SARS-CoV-2 Epidemiology on a Public University Campus in Washington State

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ABSTRACT

Background: We aimed to evaluate a testing program to facilitate control of SARS-CoV-2 transmission at a large university and measure spread in the university community using viral genome sequencing.

Methods: Our prospective longitudinal study used remote contactless enrollment, daily mobile symptom and exposure tracking, and self-swab sample collection. Individuals were tested if the participant was exposed to a known SARS-CoV-2 infected person, developed new symptoms, or reported high-risk behavior (such as attending an indoor gathering without masking or social distancing), a member of a group experiencing an outbreak, or at enrollment. Study participants included students, staff, and faculty at an urban, public university during Autumn quarter of 2020**.**

Results: We enrolled 16,476 individuals, performed 29,783 SARS-CoV-2 tests, and detected 236 infections. 75.0% of positive cases reported at least one of the following: symptoms (60.8%), exposure (34.7%), or high-risk behaviors (21.5%). Greek community affiliation was the strongest risk factor for testing positive, and molecular epidemiology results suggest that specific large gatherings were responsible for several outbreaks.

Conclusion: A testing program focused on individuals with symptoms and unvaccinated persons that participate in large campus gatherings may be effective as part of a comprehensive university-wide mitigation strategy to control the SARS-CoV-2 spread.

KEY WORDS: COVID-19 testing, outbreak, genome sequencing, university, SARS-CoV-2

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KEY POINTS: Symptomatic testing and testing of high-risk individuals identified most infected persons in our large, public university setting. In this pre-vaccination population, molecular epidemiology suggested that social gatherings were the main source of transmission for temporally clustered cases.

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INTRODUCTION

Universities are characterized by congregate living, in-person learning, and active social environments, all of which may contribute to rapid spread of infectious diseases. Between May and August 2020, persons aged 20-29 years accounted for over 20% of confirmed COVID-19 cases nationwide, and an even higher proportion in Washington state [1, 2]. Numerous outbreaks on university campuses were observed early in the SARS-CoV-2 pandemic [3]. Surveillance strategies ranged from pooled testing of asymptomatic persons to wastewater analysis, with substantial heterogeneity across universities and no clear federal guidance [3-5]. Nationwide shortages of testing supplies and reagents have prevented many universities, including ours, from adopting a strategy of testing all members of the university community on a regular basis. Given these constraints, we sought to identify an approach that would permit early identification of cases and facilitate containment of spread [6, 7].

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METHODS

Setting

This study was conducted at a large public university in Seattle, Washington, composed of approximately 60,000 students and 30,000 faculty and staff [8, 9]. In Autumn 2020, the university opened with hybrid in-person classes, and the majority courses were held fully remotely. Residence halls were populated at a limited capacity [10]. The study population included students, staff, and faculty affiliated with the main campus and two smaller campuses located 15 and 35 miles from the main campus.

Study Enrollment

Enrollment began September 24, 2020, during student resident move-in and continued during the study period. Eligibility criteria included living on-campus or within the main or satellite campus geographic area (approximately 100-mile radius), a valid university identification number, the ability to consent in English, and university-related class or work at least once per month (in-person or remotely). Exclusion criteria were living outside of the geographic area (i.e., working remotely but living in another state) and age <13 years. Participants completed informed consent and an online questionnaire that included baseline risk behaviors and demographic information. At enrollment, participants indicated a preference for either email or text communication. Data were managed using REDCap software [11, 12]. Individuals were stratified into risk tiers based on time spent on-campus, number of individuals in their household, and university affiliation (STable 1).

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Attestations and Invitations to Test

Testing was offered for four reasons: (1)Attestation positivity; (2)Outbreaks; (3)Baseline surveillance; and (4)Holidays. Due to limited testing resources, "Attestation positive" study participants were prioritized, followed by outbreak invitations, and finally, baseline and holiday invitations.

