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Title: Evaluation of SARS-CoV-2 transmission mitigation strategies on a university campus using an agent-based network model

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Running Title: SARS-CoV-2 modeling on a university campus

Summary: An agent-based network SARS-Cov-2 transmission model among university campus populations was developed to inform the UC San Diego Return to Learn program. It provides a data-driven approach to inform adaptive decision-making surrounding campus mitigation efforts.

ABSTRACT

Background: Universities are faced with decisions on how to resume campus activities while mitigating SARS-CoV-2 risk. We used an agent-based network model of SARS-CoV-2 transmission to assess the potential impact of strategies to reduce outbreaks at the University of California San Diego (UC San Diego).

Methods: We developed a SARS-CoV-2 transmission model that incorporates important features related to risk at UC San Diego, such as community composition (staff, faculty, and students on or off campus), campus residential configuration, and course registration. We investigated the relative impact of the following strategies: campus housing de-densification, class size caps and hybrid instruction, isolation and contact tracing, masking and social distancing, and asymptomatic testing (monthly to twice weekly) with tests of varying sensitivity. Outcomes examined are: basic reproduction number (R0), average/maximum outbreak size, cumulative infections and hospitalizations, and peak isolation housing.

Results: We found that structural interventions for housing (doubles to singles only) and instructional changes (from in-person to hybrid with class size caps) can substantially reduce R0, but masking and social distancing are required to reduce this to at or below 1. Within a risk mitigation scenario, increased frequency of asymptomatic testing from monthly to twice weekly has minimal impact on average outbreak size (1.1-1.9), but substantially reduces the maximum outbreak size and cumulative number of cases.

Conclusions: Our model provides a quantitative framework to inform adaptive strategies to reduce SARS-CoV-2 risk and transmission within universities. An interdependent approach incorporating risk mitigation, viral detection, and public health intervention is required to mitigate risk.

Keywords: COVID-19, prevention, modeling

INTRODUCTION

In order to mitigate the spread of SARS-CoV-2 and enhance the safety of their students, staff, and faculty, higher educational institutions are considering a number of strategies, including adjusting on-campus living arrangements, limiting the maximum number of students in a class, and conducting large-scale asymptomatic testing. As universities and colleges develop reopening policies, there is a need to provide guidance on the potential impact of each COVID-19 mitigation strategy separately as well as in combination when multiple modalities are under study.

In advance of the Fall term in 2020, UC San Diego launched the Return to Learn program, which incorporates three interdependent pillars to reduce the risk of SARS-CoV-2 on campus: risk mitigation, viral detection, and public health intervention. Risk mitigation strategies include masking [1-3], social distancing [1], sanitation, and ventilation [4], along with structural interventions such as reducing density of individuals in research and residential campus buildings as well as offering hybrid and remote class instruction, with limits to class size. Viral detection strategies incorporate symptomatic and asymptomatic testing along with other measures to detect outbreaks early such as wastewater and other environmental (e.g. surfaces and air filter) monitoring. Public health interventions include traditional case notification, isolation, contact tracing [5], and quarantine activities, along with digital exposure notification technologies [6]. The Return to Learn strategy is multi-pronged and adaptive, with the intention to revise the strategy as more data arise.

A key feature of the UC San Diego Return to Learn program is its foundation on a data-driven quantitative framework. To guide this program and inform campus decisions related to relative benefits of particular risk mitigation, viral detection, and public health intervention strategies at UC San Diego, we developed an agent-based model (ABM) that simulates SARS-CoV-2 transmission among a university campus population (of students, faculty, and staff); ABMs are ideal for informing policy decisions that influence complex social systems—such as the spread of infectious diseases in a population—as they incorporate interactions among individuals [7]. The model incorporates on- and off- campus residential information, and course schedule data. We used this model to investigate the relative impact of the following strategies in isolation or combined: campus housing de-densification, and classroom caps and hybrid instruction, asymptomatic testing with various test sensitivities, masking and social distancing, as well as isolating positive individuals, tracing their contacts, and quarantining these contacts.

METHODS

Agent-based network transmission model

Model Structure: The ABM consists of four primary components: (1) the UC San Diego population, (2) structure of contacts among members of the population, (3) transmission of SARS-CoV-2, and (4) disease progression of COVID-19. Below we provide further details for each of these components.

UC San Diego populations: The initial model population includes 38,798 students (30,285 undergraduates and 8,513 graduates) who live either on or off campus, as well as an estimated 8,000 faculty and staff who will work on campus in Fall 2020 (the remainder of faculty/staff are working remotely and are not incorporated into our model). Prior to the implementation of structural interventions, approximately 51% of students live in on-campus housing; the remaining students live off-campus along with staff and faculty. Each on-campus student is assigned a room in a UC San Diego residential hall based on their undergraduate or graduate student status. The number of rooms and their occupancy for each residential hall was based on UC San Diego housing data. Bedrooms reside in suites, where groups of bedrooms may share a bathroom and common area. Based on status as undergraduate or graduate student, each student was assigned classes using UC San Diego's Fall 2019 class registration or alternative instructional scenarios detailed below. Faculty were each assigned to teach one class.

Contact structure: The structure of a contact network—the set of contacts within a population capable of spreading SARS-CoV-2—can have profound effects on both the spread of infectious disease and the effectiveness of control programs [8-12]. The structure of the contact network differs between students living on- compared to off-campus. For on-campus students, there are three components of the contact network: (1) residential, (2) classrooms, and (3) campus encounters (contacts outside of residence and classrooms).

