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MAJOR ARTICLE

Assessment of the Effectiveness of Omicron Transmission Mitigation Strategies for European Universities Using an Agent-Based Network Model

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Background. Returning universities to full on-campus operations while the coronavirus disease 2019 pandemic is ongoing has been a controversial discussion in many countries. The risk of large outbreaks in dense course settings is contrasted by the benefits of in-person teaching. Transmission risk depends on a range of parameters, such as vaccination coverage and efficacy, number of contacts, and adoption of nonpharmaceutical intervention measures. Owing to the generalized academic freedom in Europe, many universities are asked to autonomously decide on and implement intervention measures and regulate on-campus operations. In the context of rapidly changing vaccination coverage and parameters of the virus, universities often lack sufficient scientific insight on which to base these decisions.

Methods. To address this problem, we analyzed a calibrated, data-driven agent-based simulation of transmission dynamics among 13 284 students and 1482 faculty members in a medium-sized European university. Wed use a colocation network reconstructed from student enrollment data and calibrate transmission risk based on outbreak size distributions in education institutions. We focused on actionable interventions that are part of the already existing decision process of universities to provide guidance for concrete policy decisions.

Results. Here we show that, with the Omicron variant of the severe acute respiratory syndrome coronavirus 2, even a reduction to 25% occupancy and universal mask mandates are not enough to prevent large outbreaks, given the vaccination coverage of about 85% reported for students in Austria.

Conclusions. Our results show that controlling the spread of the virus with available vaccines in combination with nonpharmaceutical intervention measures is not feasible in the university setting if presence of students and faculty on campus is required.

Keywords. COVID-19; modeling; Prevention; network; agend-based.

Many universities face increasing pressure to return to full on-campus operations, while the incidence of coronavirus disease 2019 (COVID-19) is still high. A range of simulation studies have tried to assess the transmission risk and effectiveness of nonpharmaceutical intervention measures (NPIs) in the university context, but these studies have a number of shortcomings that limit their applicability to decision making in universities. Only a small number of studies have considered NPIs in the context of vaccination coverage [1–3], and none to our knowledge have considered a situation in which the Omicron variant is dominant. A few studies have based their models on empirically determined contact networks but did not calibrate transmission dynamics against empirical data [4–6] or used small networks [4, 7, 8].

Studies that calibrate their model parameters against empirically observed outbreaks in educational settings [9–11] use simulation parameters based on virus variants that are no longer dominant. In addition, existing studies focus on residential colleges and model contacts in both classrooms and student housing. These studies have only limited applicability to the European higher education sector, where students tend to live spread out in the university's city. As a consequence, COVID-19 prevention policies adopted by European universities have no power to limit social contacts of students outside university premises. To our knowledge, no existing study combines an empirically determined colocation network with a rigorous calibration of model parameters and simulation scenarios that are relevant for current decision making processes where the Omicron variant is dominant.

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To remedy these shortcomings, we modeled transmission dynamics in a medium-sized European university (Graz University of Technology [TU Graz]) with 13 284 students and 1482 faculty members. We based our simulation on an empirically determined colocation network reconstructed from enrollment data from the last term with full on-campus operations (winter 2019–2020). At this writing, 85% of TU Graz students have been vaccinated [12]. Based on this high vaccination coverage among students, we investigated whether the university could return to full on-campus operation without risking large outbreaks, even in a situation where the Omicron variant is dominant, as was the case in January 2022.

METHODS

Colocation Network

We used course enrollment data—lectures, exercises, and examinations (called "events")—from 1 October 2019 to 28 February 2020 to construct the colocation network including students and faculty at TU Graz. The data included a total of 752 courses with several dates and 1209 examinations. This resulted in a total of 29 547 unique events at which students and faculty met. Two students enrolled in the same event were assumed to have contact with each other and the responsible lecturers. If more than a single lecturer was responsible for an event, they were also assumed to have contact with each other. The resulting colocation network includes 13 284 students and 1482 lecturers. See extended methods in the supporting information (Supplementary Materials) for additional details.