A daily attestation survey was used to determine testing eligibility. If "yes" was reported to any question, a participant was classified as "Attestation positive": In the last 24 hours, have you 1) experienced new symptoms ("symptoms"), 2) been exposed to a COVID-19 positive individual ("exposure"), or 3) attended a high-risk gathering ("gathering", defined as attending an indoor gathering of >10 people without social distancing or mask-wearing). Testing could be offered based on the daily attestation up to every three days, and repeat testing was offered immediately if new symptoms were reported. If a "gathering" or "exposure" attestation was reported, the testing invite was delayed 48 hours to account for the incubation period [13]), and a second test was offered 72 hours after the first test was completed. During outbreak testing, testing was offered every three days to all individuals in the affected group. During outbreak testing, such as in the Greek Outbreak, our objective was to identify cases for the purpose of implementing measures such as quarantine to reduce disease transmission. Holiday testing was offered before and after the Thanksgiving break during November 17-December 6, 2020.

Testing Mechanisms

Testing was conducted at in-person kiosks or via mail-in swab kits (Supplemental Methods). Participants affiliated with the main campus who received a testing invitation were offered in-person appointments of their choosing within 72 hours. Samples were collected by observed anterior nasal self-swab at on-campus kiosks. For participants at satellite campuses or who indicated mobility restrictions precluding attendance to an on-campus kiosk, a self-testing kit was sent to and picked up from their residence using rapid courier services [14, 15].

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Laboratory Methods and Results Reporting

Samples collected at kiosks were transported to the Northwest Genomics Center at the University of Washington and tested for SARS-CoV-2 using an RT-qPCR laboratory developed test (LDT). The RT-qPCR consists of assays for two SARS-CoV-2 targets in duplicate and the human marker RNase P across four multiplexed reactions (Supplemental Text) [16]. A sample was considered positive if three or four replicates for RNase P had a cycle threshold (Ct) value <36 and SARS-CoV-2 had a value <40 (Supplemental Text). If only two SARS-CoV-2 replicate reactions were positive, the result was defined as inconclusive. Inconclusive results were regarded as low-positive results and participants were counselled identically to participants with positive results [17]. If SARS-CoV-2 was not detected or detected in only one replicate, the test was considered negative. Samples were defined as failed and considered 'never tested' if RNase P was undetected in two or more reactions, or if there was a laboratory or operator error. Mid-study (November 18, 2020), we implemented an extraction-free testing method that yielded similar results, but Ct values from the two methods are not directly comparable [16]. Results were provided to participants through a research report hosted on a secure online portal that was accessed using a unique barcode identifier and date of birth. Cases were contacted by university, county, or state public health staff and contact tracing was initiated. Viral genome sequencing was attempted on all positive samples with Ct values of 30 or less using a hybrid capture enrichment method [18] or a COVID-seq amplicon method (Illumina). Raw sequencing reads were processed using the Seattle Flu Study Assembly Pipeline (GitHub [19]). Viral sequences were aligned and phylogenetic trees constructed using Nextstrain augur software [20]. Trees were visualized using the Nextstrain auspice software. All assembled genomes were publicly deposited to the Global Initiative on Sharing All Influenza Data (gisaid.org [21]) and Genbank immediately after data generation.

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University-Wide Prevention and Mitigation Strategy

Prior to and during Autumn quarter, the university deployed a communications campaign focused on masking, social distancing, handwashing, and disinfection of surfaces. Contact tracing was conducted by university public health officials for all students, staff, and faculty, except off-campus Greek community cases, which were handled by county public health. Campus isolation and quarantine housing was provided for infected students that lived in campus housing, consistent with CDC recommendations. Students and employees in private residences were given instructions for isolation/quarantine, testing, and precautions. University members also had access to free municipal SARS-CoV-2 testing outside of this research study. Data pertaining to social gatherings of university community members was not collected.

