaccination coverage amongst the students (meaning 50% and 90%, respectively, of the student body is initialized with the vaccinated infectious pathway shown in Figure 2). We assume the vaccine in question has the effect of reducing infectious duration and peak infectivity with values as indicated in Figure 2 and host susceptibility by a factor of ½ [39–41]. A fully protective vaccine could be easily simulated by sending the vaccinated pool to the recovered pool.

Once the vaccinated pool was selected, the remaining hosts are partitioned into 60% A-type and 40% S-type as in the Naïve case. All other parameters are the same as the Naïve case.

Ensembles of 50 simulations were run for each vaccination scenario with results shown in Figure 5(b) for 50% vaccination and Figure 5(c) for 90% vaccination. As seen from the figures, 50% vaccination had marginal effects on overall outbreak size apart from introducing a few outliers. Such outliers arise typically in stochastic S-I-R type models (population based or IBM) due to bimodal patterns of outbreak outputs (size and duration) with a fraction of large and small outbreaks (see Supplement Figure S1). 90% vaccination, on the other hand, helps greatly reduce outbreak size for low

environmental risk factors, and has moderate effects on moderate environmental risk factors with lower classroom distance scale (same as in Naive host pool). However, high environmental risk factors still lead to large outbreak sizes for both vaccination scenarios.

For Figure 5(b), three scenarios led to portions of outbreak burnout: d = 1.5 with low risk had 16% of simulations not lead to outbreak, d = 1.5 with high risk had 4%, and d = 2 with low risk had 8%. 90% vaccination coverage in Figure 5(c) had much higher burnout: d = 1.5 with low risk had 90%, d = 1.5 with moderate risk had 18%, d = 1.5 with high risk had 6%, d = 2 with low risk had 20%, d = 2 with moderate risk had 12%, d = 2.5 with low risk had 18%, and d = 2.5 with moderate risk had 4%.

3.2.2. Symptomatic quarantine

We now add another intervention strategy of symptomatic quarantine on top of vaccination. We fix the classroom distance scale at d = 2 and consider three choices of environmental risk, for vaccination levels of 50% vaccination (Figure 5(b)) and 90% (Figure 5(c)) as our baseline cases. Comparative results for the vaccination baseline cases (B) and vaccination plus symptomatic quarantine (Q) are shown in Figure 6(a) for 50% vaccination and Figure 6(b) for 90% vaccination.

As seen in Figure 6(a), symptomatic quarantine can lead to a significant reduction in outbreak size as environmental risk factors decrease with 50% vaccination coverage. On the other hand, 90% vaccination coverages are less likely to be quarantined, but outbreaks are still slightly reduced. This is due to the symptomatic quarantine intervention only applying to S-type pathways which constitute only 4% of the total population for 90% vaccination as opposed to 20% of the total population for 50% vaccination. The bulk of transmission is carried out now by vaccinated hosts.

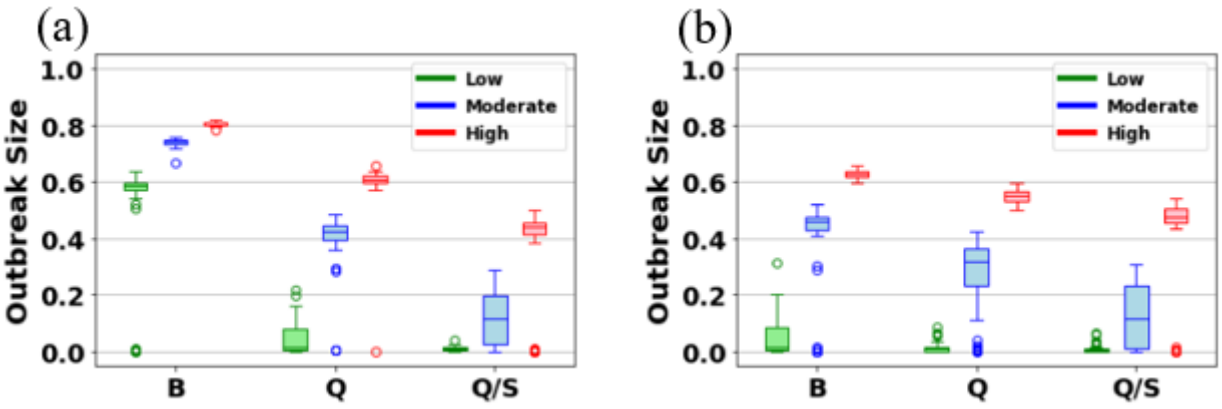

Figure 6. Relative outbreak-size distribution for (a) 50% vaccination with quarantine and screening; (b) 90% vaccination with quarantine and screening, for the d = 2 triples of Figure 5 (b) and (c) as baselines. **B** indicates baseline scenarios, **Q** indicates addition of symptomatic quarantine, **Q/S** indicates the addition of symptomatic quarantine and screening tests.