Agent-Based Model

We simulate the infection dynamics in the university, using an agent-based model with students and lecturers as agents. The model couples in-host viral dynamics with population dynamics. Depending on the viral load over the course of an infection, each agent is in 1 of 5 states: susceptible, exposed, infectious, recovered, or quarantined, as shown in Figure 1 [13]. In addition, after the presymptomatic phase, agents can stay asymptomatic or become symptomatic. Every agent has an individual exposure duration, l, incubation time, m, and infection duration, n. For every agent, we draw values for l, m, and n from Weibull distributions specified by their mean and standard deviation (SD), ensuring that $1 \leq m \leq n$.

These constraints lead to left-truncated distributions for the parameters with different means and SDs. To address this, we choose the mean and SD of the distributions before truncating, such that the difference between the effective mean and SD and the values reported in the literature are minimal (for details, see the Supplementary Materials). Specifically, we aim at an effective mean (SD) incubation time of 3 (1.9) days [14, 15] and a mean exposure duration of 2 (1.9) days, adapted from the original severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strain [16–18], accounting for the shorter incubation time of Omicron. Because to our knowledge no information about the infection duration of Omicron is available yet, we aim for a mean (SD) infection duration of 10.91 (3.95) days, as reported for the original strain [13, 19].

Infections are introduced into the university through a single, randomly chosen agent. This source case starts in the exposed state on day 0 of the simulation. All other agents start in the susceptible state. Recovered agents are assumed to be completely immune to reinfection.

Transmissions

During every interaction, an infected agent can transmit the infection to the agents they are in contact with (specified by the colocation network). Transmission is modeled as a Bernoulli trial with a probability of success, p. This probability is modified by several NPIs and biological mechanisms, q_i. Here, we consider 5 such mechanisms: the modification of the transmission risk due to the infection progression (q_1), not having symptoms q_2, mask wearing of the transmitting and receiving agent (q_3 and q_4, respectively), and immunization (q_5). Therefore, the probability of a successful transmission is given by the base transmission risk, β, modified by the combined effect of the q_i:

$$p = 1 - [1 - \beta \prod_{(i=1)}^{5} (1 - q_i)].$$

The modification of transmission risk due to a changing viral load over the course of an infection, q_1, is modeled as a trapezoid function that depends on the time an agent has already been exposed to the virus, t, given the exposure duration, l, incubation time, m, and infection duration, n, of the infected agent:

$$q_1(t) = \begin{cases} 0 & \text{if} \quad l < t < m \\ 1 - \dfrac{(t-m)}{(n-m+1)} & \text{if} \quad t > m \wedge t < n \\ 1 & \text{else} \end{cases}.$$

If an agent does not show symptoms, transmission risk is reduced by 40% (q_2).

The base transmission risk β is calibrated to reflect the observed transmission dynamics in Austrian secondary schools, following Lasser et al [20], which we assume to be similar to the university context (see Supplementary Materials for details). The calibration data were recorded in the same season that our simulation applies to (European autumn and winter), removing the need to include a seasonal effect. Calibration results in a transmission risk of 2.8% for a university contact for the original virus strain. We adjust this transmission risk to match the Omicron variant, which is about 3 times as transmissible as the Delta variant [21], which itself is about 2.25 times as transmissible as the original strain [22, 23]. This results in a transmission risk of 18.7% per contact for unvaccinated agents in a university setting. This is within the range of reported