The contacts within on-campus residences are modeled such that on-campus students have connections with their roommates, suite-mates, and building-mates. Students also have contacts with other students in classrooms. Both the residential and classroom contact networks are static, meaning that the network does not change (i.e., no contacts are formed or dissolved) during the simulation. By contrast, the campus encounters network is dynamic; that is, relationships form and dissolve daily. The number of daily campus contacts for each individual follows a negative binomial distribution ($r = 5$, $p = 0.1$). Figure 1 illustrates the contact network for an on-campus student.

Due to lack of data, we do not explicitly simulate the residential contact network for off-campus students; off-campus students (along with faculty and staff) have a daily rate of becoming infected due to outside community interactions. Off campus students with in--person classes have associated classroom network interactions, and all students are assumed to have campus population encounters.

<u>SARS-CoV-2 Transmission:</u> Transmissions among students, staff, and faculty occur through interactions defined by the contact network. The rate of SARS-CoV-2 transmission depends upon the type of contacts. For contacts within a residence, the probability of transmission is highest among roommates, decreases for individuals who are only suite-mates, and is lowest between individuals who are solely building-mates. In order to set these transmission probabilities, we used secondary attack rates measured for varying contact rates, which we denote as frequent, moderately frequent, and rare [13]. Specifically, we assumed that

roommates have a secondary attack rate proportional to frequent contact rates. We assumed that secondary attack rates associated with suite (outside the room) and building (outside the suite) contacts are proportional to moderately frequent and rare contacts. We scaled these reported rates to generate a basic reproduction number (R0) similar to other university models [14].

For classroom contacts, the probability of transmission is the same for all individuals enrolled in a given in-person course and set as the mid-point between the secondary attack rates for moderately frequent and rare contacts. The probability of transmission is constant for on-campus interactions and based on the secondary attack rates for rare contacts. The background daily incidence rate in the community was set at 15 per 100,000, informed by our county-level transmission models which estimated the true case rate at roughly 2-3 fold the observed case rate due to asymptomatic transmission and undiagnosed infection [15].

<u>Disease progression:</u> The model simulates an individual's progression through seven stages of COVID-19 infection: (1) uninfected, (2) incubation period, (3) infectious but asymptomatic, (4) infectious with symptoms, (5) hospitalized, (6) recovery, and (7) death. Figure 2 depicts these stages and possible transition pathways.

The model allows individuals to transition between stages in daily increments. The daily probability of an exposed person with SARS-CoV-2 transitioning from Stage 2 to Stage 3 (that is, being asymptomatic but infectious) follows a geometric distribution with mean 4.6 days [16].

Once individuals enter into Stage 3, they can recover (Stage 6), develop symptoms (Stage 4), or remain in Stage 3. Approximately 70% of individuals are asymptomatic for the entire duration of their infection; a study of university students and employees reported 65.9% of individuals who tested positive reported no symptoms when they were tested [17], which is on average 14 days [18]. The remaining fraction eventually develop symptoms, which define transitions to Stage 4. Individuals in Stage 4 can recover (Stage 6), require hospitalization (Stage 5), or remain in Stage 4. Death can only occur during hospitalization. Transition probabilities associated with hospitalization and death are conditional on age.

Simulated interventions

Risk mitigation: To investigate the impact of risk mitigation interventions, we assessed four scenarios with varying housing, instructional, and behavioral characteristics.

- **Double housing occupancy and in-person class instruction with no class size cap (DI)**. This scenario assumes on-campus residents reside in doubles or singles and the university has all instruction in-person without a class size limit (based on 2019 enrollment data).
- **Double housing occupancy and in-person class instruction with a class size cap (DI-Cap).** Similar to DI, except that the maximum class size is capped at 50.
- **Single housing and hybrid instruction with in-person class size cap (SH-Cap).** This scenario assumes on-campus residents reside only in singles and instruction is mostly

remote (12% of sections in-person) with a maximum class size capped at 50 for in-person classes. In this scenario, we assume that students who are unable to be accommodated with on campus housing would instead reside off campus.

- **Single housing and hybrid instruction with in-person class size cap and behavioral intervention with masking and social distancing (SH-Cap-Mask).** Here we implement the same structural interventions as SH-Cap, but additionally assume that students wear masks and socially distance everywhere except within their bedrooms, leading to an effective reduction in transmission of 50%.

Isolation and quarantine: We assume that diagnosed individuals adhere to isolation recommendations and move to on-campus isolation housing (if on-campus residential students) or isolate in their own residences (if off-campus students, faculty, or staff). We assume that individuals who are isolating are not at risk of transmission to others in the UC San Diego community.

For all confirmed positive students, we simulate contact tracing efforts as performed by the public health team. In the simulation, we assume contact tracing will identify close contacts among an infected individual's room- and suite- mates, as well as students in their classroom who sit adjacent to them based on an assumed grid sitting assignment. Students who are close contacts are assumed to adhere to quarantine (and are offered quarantine housing on campus), therefore we assume those who are in quarantine are not at risk of transmission to others during this period. If any of the close contacts are confirmed to have SARS-CoV-2 and are an on-campus resident, they will be relocated to isolation housing and their contacts will be traced.

Asymptomatic testing: We simulate entry testing at the start of term as planned by UC San Diego. All students are tested on residential move in (two weeks prior to the start of classes) and again on day 12. Off-campus students are required to test before the start of classes. After the start of classes, individuals with in-person classes or who reside on-campus (referred to as campus testing) will be tested at differential rates compared to individuals with no in-person classes or a non-resident (referred to as non-campus testing). We investigated on-campus testing rates of monthly, every 2 weeks, every week, 2x weekly. We assumed that non-campus populations will test monthly.

