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

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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

Universities are faced with decisions on how to resume campus activities while mitigating SARS-CoV-2 risk. To provide guidance for these decisions, we developed an agent-based network model of SARS-CoV-2 transmission to assess the potential impact of strategies to reduce outbreaks. The model incorporates important features related to risk at the University of California San Diego. We found that structural interventions for housing (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. We conclude that 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], quarantine, and 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, classroom caps and hybrid instruction, asymptomatic testing with various test sensitivities, and 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 population: We simulated 38,798 students (30,285 undergraduates and 8,513 graduates) who live either on or off campus and 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 simulated). Prior to the implementation of structural interventions, approximately

51% of students live in on-campus housing; the remaining students, staff, and faculty live off-campus. Each on-campus student is assigned a room in a 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, 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. See Supplementary Section S1 for additional details on the UC San Diego class and residence information.

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. On-campus students have three types of contacts: (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 no connections 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. The model assumes that students living on-campus do not have contact with individuals outside the university.

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; these transmission probabilities were derived from secondary attack rates for frequent, moderately frequent, and rare contacts, respectively [13]. These secondary attack rates were rescaled by a factor of four to generate a basic reproduction number (R0) for on-campus residents (individuals with the highest risk in the model) of 6.2 without intervention and between 1.3 and 3.6 with interventions (Table 1), which are comparable to estimates in the literature. Sanche et al. (2020) estimated an R0 value of 5.7 [14], while Gressman and Peck (2020) assumed an R0 of 3.8 prior to inclusion of residential contacts in their university model [15]; the inclusion of residential contacts would increase the R0. Paltiel et al. (2020) investigated R0 values from 1.5 to 3.5 for their university model [16]; however, their model only included 4990 students; by contrast, UC San Diego has over 30,000 students, including potential classes exceeding

400 students and residential suites that accommodate up to 18 roommates in a single suite. Therefore, we believe our R0 calibration to be reasonable given the literature. The rescaling also ensures that—to aid in planning—especially adverse scenarios are examined. See Supplementary Section S2 for additional details on the transmission probabilities.

Airborne transmission of SARS-CoV-2 is known to be an important source of transmission [3], but the precise association between proximity and transmission probability in enclosed classrooms is not known [17]. Therefore, we modeled the probability of transmission as being the same for all individuals enrolled in a given in-person course. The probability was 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, as informed by the UCSD-COVIDReadi (COVID-19 Resource Allocation Decisionmaking Information model) county-level transmission model, which estimated the true case rate at 2-3 fold the observed case rate due to asymptomatic transmission and undiagnosed infection in August 2020. Additional details regarding the UCSD-COVIDReadi model can be found at the application website [18].

Disease progression: 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.

Transitions between stages occur in daily increments. The daily probability of an exposed person with SARS-CoV-2 transitioning from Stage 2 to Stage 3 (asymptomatic but infectious) follows a geometric distribution with mean 4.6 days [19]. From Stage 3, individuals can recover (Stage 6), develop symptoms (Stage 4), or remain in Stage 3. We assume 70% of our population (predominantly college-aged individuals) are asymptomatic for the duration of infection [20], lasting on average 14 days [21]. Symptomatic 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; see Supplementary Section S3 for additional details on transition probabilities.

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, with maximum in-person class size 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 in-person class size capped at 50. Students who are unable to be accommodated with on-campus housing 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).** Similar to SH-Cap, but additionally assume 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 diagnosed individuals 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 individuals who are isolating are not at risk of transmission to others.

For confirmed positive students, we simulate contact tracing efforts performed by the public health team. We assume contact tracing identifies close contacts among an infected individual's room- and suite- mates, as well as students in their classroom who sit adjacent based on an assumed grid sitting assignment. Close contacts are assumed to adhere to quarantine, and we assume those in quarantine are not at risk of transmission to others. If close contacts are confirmed to have SARS-CoV-2 and are an on-campus resident, they are relocated to isolation housing and their contacts traced.