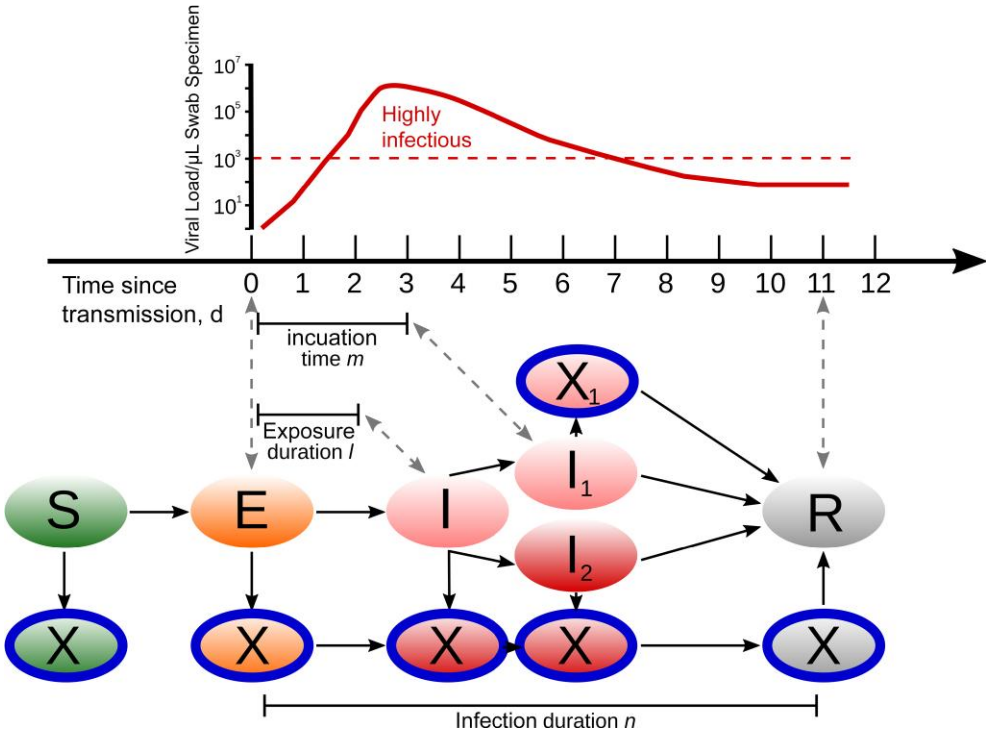

Figure 1. Agents in the epidemiological model can be in the states (displayed as ellipses) susceptible (S), exposed (E), infectious (I), infectious without symptoms (I_1), infectious with symptoms (I_2) and recovered (R). Possible state transitions are shown by black arrows. In each of these states, agents can also be quarantined (X), preventing them from interacting with other agents. Transitions between states follow the development of the viral load in the host sketched above, reproduced from Walsh et al [13].

secondary attack rates for Omicron of 10.1%–38% in the literature [24–27].

Intervention Measures

In all simulations, on developing symptoms, agents are immediately isolated for 10 days. There are no additional contact tracing and quarantine measures for contacts of the infected agent in place. This reflects the situation currently prevalent in many European countries: vaccinated people or people who were wearing a mask during the contact are considered only low-risk contacts and are not quarantined. If additional contact tracing measures are introduced, all contact persons will be quarantined for 10 days 2 days after the infected agent showed symptoms. This reflects the delay in contact tracing efforts caused by the time it takes for a test result to arrive and to reach contact persons.

For every event location, the seating capacity of the room is known. If occupancy is 100%, all students enrolled in a given event are allowed to attend the event, even if the number of enrolled students surpasses the seating capacity. If occupation is reduced to 50% (or 25%), students are picked at random and removed from the contact network until 50% (or 25%) of the seating capacity is reached.

If masks are mandated, all students and lecturers wear masks, which reduces the probability of transmission by 50% if only the infected agent wears a mask (q_3) and by 30% if only the receiving agent wears a mask (q_4). If both agents wear a mask, transmission risk is reduced by 65%. This models the reduction of transmission risk for surgical masks [28], in line with a 2021 review on mask effectiveness [29].