Model outcomes

We assess the basic reproduction number (R0), outbreak size (number of linked infections per each viral introduction), peak isolation housing, and cumulative hospitalizations and infections across an 80-day term.

RESULTS

Structural interventions such as hybrid instruction, class size caps, and de-densification of housing can substantially reduce the R0 on campus (Figure 3). With doubles and in person instruction (DI), the R0 is 6.2, whereas implementing a class size cap of 50 reduces this to 3.6

(DI-Cap), which is further reduced to 2.7 for singles with hybrid instruction (SH-Cap). The SH-Cap-Mask scenario indicates that masking and social distancing is important in reducing the R0 further; for instance, to 1.3 if these interventions reduce transmission by 50%. Reducing R0 to below 1 likely requires strict adherence to masking and social distancing guidelines.

These interventions similarly have a strong impact on reducing the number of individuals infected for each viral introduction (defined as the outbreak size). As shown in Figure 4, the average outbreak size could exceed 60 with the DI scenario, halving to below 30 for the DI-Cap, and further reducing to below 20 for SH-Cap. Masking and social distancing dramatically reduce the average outbreak size, leading to an average outbreak size of 1.4 for the SH-Cap-Mask scenario.

Variations in asymptomatic testing frequency (from monthly to twice-weekly) had relatively little impact on average outbreak size assuming a SH-Cap-Mask scenario, ranging from 1.9 to 1.1 (Figure 5a). However, despite the small size of the large majority of outbreaks (<10 infections, Figure 5b), a small number of outbreaks could be large (>20); there was more of an effect of asymptomatic testing on maximum outbreak size. The maximum outbreak size was predicted to be 158 (95% interval 45-345) with monthly testing in the SH-Cap-Mask scenario, reducing to 65 (16-142) for every 2 weeks testing, 14 (7-29) with every week testing, and 7 (5-13) with twice weekly testing (Figure 5c).

Under the SH-Cap-Mask scenario, the model estimated a peak isolation housing need of approximately 200 beds. Slightly more isolation beds were required when moving from monthly testing to testing every 2 weeks (Figure 6a). The additional testing identifies more infections requiring isolation, but this is offset by prevention of infections with increased testing. More frequent testing decreases the cumulative hospitalizations and associated hospital resource need (Figure 6b).

More frequent testing can reduce the cumulative number of infections predicted across an 80-day term (Figure 6c); testing markedly reduced the number of cumulative infections which occur due to transmission on campus (blue bars). However, the model predicts that a fraction of infections (from 34% with monthly testing to 78% with twice weekly testing) occurs from the community which is not affected by campus testing (yellow bars). Finally, Figure 8 indicates that the benefits of testing at a higher frequency with less sensitive tests (70% sensitivity compared to 80% sensitivity) offsets the loss in individual test sensitivity.

DISCUSSION

Universities are grappling with how to resume on-campus educational and research activities while mitigating the risk of SARS-CoV-2 transmission and morbidity. Our modeling study indicates that structural interventions (through housing de-densification and hybrid instructional approaches with class size caps), viral detection (through asymptomatic and symptomatic testing), public health intervention, and masking and social distancing can work together to reduce the risk of transmission and large outbreaks on a university campus. We find that even with structural interventions, adherence to masking and social distancing are critical to reducing the transmission rate and ensuring average outbreak sizes are small. Asymptomatic testing plays an additional role in detecting outbreaks early and preventing the risk of very large outbreaks.

Our findings informed the UC San Diego Return to Learn program, which invited students to return in the Fall 2020 term in singles housing with hybrid instruction with a maximum class size cap of 50 for in person courses. Asymptomatic testing every two weeks is mandatory for students living on campus or coming on to campus, and highly recommended for all others every two weeks (students living off campus who are not coming on to campus, faculty, and staff). Additionally, the Return to Learn program incorporates other elements not captured yet in our modeling, including: wastewater and surface monitoring for early viral detection, digital exposure notification through our participation as a pilot site for the Apple/Google CA COVID Notify program [6], and molecular sequencing, among other efforts. A key element to the Return to Learn approach (and modeling within) is our adaptive strategy. We are continually collecting data, refining our understanding of the situation (and associated modeling), and adapting the strategy accordingly to ensure we enact a data-driven strategy for SARS-CoV-2 prevention.

Our modeling is consistent with other modeling studies examining the role of asymptomatic testing [14] and combination intervention approaches [19, 20] to reduce the risk of transmission on university campuses. Our study advances these previous studies by leveraging classroom and housing network data to examine the impact of these interventions on the predicted distribution of outbreak sizes.