Asymptomatic testing: We simulate entry testing at term start as planned by UC San Diego. All students are tested on residential move in (two weeks prior to class start) and again on day 12. Off-campus students are required to test before class start. After the start of classes, individuals with in-person classes or who reside on-campus (referred to as campus testing) are tested at differential rates compared to individuals with no in-person classes or are 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 non-campus populations 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. The R0 is measured for the average on-campus index case without the impact of isolation and quarantine.

RESULTS

Structural interventions such as hybrid instruction, class size caps, and de-densification of housing can substantially reduce the R0 on campus (Table 1). With doubles and in-person instruction (DI), the R0 is 6.2; 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 structural interventions similarly have a strong impact on reducing the number of individuals infected for each viral introduction (defined as the outbreak size). 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 1.9 for the SH-Cap-Mask scenario (Table 1).

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 3a). However, despite the small size of the large majority of outbreaks (<10 infections, Figure 3b), 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 (90% 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 3c).

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 (Table 2). 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 (Table 2).

More frequent testing can reduce the cumulative number of infections predicted across an 80-day term (Figure 4); 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 total infections (from 34% with monthly testing to 78% with twice weekly testing) occurs from the community, with the number of community infections not affected by campus testing (yellow bars). Finally, Figure 4 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 approach accordingly to ensure we enact a data-driven strategy for SARS-CoV-2 prevention.

Our modeling is consistent with other studies examining asymptomatic testing [16] and combination intervention approaches [15, 22] to reduce transmission on university campuses. Our study advances these studies by leveraging classroom and housing network data to examine the impact of interventions on the predicted distribution of outbreak sizes.

Our study has several 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 making absolute predictions. Collection of behavioral data (in terms of masking, social distancing, and contact rates) will aid in refinement of the model and reduction in uncertainty. Second, as mentioned above, our model does not incorporate additional activities that 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 the impact of them. Third, our model does not account for superspreading events. Despite the fact that such events play an important role in SARS-CoV-2 transmission [23, 24], 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. R.S. is chair of Data Monitoring Committees for Merck and VIR Biotechnology, reports advisory board membership for Arcturus Therapeutics, and reports patents pending for orally bioavailable anti-coronavirus drugs. All other authors have no potential conflicts.

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FIGURE LEGENDS

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 (denoted as lines) with roommates (orange triangle), suite-mates (green diamonds), and building-mates (yellow squares). The student also has contacts with other students/faculty in classrooms (blue pentagons); 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 hexagons and change every day.

Figure 2: Schematic of the natural history of infection in the model. The agent-based 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: Predicted outbreak characteristics with various testing frequencies for students residing on or coming to campus for classes (monthly to twice weekly). Plots present (A) the average outbreak size; (B) a histogram of outbreak sizes; and (C) the maximum outbreak size. All plots assume an 80-day term and with the scenario with single housing, hybrid instruction with an in-person class size cap of 50, adherence to behavioral interventions (masking and social distancing), and test sensitivity of 80%.

Figure 4: 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).

TABLES

Table 1: The on-campus basic reproduction number (R0) and 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. The 90% prediction intervals are presented within the parentheses.

Scenarios	On-campus basic reproduction number (R0)	Average outbreak size, mean (90% prediction interval)
Doubles and in-person instruction	6.2	65.3 (64.8 – 65.9)
Doubles and in-person instruction with in-person class size cap of 50	3.6	28.8 (27.2 – 28.4)
Singles and hybrid instruction with in-person class size cap of 50	2.7	16.9 (15.7- 17.9)
Singles, hybrid instruction, in-person class size cap of 50, and masking/distancing reducing transmission by 50%	1.3	1.9 (1.4-2.3)

Table 2: Predicted peak isolation housing and hospitalizations across an 80-day term for various testing frequencies for students residing on or coming to campus for classes (monthly to twice weekly). All scenarios assume the scenario with single housing, hybrid instruction with an in-person class size cap of 50, adherence to behavioral interventions (masking and social distancing), and test sensitivity of 80%. The 90% prediction intervals are presented within the parentheses.