At the beginning of a simulation, 85% of students and lecturers are chosen at random and assigned a "vaccinated" status. This includes immunity from previous infection with other variants of the virus but assumes a population naive to infection with the Omicron variant, as was the case in Austria in October 2021. Being vaccinated reduces an agent's chance of becoming infected. Because vaccination effectiveness against infection greatly depends on the number of vaccination doses [30, 31] and wanes with time [32], we model different levels of vaccine effectiveness (q_5). For the Delta variant, the viral load of vaccinated people was similar to that of unvaccinated people [33]. To our knowledge, similar data do not yet exist for Omicron. We therefore do not assume a lower infectiousness of infected vaccinated agents. Vaccination status and effectiveness do not change throughout the simulation.

RESULTS

We developed an agent-based model to simulate transmission dynamics on a colocation network determined by the interactions of students and faculty at TU Graz. We assume a

vaccination coverage of 85% among students and staff [12]. We study 3 lecture hall occupancy levels (100%, 50%, and 25%) and 2 masking mandate options (no masks or masks), as well as different vaccine effectiveness against infection (0%, 30%, 50%, and 70%). We report distributions of the mean outbreak size (number of infected individuals minus the source case) for 1000 simulations for each scenario. Figure 2*A* shows the distribution of outbreak sizes for different NPI combinations at a vaccination effectiveness level of 50%—an optimistic estimate after 2 doses of the BNT162b2 or mRNA-1273 vaccines [30]. Figure 2*B* shows the distribution of outbreak sizes for different vaccination effectiveness levels at 25% lecture hall occupancy with masks.

In addition to outbreak sizes, we calculate the average number of secondary infections caused by each agent over the course of their infectious period, R_{eff}. For our agent-based model, R_{eff} is calculated as an individual-based measurement and averaged over all infected individuals in a given simulation, following Breban et al [34]. Owing to the finite size and heterogeneity of the contact network, R_{eff} varies over time. In our simulations most outbreaks do not last longer than 100 days (time steps), and after this time R_{eff} has converged to a stable value (see Supplementary Materials). We therefore report R_{eff} averaged over the first 100 time steps of the simulation. Distributions of R_{eff} for the 6 scenarios are shown in Figure 3.

If we assume a vaccination effectiveness of 50% at a vaccination rate of 85%, with 100% lecture hall occupancy and no masking mandate, the mean outbreak size is 6713 (95% credible interval, 0–11 181) (95% credible interval [CrI]) with an R_{eff} of 2.0 (.0–3.4).The maximum observed outbreak size is 11 270. In 36.0% of the simulation runs, the source cases does not infect another person. If both students and lecturers wear masks, the mean outbreak size is reduced to 3342 (95% CrI, 0–8202), and the maximum observed outbreak size is 8335, with an R_{eff} of 1.2 (.0–3.0). On the other hand, if no mask mandate is implemented but instead lecture hall occupancy is reduced to 50%, the mean outbreak size is 4183 (95% CrI, 0–9561), with an R_{eff} of 1.4 (.0–3.1).

In a maximum mitigation scenario, if occupancy is reduced to 25% and masks are mandated, mean outbreak sizes are reduced to 4 (95% CrI, 0–29), with an R_{eff} of 0.4 (.0–2.9),

with a maximum observed outbreak size of 517, while 77.3% of the source cases do not lead to another transmission. This shows that even if with an average R_{eff} of <1, very large outbreaks are still possible. If 95% instead of 85% of the population are vaccinated, outbreak sizes do not substantially change: on average, 6949 (95% CrI, 0–11 148) people are infected with 100% occupancy and no masks, 4290 (0–9494), with 50% occupancy and no masks, and 5 (0–52) with 25% occupancy and masks. If vaccine effectiveness is assumed to be 70%—a value that is not realistic with current vaccines against Omicron—in the maximum mitigation scenario the mean outbreak size drops to 1 (95% CrI, 0–7), with a maximum observed outbreak size of 115 and an R_{eff} of 0.3 (.0–2.4). With a vaccine effectiveness of 90%, occupancy could be increased to 50% (while still mandating masks), resulting in a mean outbreak size of 1 (95% CrI, 0–13), with an R_{eff} of 0.3 (.0–3.0) and a maximum observed outbreak size of 55.