Despite these strengths, our study has limitations. First, there is substantial uncertainty in many parameters, most notably the transmission rate on campus. This rate is determined by a number of factors, including behaviors which have not yet occurred. As such, our model is most useful in assessing the relative benefits of different scenarios rather than absolute predictions. Collection of behavioral data (in terms of masking, social distancing, and contact rates) will aid in refinement of the model and reductions in uncertainty. Second, as mentioned above, our model does not incorporate additional activities which may serve to additionally reduce risk on campus such as wastewater monitoring and digital exposure notification. As we collect data on the effectiveness of these activities, future iterations of the model will incorporate these factors. Third, our model does not account for superspreading events. Despite the fact that superspreading events play an important role in SARS-CoV-2 transmission [21, 22], much is still unknown about the dynamics of these events and the mechanisms that contribute to them. In particular, the relative importance of individual-level factors (in transmissibility between individuals) and structural factors (in setting ventilation, air flow, population density, etc.) that contribute to superspreading events is not well understood. Should such events occur at UC San Diego, we will investigate these dynamics from the data to be collected and our modeling approaches. Large-scale studies assessing the implications of superspreading events on transmission are urgently needed. Finally, we do not include the effect of vaccination strategies nor do we incorporate the potential impact of therapeutics that may reduce hospital utilization and mortality rates as these were unavailable during our study.

In the absence of an effective vaccine, universities and the broader society may face the challenge of reopening activities while attempting to reduce SARS-CoV-2 transmission for years. Our study provides a flexible modeling approach which can be used to inform adaptive, data-driven decisions on how to reduce SARS-CoV-2 outbreaks through risk mitigation, viral detection, and public health intervention strategies.

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DISCLOSURE

NM has received unrestricted research grants from Gilead and Merck unrelated to this work.

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FIGURES

Figure 1: An illustration of a contact network for an on-campus student. An on-campus student, which is denoted as the red circle, has residential connections (denotes as lines) with roommates (peach circle), suite-mates (green circles), and building-mates (yellow circles). The student also has contacts with other students/faculty in classrooms (blue circles); the illustration shows the student is enrolled in three classes (classes A to C). Both the residential and classroom connections do not change during the simulation. The student also has contacts with other university individuals outside the residential building and classroom, referred to as campus encounters; these individuals are denoted by gray circles and change every day.

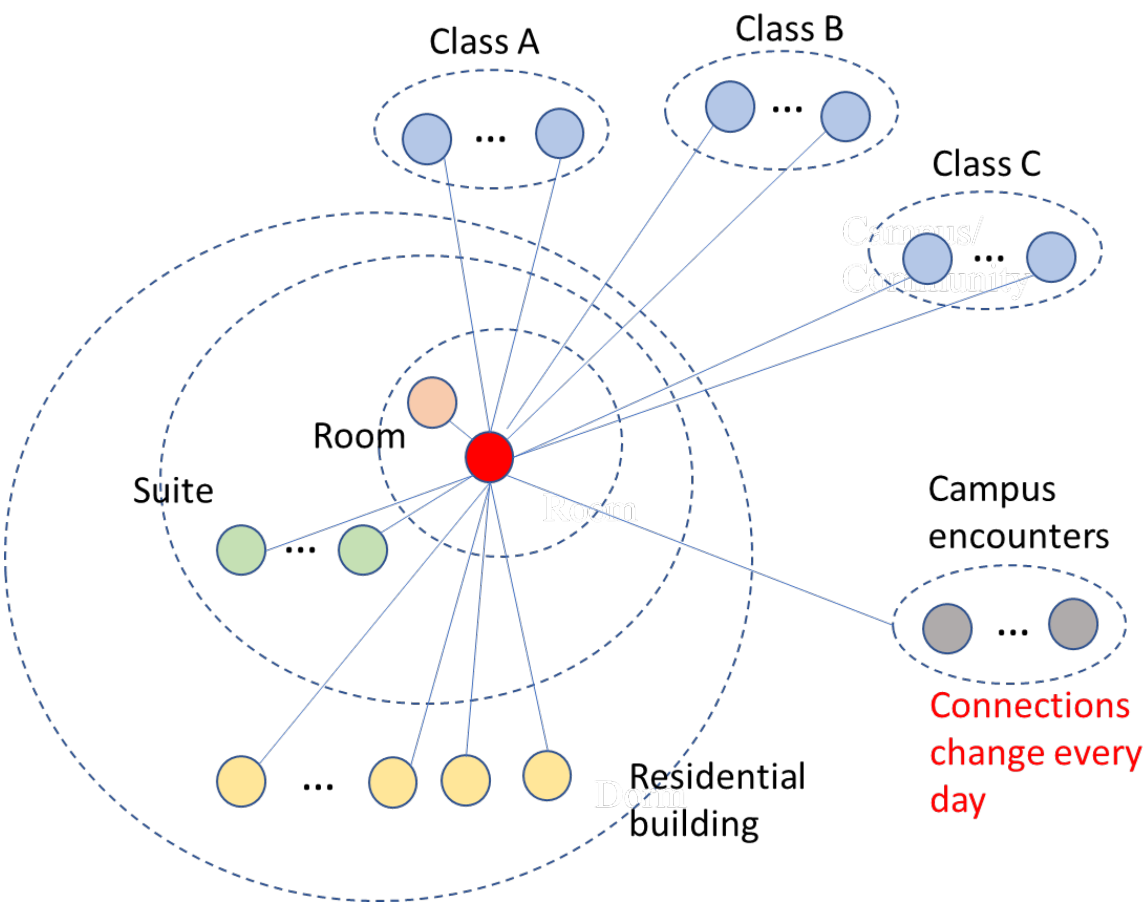


Figure 2: Schematic of the natural history of infection in the model. The transmission model simulates an individual's progression through seven stages of SARS-CoV-2 infection: (1) uninfected, (2) incubation period, (3) infectious but asymptomatic, (4) infectious with symptoms, (5) hospitalized, (6) recovery, and (7) death. Each day, an individual either remains in the current stage or transitions to another stage. The figure depicts these stages (blue circles) as well as possible transition pathways between stages (blue arrows).