3.2.3. Screening and tests

Next, we combine Test Screening with symptomatic quarantine intervention for the same cases as above. We assume that 5% of the student population can be screened on a daily basis (i.e., about 100%

of the population every three weeks). The test pool is drawn randomly. The test sensitivity depends on the host infective stage (Figure 3). We run symptomatic quarantine as before.

Results for symptomatic quarantine plus screening (Q/S) are shown in Figure 6(a) for 50% vaccination and Figure 6(b) for 90% vaccination. Similar to the intervention of symptomatic quarantine alone, the addition of screening has a considerable impact on lowering outbreak size as environmental risk factors decrease for 50% vaccination. Additionally, added screening reduces the outbreak size for 90% vaccination but comparatively less so than for 50% vaccination.

For Figure 6(a) and (b), portions of outbreak burnout occurred for nearly every scenario. In Figure 6(a): Q with low risk had 58% burnout, Q with moderate risk had 6%, Q with high risk had 2%, Q/S with low risk had 98%, Q/S with moderate risk had 2%, and Q/S with high risk had 12%. In Figure 6(b): Q with low risk had 88%, Q with moderate risk had 16% Q with high risk had 0%, Q/S with low risk had 94%, Q/S with moderate risk had 16%, and Q/S with high risk had 10%.

One interesting point to note: our particular selections for (Q/S) interventions for 90% vaccination led to marginally higher outbreaks than for 50% vaccination as seen by comparing Figure 6(a) with Figure 6(b). It appears the effect of test screening becomes less significant above 50% vaccination. It is important to realize, however, that the severity of the infections will be much less for higher vaccination coverages as more individuals will follow the vaccinated pathway (Figure 2).

4. Discussion

Controlling the spread of COVID-19 has been an ongoing critical challenge for colleges and universities. Though most colleges required or encouraged their students to get vaccinated, many highly vaccinated colleges have experienced large scale COVID-19 outbreaks which in some cases have resulted in interruption of campuses in-person activities. University administrators are still wondering to what degree they should continue to implement non-pharmaceutical interventions and what are the most efficient control strategies.

To understand the disease dynamic on college campuses and help answer those questions, we developed an individual-based model (IBM) of COVID-19 transmission that accounts for heterogeneity in social interactions, disease progression, and control interventions. Since social mixing plays an important part in COVID-19 transmission, we considered two basic types of mixing typical for college communities: (i) scheduled contacts (classes and dorm residence), (ii) random contacts (e.g., dining and/or other forms of unstructured social activity). Once infected, each host undergoes a prescribed disease progression history, with a time-dependent infectivity pattern, viewed as a proxy for variable viral load during the course of infection. Such a computational framework allows us to generate and simulate more realistic college communities than standard SEIR models [10], and quantitatively assess the efficacy of different intervention strategies.

In our IBM setup, daily activities (class, dorm, and social mixing) take place in a suitable environment, and each environment is assumed to have an associated risk factor. These factors mitigate the probability of transmission (exposure risk) in a given environment, so they could represent site-specific control interventions (e.g., wearing facial masks, or providing clean contact space). Since these factors are highly uncertain and could vary in different colleges, we explore a range of choices of environmental risk factors, by taking three values (low, moderate, high) of each environmental risk factor (dorm, class, social mixing). Another control focus could be social activities (e.g. reduce class attendance or random social mixing). Our model setup can be easily adjusted to run such simulations.

We conducted an analysis with imperfect vaccination that allows infection transmission by the vaccinated pool. We considered 50% and 90% vaccination of the student body. In most cases, vaccination alone was not enough to prevent an outbreak, though it could significantly mitigate its size. The addition of symptomatic quarantine can have a large impact on outbreak reduction in lower vaccinated populations due to the larger prevalence of symptoms. We found that moderate frequency (every 3 weeks) random screening is effective in reducing outbreak size in all cases explored. The most important feature in all scenarios of vaccination and intervention is environmental/behavioral control measures (i.e., wearing facial masks in class, dorms, or at social events). These are required to ensure low environmental risk factors to mitigate disease spread.