Our simulations assume testing and isolation of agents as soon as they show symptoms. If additional contact tracing and quarantine measures are introduced, outbreak sizes are slightly reduced, which is consistent with previous findings [8]: with 100% occupancy and no masks, on average 6634 (95% CrI, 0–11 177) agents are infected. With 50% occupancy and no masks, the outbreak size is 4182 (95% CrI, 0–9561); with 25% occupancy and masks, it is 4 (0–25). On average, this causes 0.22 quarantine days per student and 0.15 quarantine days per lecturer.

DISCUSSION

Decreasing lecture hall occupancy to 50% or 25% and imposing masking mandates are 2 of the most widespread NPIs to control the spread of COVID-19 adopted by universities (see for example [35]). Frequent preventive testing is another NPI frequently implemented in institutions, which our group investigated in 2 studies in schools [20] and nursing homes [36], using the same simulation framework. With the widespread adoption of so-called 3G entry rules in Austria, by which students and faculty have to be vaccinated, recently tested, or recovered from a SARS-CoV-2 infection, frequent preventive testing of students has become less desirable, especially given its high cost and implementation complexity. We therefore think that decreasing lecture hall occupancy and mandating masks are the only 2 feasible NPI options that universities can implement.

It is hard to define what an *acceptable* size is for an outbreak, because this depends on many factors, such as the likelihood of causing a severe outcome or long-term damage as well as current hospital and intensive care occupation. The decision as to what constitutes too large a burden for a society is ultimately a political one. We therefore refrain from defining a fixed outbreak size that is acceptable and rather report results for different scenarios.

Our findings suggest that, even in a maximum mitigation scenario with only 25% occupancy and a mask mandate, very large outbreaks that reach >500 people can occur. If the goal is to prevent virus transmission within university premises this is likely not acceptable for university leadership. Given high rates of community transmission, many introductions of the virus in the university setting are to be expected and the occurrence of large outbreaks cannot be ruled out. Because vaccines with a higher effectiveness against infection with the Omicron variant are not available yet, this leaves universities with few options: if the presence of students and faculty on the university campus is a priority, large outbreaks are likely to be unavoidable.