Statistical methods

Positive and inconclusive results were counted as cases. 95% confidence intervals were calculated, and p-values were considered significant at alpha level of 0.05. Statistical testing for the comparison of averages was completed using Welch's two sample t-tests. For multivariate regression, the reference group for race was White and non-Latinx/Hispanic for ethnicity.

Persons testing positive for SARS-CoV-2 were categorized as symptomatic, presymptomatic, asymptomatic, and possible asymptomatic. A case who tested positive/inconclusive was defined as symptomatic if they reported symptoms on their daily attestation survey within the seven days prior to testing or the day of testing. Presymptomatic was defined as those who only reported symptoms in the week after testing on their daily attestation or follow-up survey. If no symptoms were reported before or after testing on the daily attestation or follow-up survey, a participant was classified as asymptomatic. Participants who did not complete their daily attestations or the follow-up

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survey, and who reported no symptoms at the time of testing were classified as “possible asymptomatic” cases.

A Generalized Estimating Equation with a logit link, robust variance, and an independent working correlation matrix was used to analyze risk factors for testing positive, allowing for dependence within individuals longitudinally. Odds ratios (OR) and their 95% confidence intervals were calculated adjusting for race, Latinx/Hispanic ethnicity, university or Greek affiliation, number of household members, attesting positive, mask wearing behavior, social distancing behavior, and on-campus frequency. Analyses were performed in R version 3.6.1.

Human Subjects

The University of Washington Institutional Review Board approved this study. All participants (or their guardians) provided written informed consent.

RESULTS

Between September 24 and December 18, 2020, 16,476 individuals enrolled in the study, and 29,783 samples from 11,644 unique individuals were collected and tested for SARS-CoV-2 (SFigure 1). 25.5% (15,930/62,591) of matriculated students during Autumn quarter were enrolled in at least one course with in-person instruction, and 19.9% (8,204/41,296) of all matriculated undergraduates and 18.4% (2,719/14,765) of graduate students participated in the study [22-24]. Due to remote instruction, many students were not living in the surrounding area and were not eligible for the study. More female (61.4% in the study vs. 54% in the student body), and White students (62.6% in the study vs. 40.8% in the student body; SFigure 2 and Table 1A) were enrolled. Of an estimated 4,100 eligible Greek community students, 2,672 (65.2%) were enrolled, and these students were more likely to be White than non-Greek students (STable 2).

The daily attestation survey was completed by a mean of 47.7% (6,203) participants per day (Figure 1A-B). Among participants attesting positive over the study period, 40.4% reported

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symptoms, 12.1% reported recent exposure to a SARS-CoV-2 positive individual, 36.4% reported attending an indoor gathering with >10 people without distancing or mask wearing, and 11.1% reported multiple reasons. During the study, 409 (2.5%) participants opted to stop receiving attestation alerts and were given the option of completing attestations on the study website. Results on participant preventative behaviors are shown in STable 3.

SARS-CoV-2 Testing Results

A total of 11,633 (70.6%) participants were tested at least once (STable 4). Tests were resulted and available for participants to view online the day of sample collection (26.3%) or the following day (62.6%), and a minority of students received their results >24 hours after testing. 265 out of 29,783 samples (0.80%) tested positive or inconclusive for SARS-CoV-2 (Table 1B). Among the 265 cases, there were 60.8% (61) symptomatic, 19.6% (52) presymptomatic, 3.4% (9) asymptomatic, and 16.2% (43) possible asymptomatic. Based on the total 29,723 samples tested, 1.4% of participants reporting symptoms at the time of testing were positive (161/11,116) and participants not reporting symptoms at the time of testing had a low likelihood of positivity (0.56%, 104/18,607, Table 1B). The symptoms associated with the highest percent positivity were loss of taste/smell (19/382, 5.0%), fever (52/1,518, 3.4%), and chills (36/1,365, 2.6% (STable 5). 92/256 (34.7%) of participants testing positive reported exposure to a known positive case. By group, the Greek community had 1.5% test positivity (1796/12,045), on-campus dorm residents 1.2% positivity (43/3,507), and staff and faculty 0.4% (19/4,417) and 0.3% (4/1,467), respectively. Test positivity by affiliation and race is shown in STable 6. Overall during the Autumn quarter, the university was aware of 745 positive SARS-CoV-2 individuals, of which 31.7% (236/745) were detected as part of this study [25].