We developed a flexible methodology and computational framework to generate and simulate college communities for a broad range of conditions including student body size, class schedules, et. al. While we chose students to attend three classes to illustrate our analysis here, our model allows for any class schedule with any class number and a more structured student body. The basic setup combines the social mixing component of the system and disease progression. The inputs can be easily modified for all components, and a wide range of COVID like pathogens can be simulated with this model, for synthetic college communities to derive robust prediction. Moreover, our methodology can be extended to other local community settings such as workplaces, primary and secondary schools, or hospitals.

Many additional topics could be explored by our IBM methodology, including assessment of environmental/behavioral risk factors and relative contributions of different transmission environments on disease outbreaks. Additionally, various other control measures not explored here such as contact tracing can be implemented with minor modification to the model.

Different outbreak measures can be explored, which we did not discuss. For instance, we can extract daily quarantine counts from the infection history over the outbreak period. This measure could provide some guidelines to the University administration on how many quarantine pool capacity rooms are needed to sustain an outbreak, and could also give a simple economic measure of outbreak impact and putative intervention.

Such assessment could guide effective intervention strategies. Our social mixing setup (scheduled and random) could be further expanded to account for more realistic intermediate levels of social connectivity. This work could also be extended to account for partial or dynamic vaccine schedules. Besides, since college campuses are often not isolated, we could extend the current model to couple college campus transmission to the local community.

Our analysis has implications for informing control strategies against COVID-19 on college campuses. The risk of COVID-19 outbreak could be efficiently controlled or mitigated using existing control measures. Our model shows that COVID-19 outbreaks may occur on college campuses regardless of their vaccination coverage. Our analysis suggests that the use of random screening and quarantine remains effective tools to mitigate and even prevent an outbreak even on highly vaccinated college campuses.

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Conflict of interest

The authors declare there is no conflict of interest.

References

1. Here's our list of colleges' reopening models. https://www.chronicle.com/article/heres-a-list-of-colleges-plans-for-reopening-in-the-fall
2. N. Ghorui, A. Ghosh, S. Mondal, M. Bajuri, A. Ahmadian, S. Salahshour, et al., Identification of dominant risk factor involved in spread of COVID-19 using hesitant fuzzy MCDM methodology, *Results Phys.,* **21** (2021), 103811. https://doi.org/10.1016/j.rinp.2020.103811
3. How colleges are dealing with high COVID case counts on campus. NPR Houston Public Media **2022**. Available from: https://www.npr.org/2022/01/23/1072730869/omicron-college-campuses-covid-outbreaks
4. Cornell University reports more than 900 Covid-19 cases this week. Many are Omicron variant cases in fully vaccinated students, CNN **2021**. Available from: https://www.cnn.com/2021/12/14/us/cornell-university-covid-cases/index.html
5. L. Rennert, C. McMahan, C. A. Kalbaugh, Y. Yang, B. Lumsden, D. Dean, et al., Surveillance-based informative testing for detection and containment of SARS-CoV-2 outbreaks on a public university campus: An observational and modelling study, *Lancet Child Adolescent Health,* **5** (2021), 428–436. https://doi.org/10.1016/S2352-4642(21)00060-2
6. L. Rennert, C. A. Kalbaugh, L. Shi, C. McMahan, Modelling the impact of presemester testing on COVID-19 outbreaks in university campuses, *BMJ Open,* **10** (2020), e042578. http://dx.doi.org/10.1136/bmjopen-2020-042578
7. A. Elbanna, G. N. Wong, Z. J. Weiner, T. Wang, H. Zhang, Z. Lui, et al., Entry screening and multi-layer mitigation of COVID-19 cases for a safe university reopening, *medRxiv* **2020**. https://doi.org/10.1101/2020.08.29.20184473
8. B. Lopman, C. Y. Liu, A. Le Guillou, A. Handel, T. Lash, A. Isakov, et al., A modeling study to inform screening and testing interventions for the control of SARS-CoV-2 on university campuses, *Sci. Rep.*, **11** (2021), 1–11. https://doi.org/10.1038/s41598-021-85252-z
9. H. L. Hambridge, R. Kahn, J. P. Onnela, Examining sars-cov-2 interventions in residential colleges using an empirical network, *Int. J. Infect. Dis.,* **113** (2021), 325–330. https://doi.org/10.1016/j.ijid.2021.10.008
10. R. Bahl, N. Eikmeier, A. Fraser, M. Junge, F. Keesing, K. Nakahata, et al., Modeling COVID-19 spread in small colleges, *PLoS One*, **16** (2021), e0255654. https://doi.org/10.1371/journal.pone.0255654