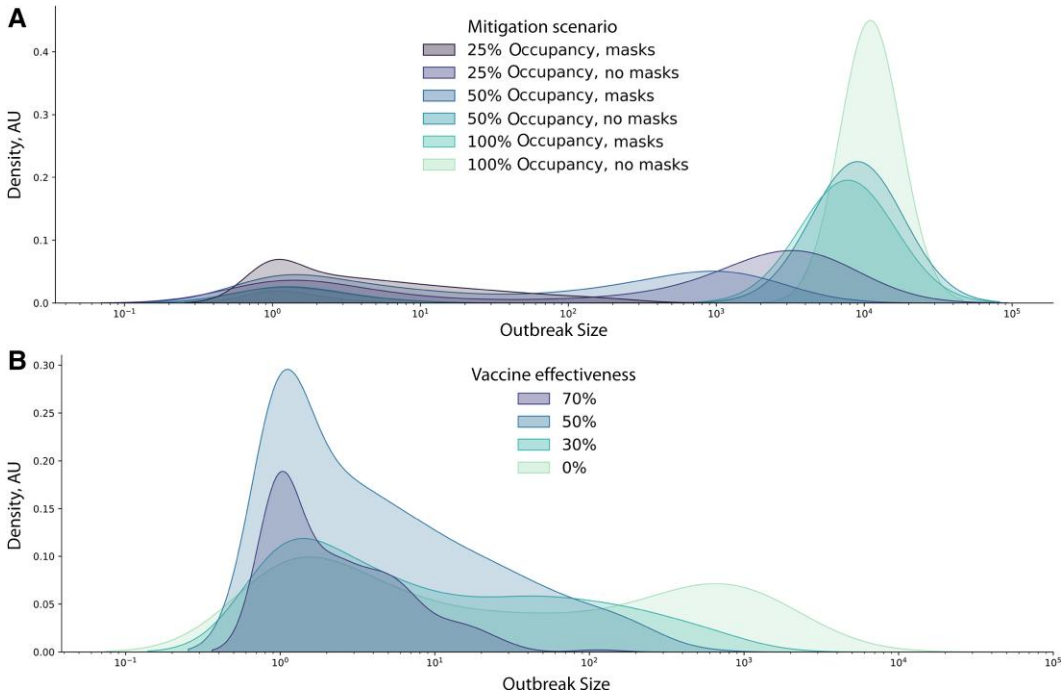

Figure 2. Kernel density estimation of the distribution of outbreak sizes for different mitigation scenarios at a vaccination efficacy against infection of 50% (*A*) and different vaccination effectiveness levels at 25% occupancy with masks (*B*). Distributions show outbreak sizes for 1000 simulation runs where the source case infected ≥1 other agent. Simulation runs where the source case did not cause a secondary infection are excluded. Abbreviation: AU, arbitrary units.

If the prevention of outbreaks is a priority, conducting courses in presence is not a feasible option. If, on the other hand, vaccines with a higher effectiveness become available, our simulations indicate that a high vaccination rate in combination with NPIs can effectively prevent large outbreaks. We note that in an earlier draft version of the present publication, published as a preprint in November 2021 [37], we came to very different conclusions, that is, that minimal NPIs were sufficient to prevent large outbreaks. This was based on the then-dominant Delta strain of the virus. The very high transmissibility of Omicron changed the outbreak dynamics completely. This comparison of results shows the importance of model calibration and adaptive strategies to the spreading of the virus, where oversimplifications of the spreading dynamics lead to misleading predictions.

Because our model rests on a set of assumptions, an analysis of its shortcomings and the uncertainties associated with these assumptions is warranted. Our model does not include contact situations apart from courses on the university premises. This is a deliberate choice: including such contacts would correspond to multiple concurrent introductions of the infection into the university network, which would further increase the number of transmissions in the university context. Since even without the inclusion of such contacts outbreak sizes are already large, we do not think that adding such contacts would add additional information to our study, while it would introduce a number of additional assumptions to our model. We note that, owing to this assumption, the outbreak sizes reported here are a lower bound to the outbreak dynamics that are to be expected. We base our contact network on enrollment data of students for courses. Not all students that enroll in a given event show up, as there often is no mandatory attendance, especially under the current circumstances. The density of the contact network used in our simulation in the case of 100% occupancy is therefore an upper bound of the number of contacts caused by the courses organized by the university.

Since students are on average young (currently 27 years old in Austria [38]) and have had to wait longer for their first and second vaccine doses in many national vaccination schemes, they will most likely have had their second dose during the summer, and most will not have had a booster shot yet. We assume the vaccine effectiveness against infection to be 50% for most of our scenarios. This number was reported by Tartof et al [32] for the BNT162b2 vaccine 4-5 months after the second dose and against the Delta strain of the virus. Vaccine effectiveness against Omicron is still being evaluated at the point of writing, but we assume that 50% effectiveness is very optimistic, as Omicron has demonstrated significant immune escape capabilities [39]. If the vaccination effectiveness is assumed to be lower, outbreak sizes increase even further. To account for this uncertainty, we simulated the different mitigation scenarios for different levels of vaccine effectiveness. Therefore, our results should still be applicable once more effective vaccines become available in the future.