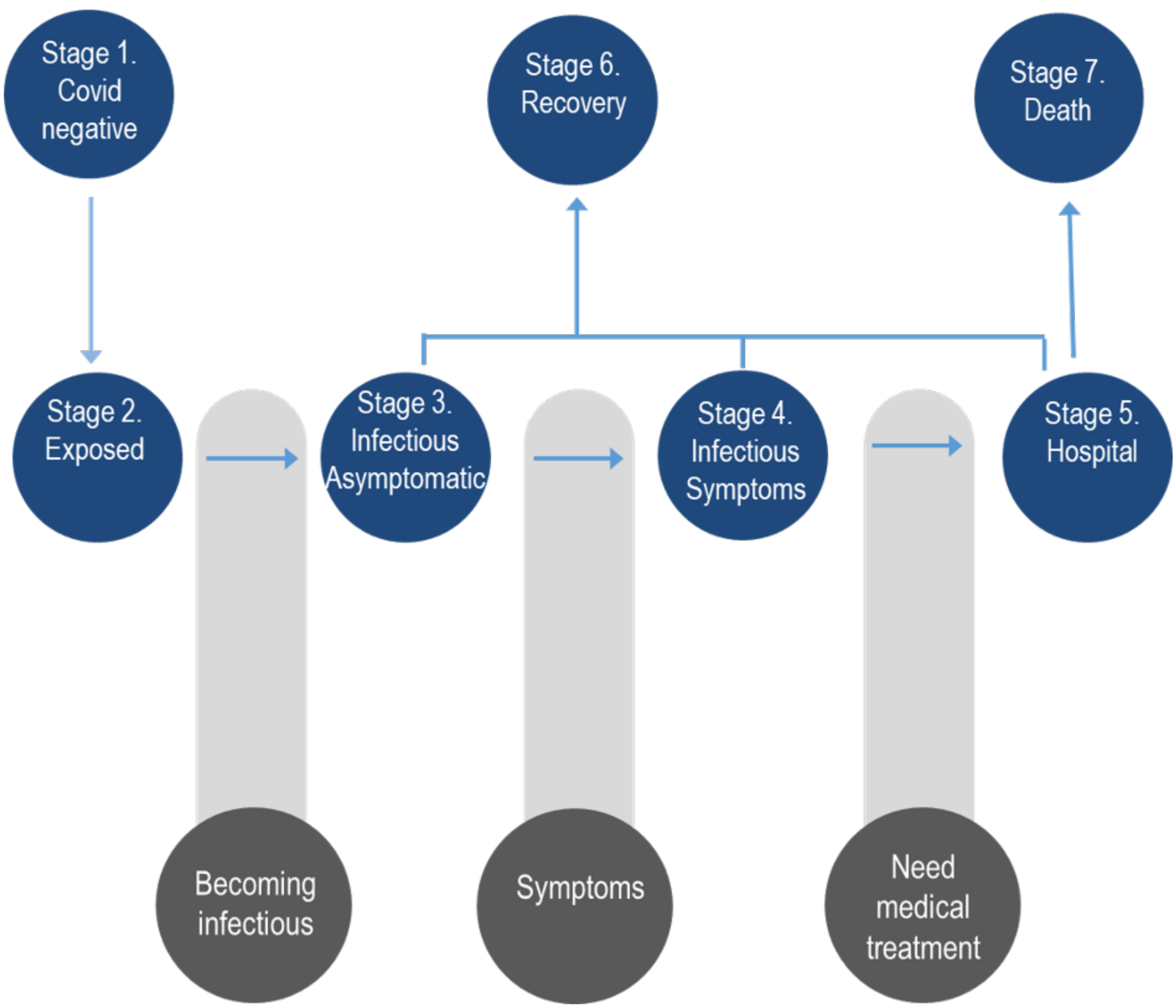


Figure 3: The on-campus basic reproduction number (R0) for four scenarios that include structural interventions such as hybrid instruction, class size caps, and de-densification of housing.