For comparison of Ct values, we restricted comparisons to the time period before the change in testing methods, since methods used before and after November 18, 2020 were not comparable. Among samples collected from September 24-November 18, 2020, mean Ct

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values were higher in presymptomatic compared to symptomatic cases (28.7 vs. 24.2, p=0.001), corresponding to a lower viral load (Figure 2, SFigure 3).

Risk Factors for SARS-CoV-2 Infection

On multivariable analysis, Greek affiliation had the strongest association with test positivity (OR: 2.71, 95% CI:1.84-4.00, p<0.001). Latinx/Hispanic ethnicity (OR: 2.12, 95% CI:1.28-2.18, p=0.002) and positive attestations (OR 1.86, 95% CI:1.43-2.41, p<0.001) were also risk factors for positivity (STable 7). Reported frequency of hand washing, mask-wearing, and social distancing were not associated with positivity.

Greek Community Outbreak

Thirty cases were identified in the Greek community during the first 10 days of the study, which prompted outbreak testing. Test positivity trends in the Greek community demonstrated a unique epidemiologic curve compared to the non-Greek students, employees, and the county (Figure 3A [26]). Outbreaks within Greek houses were concurrent, but with unique individual timelines, and involved both fraternities and sororities (Figure 3B). 68.3% of Greek members reported sharing a living space with 6 or more people, compared to only 14.0% of non-Greek students. During 37 days of outbreak testing in the Greek community, serial testing frequently identified individuals who tested negative several times prior to testing positive (Figure 3C).

SARS-CoV-2 Molecular Epidemiology

Genome sequences were generated from 88 SARS-CoV-2 samples collected from unique individuals between September 27-November 28, 2020. 59 samples were from Greek-affiliated students, 24 from non-Greek-affiliated students, and 5 from faculty/staff. In a phylogenetic tree of 1,700 SARS-CoV-2 genomes collected statewide, including the 88 from this study, samples included viruses from each of the four major clades (20A, 20B, 20C, 20G) circulating in the county and state during this timeframe (Figure 4A).

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Most viral genomes from this study (56/88, 63.6%) grouped into one large cluster that included genomes from 49 Greek-affiliated and 7 non-Greek-affiliated students (large black box in Figure 4A, detailed in Figures 4B,C and SFigure 4). This cluster also included genomes from four samples collected but outside of our study. Samples in this cluster were collected between September 27-November 28, 2020, and all samples in this cluster collected prior to October 7 originated from Greek-affiliated students.

Closer inspection of this cluster (Figure 4B,C) demonstrates two sub-clusters (branch support values are 0.94 for larger sub-cluster and 0.78 for smaller sub-cluster) containing both sorority and fraternity members. Samples within clusters are closely related with a maximum pairwise distance between any two samples in the same sub-cluster of four single nucleotide changes. Molecular clock estimates place the common ancestor of the larger cluster on September 22, 2020 (95% CI:September 1-29) and the smaller cluster at September 27, 2020 (95% CI:September 20-October 4). These two dates are just prior to the sharp increase in cases observed in our study among Greek students, which peaked on approximately October 7-8, 2020 (Figure 3A). The last sample mapping to either of these sub-clusters was collected November 12, 2020. This date roughly coincides with the end of the Greek outbreak as measured by the percent positivity rate (Figure 3A). Among the hundreds of genomes sequenced state-wide November 12, 2020-March 17, 2021, none are descendants of the viruses responsible for the Greek community outbreak.