11. A. D. Paltiel, A. Zheng, R. P. Walensky, Assessment of SARS-CoV-2 screening strategies to permit the safe reopening of college campuses in the United States, *JAMA Network Open,* **3** (2020), e2016818-e. https://doi.org/10.1001/jamanetworkopen.2020.16818
12. K. A. Weeden, B. Cornwell, The small-world network of college classes: Implications for epidemic spread on a university campus, *Sociol. Sci.,* **7** (2020), 222–241. https://doi.org/10.15195/v7.a9
13. P. T. Gressman, J. R. Peck, Simulating COVID-19 in a university environment, *Math. Biosci.,* **328** (2020), 108436. https://doi.org/10.1016/j.mbs.2020.108436
14. R. Goyal, J. Hotchkiss, R. T. Schooley, V. De Gruttola, N. K. Martin, Evaluation of severe acute respiratory syndrome coronavirus 2 transmission mitigation strategies on a university campus using an agent-based network model, *Clin. Infect. Diseases,* **73** (2021), 1735–1741. https://doi.org/10.1093/cid/ciab037
15. B. Lopman, C. Liu, A. Le Guillou, A. Handel, T. Lash, A. Isakov, et al., A model of COVID-19 transmission and control on university campuses, *medRxiv* **2020**. https://doi.org/10.1101/2020.06.23.20138677
16. J. Mossong, N. Hens, M. Jit, P. Beutels, K. Auranen, R. Mikolajczyk, et al., Social contacts and mixing patterns relevant to the spread of infectious diseases, *PLoS Med*., **5** (2008), e74. https://doi.org/10.1371/journal.pmed.0050074
17. X. Ma, X. Luo, L. Li, Y. Li, G. Sun, The influence of mask use on the spread of COVID-19 during pandemic in New York City, *Results Phys.,* **2022**. https://doi.org/10.1016/j.rinp.2022.105224
18. G. Sun, S. Wang, M. Li, L. Li, J. Zhang, W. Zhang, et al., Transmission dynamics of COVID-19 in Wuhan, China: Effects of lockdown and medical resources, *Nonlinear Dynam.,* **2020**. https://doi.org/10.1007/s11071-020-05770-9
19. N.M. Ferguson, D. A. Cummings, C. Fraser, J. C. Cajka, P. C. Cooley, D. S. Burke, Strategies for mitigating an influenza pandemic, *Nature*, **442** (2006), 448–452. https://doi.org/10.1038/nature04795
20. J. M. Epstein, Modelling to contain pandemics, *Nature*, **460** (2009), 687. https://doi.org/10.1038/460687a
21. N. M. Ferguson, D. Laydon, G. N. Gilani, N. Imai, K. Ainslie, M. Begulin, et al., Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand, 2020.
22. D. K. Sewell, A. Miller, CDC MInD-Healthcare Program, Simulation-free estimation of an individual-based SEIR model for evaluating nonpharmaceutical interventions with an application to COVID-19 in the District of Columbia, *PLoS One,* **15** (2020), e0241949. https://doi.org/10.1371/journal.pone.0241949
23. H. Tian, Y. Liu, Y. Li, C. Wei, B. Chen, M. Kraemer, et al., An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China, *Science* **2020**. https://doi.org/10.1126/science.abb6105
24. Z. Du, X. Xu, Y. Wu, L. Wang, B. Cowling, L. A. Meyers, Serial interval of COVID-19 among publicly reported confirmed cases, *Emerg. Infect. Dis.,* **2020**. https://doi.org/10.3201/eid2606.200357
25. E. Bonabeau, Agent-based modeling: Methods and techniques for simulating human systems, *Proceed. Nat. Acad. Sci.,* **99** (2002), 7280–7287. https://doi.org/10.1073/pnas.082080899
26. W. T. Enanoria, F. Liu, J. Zipprich, K. Harriman, S. Ackley, S. Blumberg, et al., The effect of

contact investigations and public health interventions in the control and prevention of measles transmission: A simulation study, *PLoS One*, **11** (2016), e0167160. https://doi.org/10.1371/journal.pone.0167160