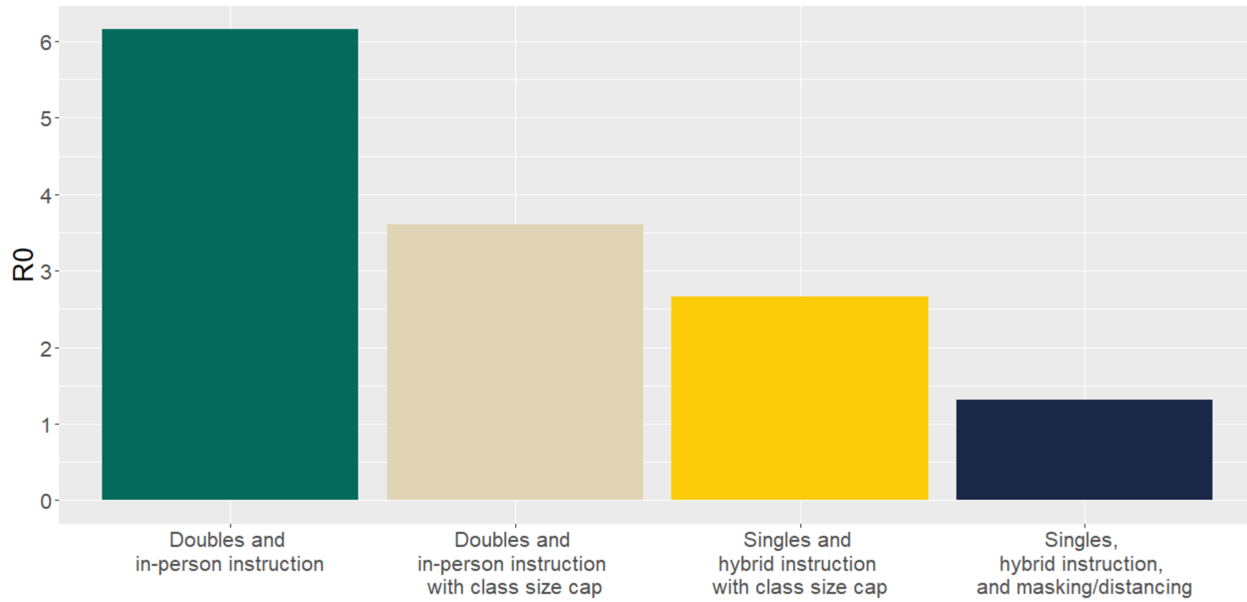


Figure 4: The average outbreak size (average number of individuals infected for each viral introduction), for four scenarios that include structural interventions such as hybrid instruction, class size caps, and de-densification of housing. Bars represent the mean across all simulations, and whiskers represent the 90% prediction intervals.

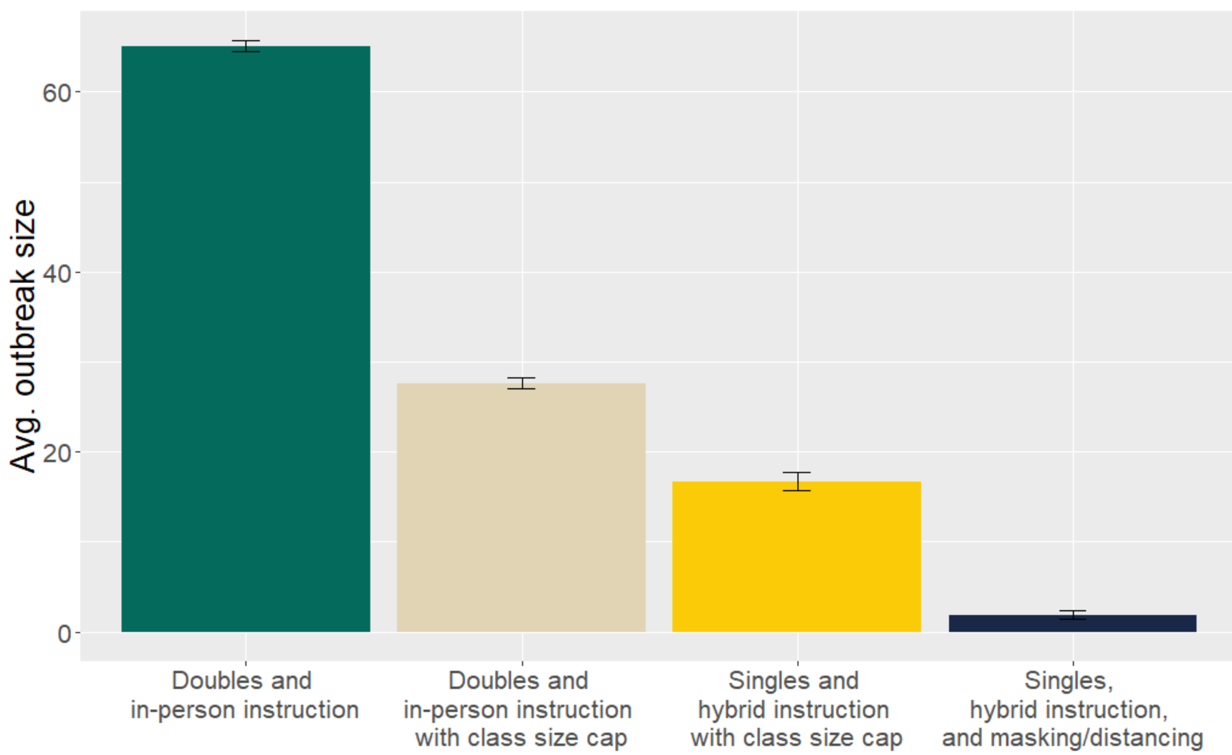
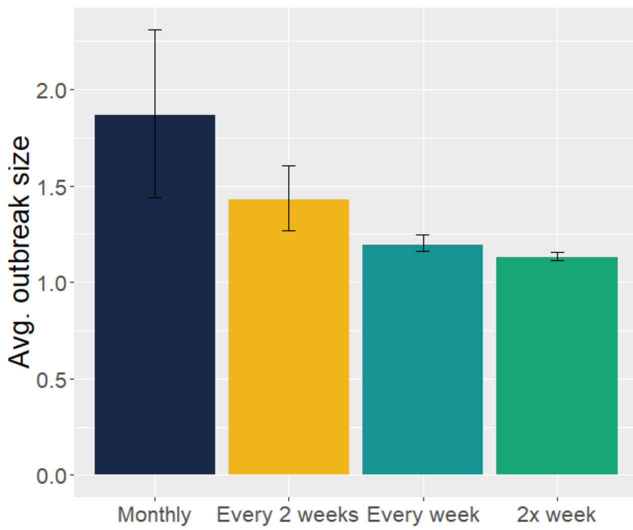
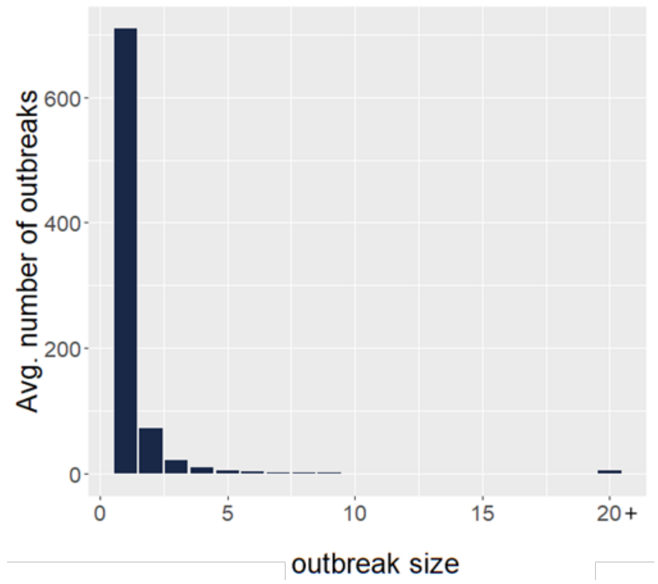