Outcome	Testing frequency			
	Monthly	Every 2 weeks	Every week	2x week
Peak isolation housing	169 (130-242)	196 (143-264)	194 (165-223)	191 (168-215)
Cumulative hospitalizations	7 (3-11)	6 (3-10)	5 (3-8)	5 (3-8)

Figure1

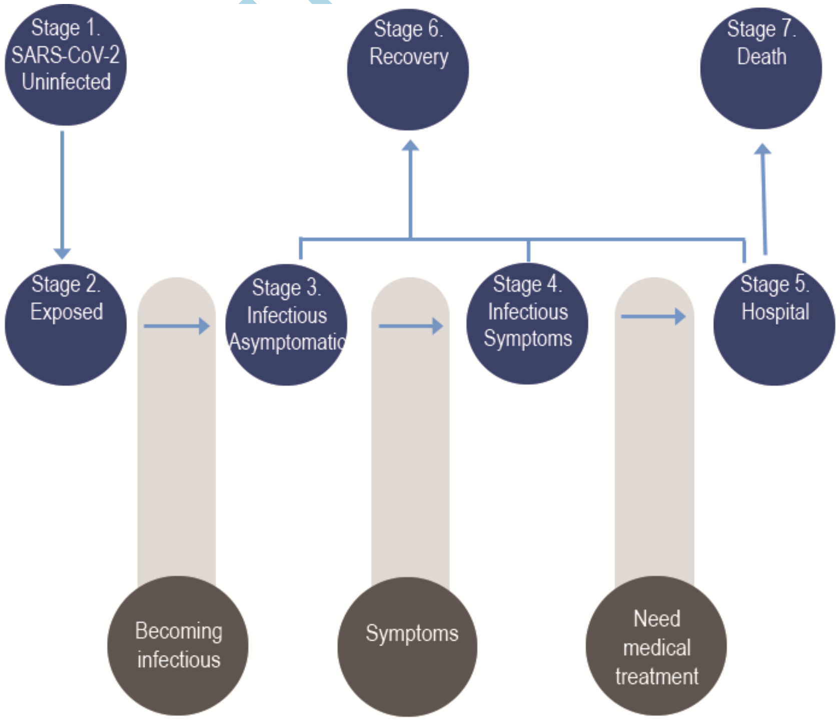
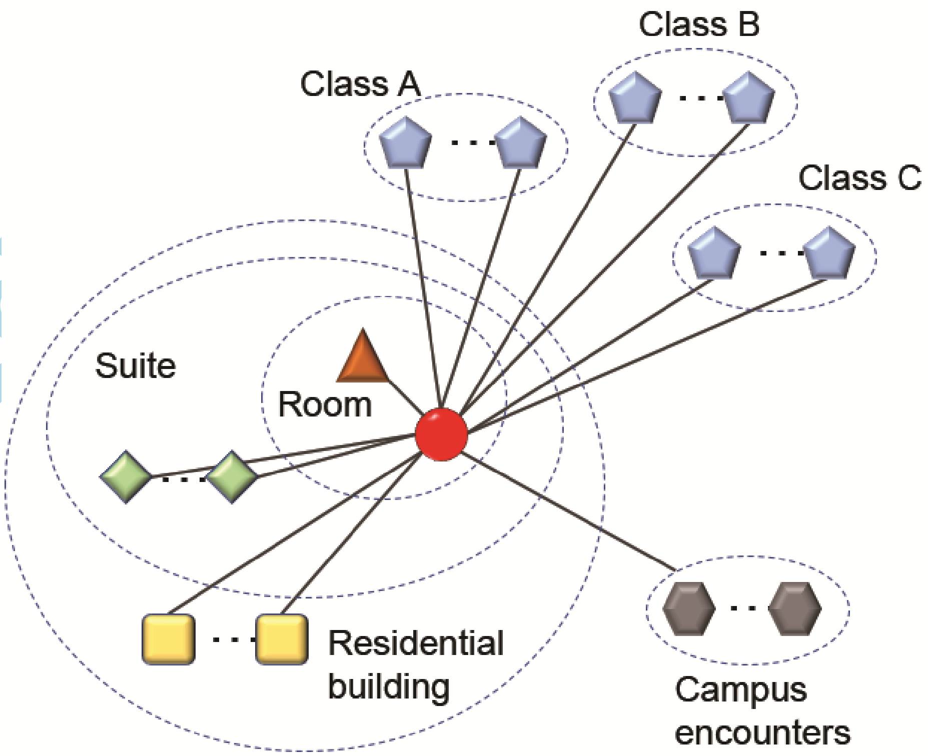
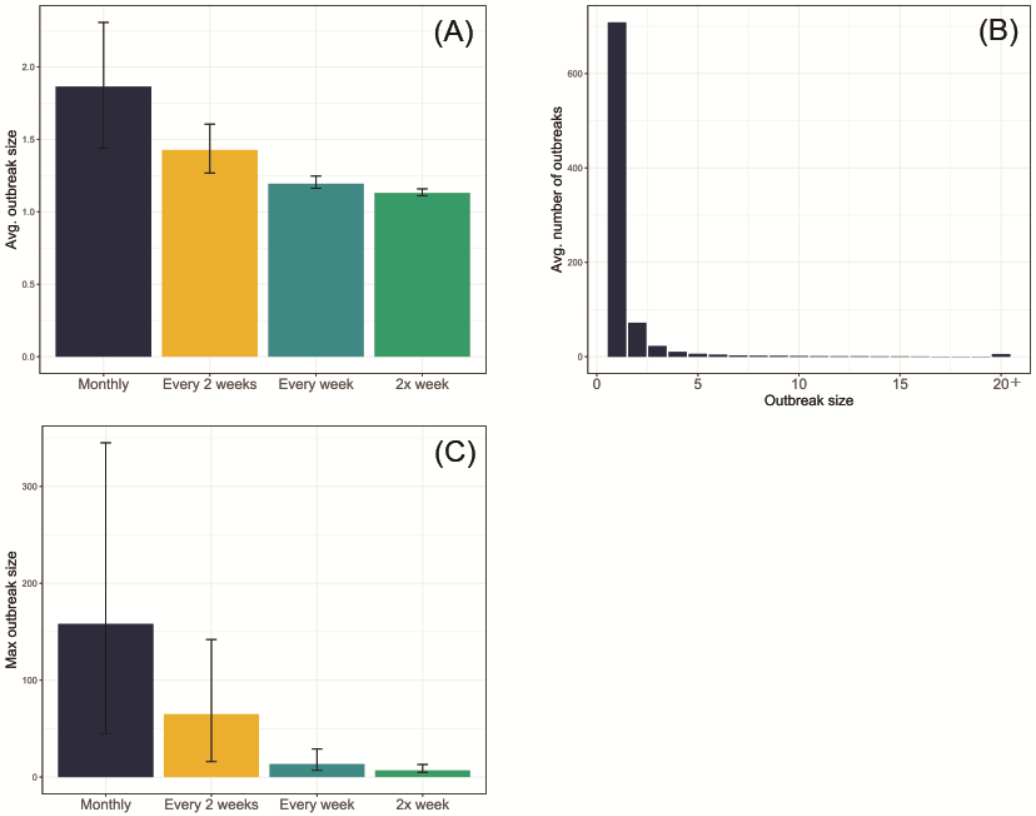