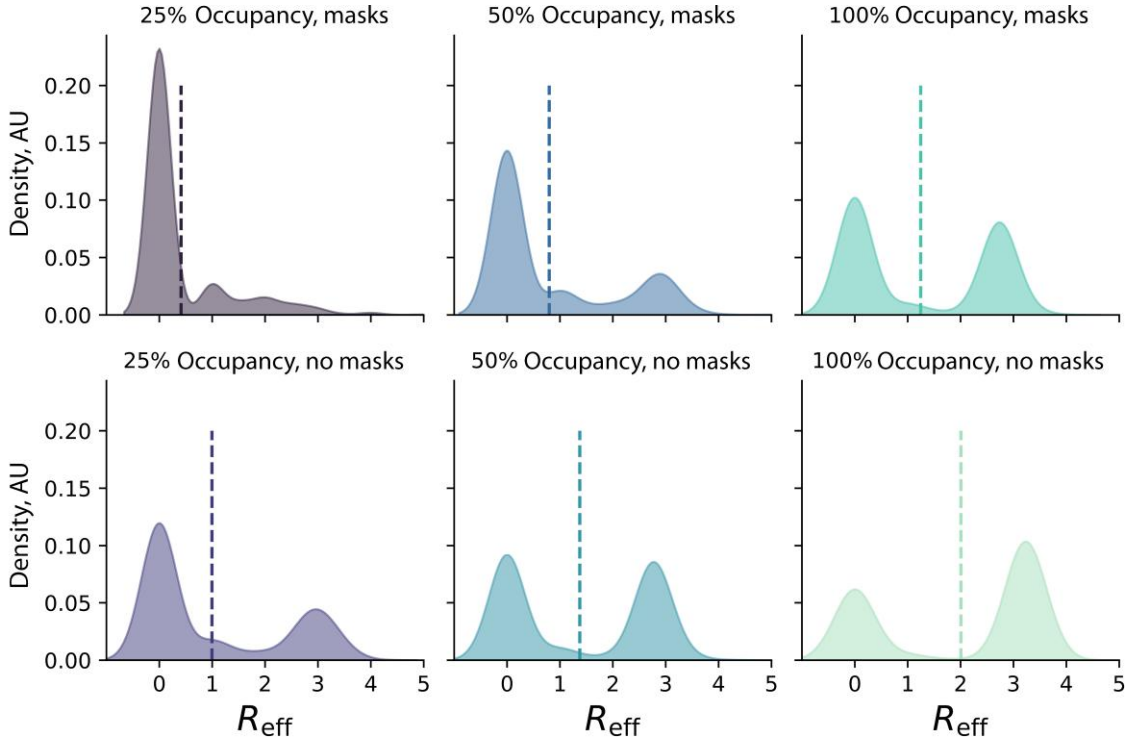

Figure 3. Kernel density estimation of the distribution of R_{eff} for different mitigation scenarios at a vaccination efficacy against infection of 50%. Dotted lines denote the average of R_{eff} in each scenario. Distributions show outbreak sizes for 1000 simulation runs where the source case infected ≥1 other agent. Abbreviation: AU, arbitrary units.

We calibrated our model using empirical observations of distributions of cluster sizes in Austrian secondary schools in autumn 2020 [20]. University students tend to have sparser schedules than students in secondary schools, resulting in an overall decreased duration of contact time between people. On the other hand, the space available per student in university lecture halls is on average smaller than for students in secondary schools (see Supplementary Materials for details). It is hard to quantify the difference in contact intensity that the difference in contact duration and proximity introduce. Nevertheless, the differences act in different directions and are expected to at least partially cancel each other. We therefore think it is warranted to assume that contact situations in universities and secondary schools are similar enough to use the available data on outbreaks in school settings to calibrate our simulation for an application in the university context.

Overall, our study assessed the 2 most common policies to curb the spread of SARS-CoV-2 in European universities: reduction of occupancy and mask mandates, in the context of high vaccine coverage and a dominant high transmissibility variant (Omicron). We found that—given the currently reported vaccination rates among students of ≥85% and an assumed optimistic vaccination effectiveness against infection of 50%—even a maximum mitigation scenario with 25% occupancy combined with a mask mandate for students and lecturers is not enough to prevent large outbreaks.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Data archival. The simulation code is published as Python package, version 1.4.2 (https://pypi.org/project/scseirx/). The code used to simulate the transmission dynamics at TU Graz is available at https://github.com/JanaLasser/uni_SEIRX. Data used to calibrate the model are available at https://doi.org/10.17605/OSF.IO/UPX7R, along with contact networks and simulation results.

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