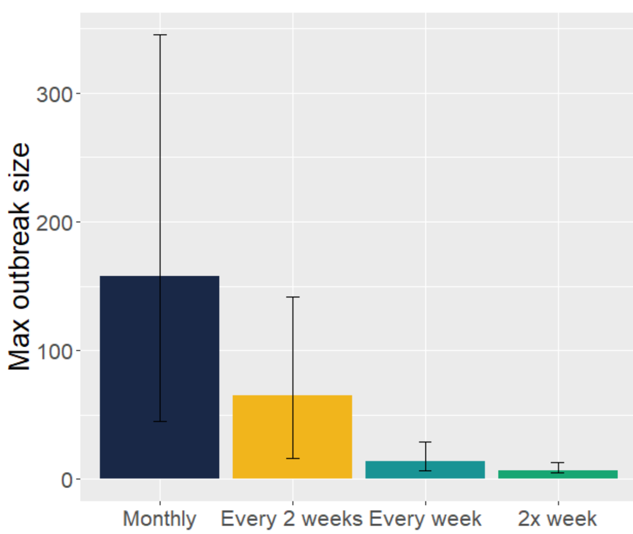
Figure 5: Predicted outbreak characteristics with various testing frequencies for students residing on or coming to campus for classes (monthly to twice weekly). Figures present (A) The average outbreak size; (B) a histogram of outbreak sizes; and (C) the maximum outbreak size, all assuming an 80-day term and with the scenario with single housing, hybrid instruction with an in-person class size cap of 50, and adherence to behavioral interventions (masking and social distancing.



(A)

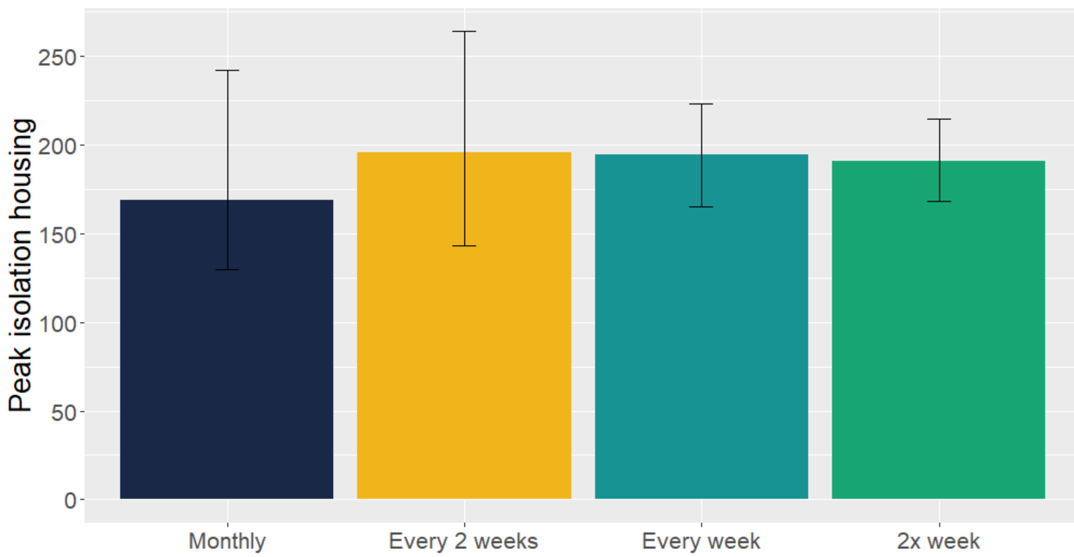


(B)