27. A. H. Auchincloss, A. V. Diez Roux, A new tool for epidemiology: The usefulness of dynamic-agent models in understanding place effects on health, *Am. J. Epidemiol.,* **168** (2008), 1–8. https://doi.org/10.1093/aje/kwn118
28. C. Wolfram, An agent-based model of covid-19, *Complex Systems,* **29** (2020).
29. Q. Huang, A. Mondal, X. Jiang, M. A. Horn, F. Fan, P. Fu, et al., SARS-CoV-2 transmission and control in a hospital setting: An individual-based modelling study, *Royal Soc. Open Sci.,* **8** (2021). https://doi.org/10.1098/rsos.201895
30. K. Azuma, U. Yanagi, N. Kagi, H. Kim, M. Ogata, M. Hayashi, Environmental factors involved in SARS-CoV-2 transmission: Effect and role of indoor environmental quality in the strategy for COVID-19 infection control, *Environ. Health Prevent. Med.,* **2020**. https://doi.org/10.1186/s12199-020-00904-2
31. M. Cevik, M. Tate, O. Lloyd, A. E. Maraolo, J. Schafers, A. Ho, SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: A systematic review and meta-analysis, *Lancet Microbe***, 2020**. https://doi.org/10.1016/S2666-5247(20)30172-5
32. M. A. Johansson, T. M. Quandelacy, S. Kada, V. Prasad, M. Steele, J. Brooks, et al., SARS-CoV-2 transmission from people without COVID-19 symptoms, *JAMA Network Open*, **4** (2021), e2035057-e. https://doi.org/10.1001/jamanetworkopen.2020.35057
33. X. He, E. H. Y. Lau, P. Wu, X. Deng, J. Wang, X. Hao, et al., Temporal dynamics in viral shedding and transmissibility of COVID-19, *Nat. Med.,* **26** (2020), 672–675. https://doi.org/10.1038/s41591-020-0869-5
34. P. Ashcroft, J. S. Huisman, S. Lehtinen, J. A. Bouman, C. L. Althaus, R. R. Regoes, et al., COVID-19 infectivity profile correction, *Swiss Med. Wkly.,* **150** (2020), w20336. https://doi.org/10.4414/smw.2020.20336
35. C. Fraser, S. Riley, R. M. Anderson, N. M. Ferguson, Factors that make an infectious disease outbreak controllable, *Proceed. Nat. Acad. Sci.,* **101** (2004), 6146–6151. https://doi.org/10.1073/pnas.030750610
36. M. Ebell, D. Forgacs, Y. Shen, T. Ross, C. Hulme, M. Bentivegna, et al., High prevalence of both previous infection with SARS-CoV-2 and persistent symptoms, *J. Am. Board Family Med.,* **2021**. https://doi.org/10.3122/jabfm.2022.03.210348
37. P. Poletti, M. Tirani, D. Cereda, F. Trentini, G. Guzzetta, G. Sabatino, et al., Association of age with likelihood of developing symptoms and critical disease among close contacts exposed to patients with confirmed SARS-CoV-2 infection in Italy, *JAMA Network Open*, **2021**. https://doi.org/10.1001/jamanetworkopen.2021.1085
38. D. Buitrago-Garcia, D. Egli-Gany, M. Counotte, S. Hossmann, H. Imeri, A. Ipekci, et al., Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis, *PLoS Med.,* **2020**. https://doi.org/10.1371/journal.pmed.1003346
39. S. Malhotra, K. Mani, R. Lodha, S. Bakhshi, V. Mathur, P. Gupta, et al., COVID-19 infection, and reinfection, and vaccine effectiveness against symptomatic infection among health care workers in the setting of omicron variant transmission in New Delhi, India, *Lancet Regional Health,* **2022**.

https://doi.org/10.1016/j.lansea.2022.100023
40. H. Tseng, B. Ackerson, Y. Luo, L. Sy, C. Talarico, Y. Tian, et al., Effectiveness of mRNA-1273 against SARS-CoV-2 Omicron and Delta variants, *Nat. Med.,* **28** (2022), 1063–1071. https://doi.org/10.1038/s41591-022-01753-y
41. N. Andrews, J. Stowe, F. Kirsebom. S. Toffa, T. Rickeard, E. Gallagher, et al., Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) Variant, *N Engl. J. Med.,* **386** (2022), 1532–1546. https://doi.org/10.1056/NEJMoa2119451

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