Stage 1. SARS-CoV-2 Uninfected
Stage 6. Recovery
Stage 7. Death
Stage 2. Exposed
Stage 3. Infectious Asymptomatic
Stage 4. Infectious Symptoms
Stage 5. Hospital
Becoming infectious
Symptoms
Need medical treatment

Figure2



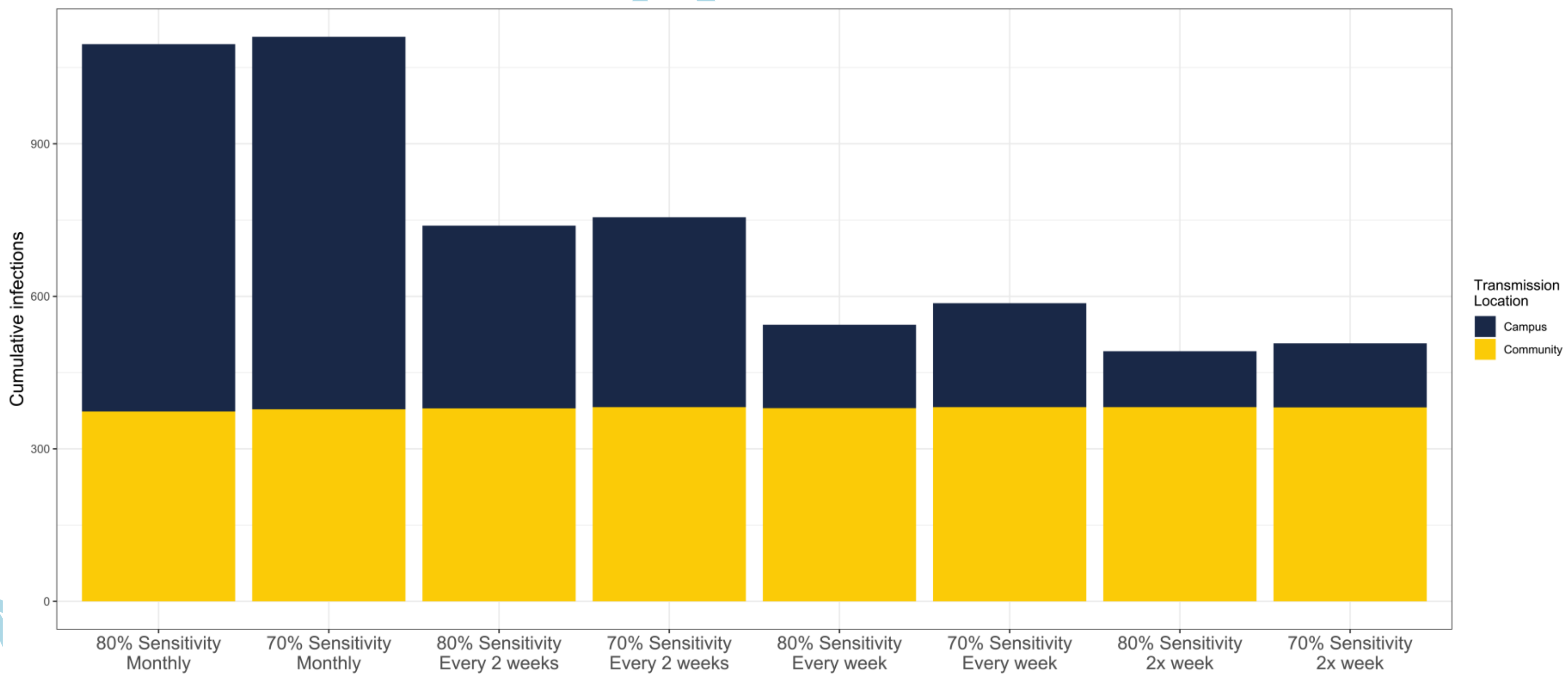
Class A
Class B
Class C
Suite
Room
Residential building
Campus encounters

Figure3



(A)
Avg. outbreak size
2.0
1.5
1.0
0.5
0.0
Monthly
Every 2 weeks
Every week
2x week
(B)
Avg. number of outbreaks
600
400
200
0
0
5
10
15
20+
Outbreak size
(C)
Max outbreak size
300
200
100
0
Monthly
Every 2 weeks
Every week
2x week

Figure4


Cumulative infections
0
300
600
900
80% Sensitivity Monthly
70% Sensitivity Monthly
80% Sensitivity Every 2 weeks
70% Sensitivity Every 2 weeks
80% Sensitivity Every week
70% Sensitivity Every week
80% Sensitivity 2x week
70% Sensitivity 2x week
Transmission Location
Campus
Community