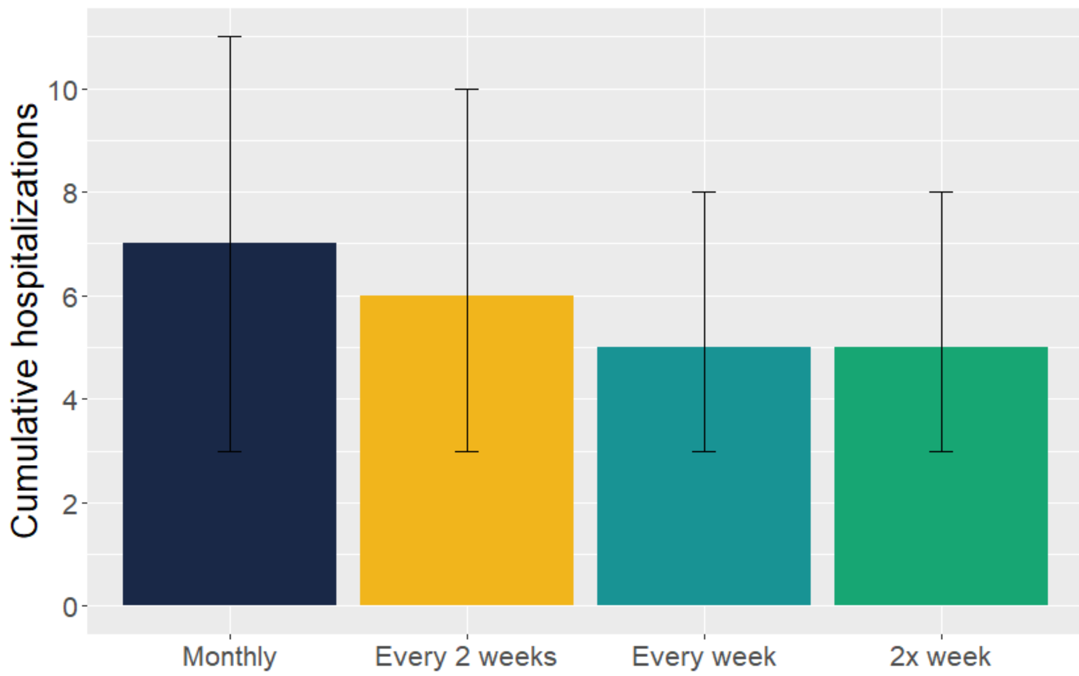


(C)

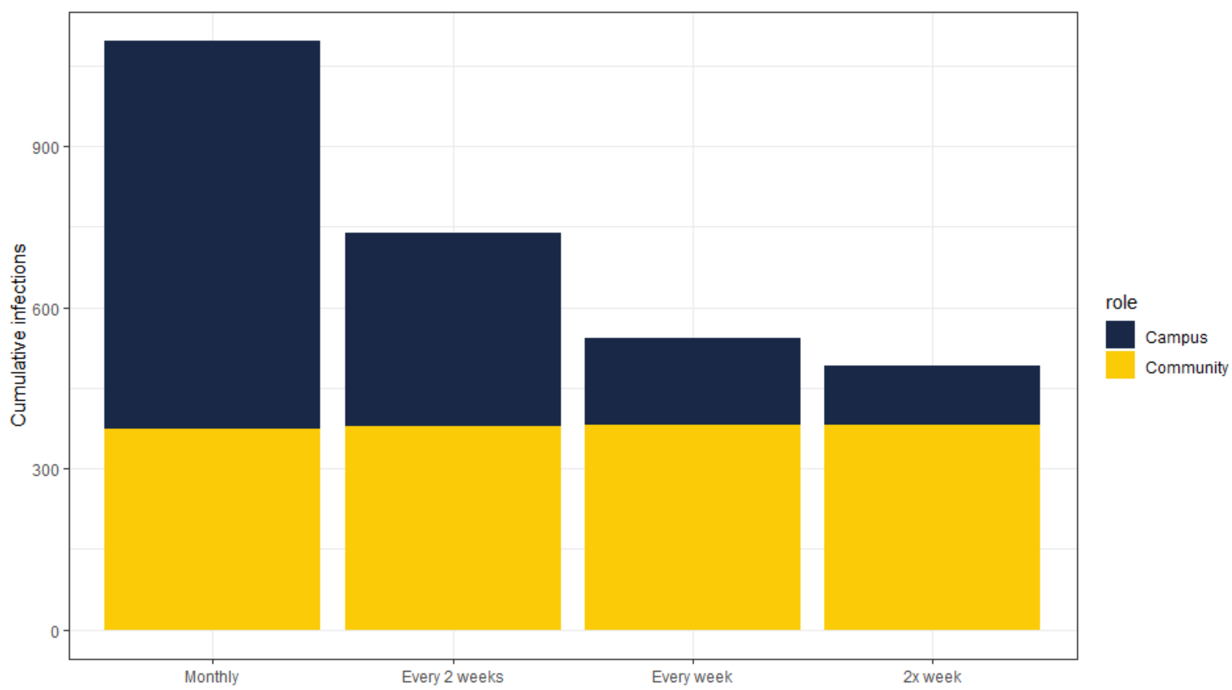
Figure 6: Peak isolation housing need (A), cumulative hospitalizations (B), and cumulative numbers of infections stratified by location of transmission (C) across an 80-day term for the scenario with single housing, hybrid instruction with an in-person class size cap of 50, and adherence to behavioral interventions (masking and social distancing. The frequency of testing campus residents varied was from monthly to twice a week. Bars represent the mean across all simulations, and whiskers represent the 90% prediction intervals.



(A)


Cumulative hospitalizations
0
2
4
6
8
10
Monthly
Every 2 weeks
Every week
2x week

(B)


Cumulative infections
0
300
600
900
Monthly
Every 2 weeks
Every week
2x week
role
Campus
Community

(C)

Figure 7: Cumulative number of infections predicted across an 80-day term for various testing frequencies (monthly to twice weekly) and test sensitivities (70% and 80%). Results shown for the scenario where residents live in single housing, have hybrid instruction with in-person class size cap, and adhere to behavioral interventions (masking and social distancing). The infections are stratified by location of transmission: community (yellow) or campus (blue).