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Two smaller clusters of viral genomes from this study are shown in Figure 4A (two small boxes) and SFigures 5,6. One cluster contains four genomes from Greek-affiliated students and one from a non-Greek student. This cluster has a most recent common ancestor dating to October 31, 2020 (95% CI:October 17-November 1). The second contains three genomes from non-Greek-affiliated students and one faculty/staff member with a most recent common ancestor dating to November 3, 2020 (95% CI:October 11-November 16). Viral genomes from Greek-affiliated students were most likely to cluster with other study samples; 88.1% of genomes from Greek-affiliated students were genetically identical to at least one other study SARS-CoV-2 genome, and 45.8% of genomes from non-Greek students and 0% of genomes from faculty/staff were identical to another study genome.

DISCUSSION

We report a large-scale COVID-19 longitudinal study of students, faculty, and staff at a university campus allocated testing based on self-reported risk of infection, rather than mass surveillance. Most cases were identified through daily attestation surveys, and participants reporting a recent exposure to a case had the highest positivity rate of 2.4%, followed by 1.4% for participants reporting symptoms. Baseline testing had a much lower positivity rate of 0.56%, identifying only 15% of cases. Phylogenetic analysis of SARS-CoV-2 genomes from this study suggest differences in transmission patterns among Greek community members and non-Greek members. SARS-CoV-2 genomes from Greek-affiliated students primarily fell into closely related clusters, suggesting transmission related to Greek associated housing or activities, while samples from non-Greek students and faculty/staff were more genetically diverse. Most viral genomes from Greek-affiliated students were members of a large cluster that may have resulted from a single SARS-CoV-2 transmission event. 84% of the samples in this cluster represented just 5 unique viral genotypes, suggesting rapid spread. Identical viruses were commonly collected from members of

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several different sororities/fraternities, and this supports the theory that social behaviors, rather than housing arrangements, drove this outbreak.

Outbreak testing was an essential part of our testing strategy. In our study, Greek affiliation was the most important risk factor for testing positive, and more than two-thirds of cases detected in this study were in Greek-affiliated students, similar to findings at other universities [27]. We observed cases in most of our university's Greek chapters, and the genomic analysis and outbreak dynamics indicate that rapid transmission occurred within and among fraternities and sororities. However, later in the quarter, the decreased test positivity rate among this group became comparable to rates observed among the non-Greek participants. This decline may have been driven in part by our aggressive testing strategy in this group, and effective contact tracing, quarantine, and other risk mitigation strategies. This analysis suggests that policies that limit large gatherings and provide regular testing to high-risk populations can mitigate outbreaks.

Consistent with our findings, random testing of asymptomatic people at the University of Pittsburgh yielded a positivity rate of only 0.4% prior to widespread vaccination {O'Donnell, 2021 #18}. Among partially vaccinated communities, one report indicates that surveillance testing yielded even fewer case detections [28]. Campus outbreaks are known risk factors for broader community transmission [29, 30]. In our study, SARS-CoV-2 test positivity rates in the university community were substantially lower than in the surrounding area. This may have been due to increased test availability, particularly for asymptomatic persons. However, it is also possible that focused testing of high-risk groups prevented and mitigated campus-wide outbreaks. In addition to members of the Greek community, participants who identified as Latinx or Hispanic experienced increased positivity rates. This is consistent with COVID-19 incidence rates in Washington State, where Hispanic individuals represented 13% of state residents, but 33% of COVID-19 cases [26]. This highlights the need for more targeted and equitable distribution of testing and contact tracing resources in this population.

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Testing and behavioral interventions are cost-effective to control outbreaks on college campuses; however, prioritization of testing is critical, and scarcity of laboratory supplies were present during our study [31]. We employed several mechanisms to conserve testing resources. First, we used the daily attestation surveys to screen for symptoms predictive of SARS-CoV-2 infection [32] to prioritize tests for those at highest risk. Second, we used mass produced swabs that are shipped dry and eluted in PCR-friendly buffer to allow an extraction-free RT-qPCR method. By avoiding the need for limiting reagents such as transport media and RNA extraction kits, we avoided supply chain challenges, reduced the price per test, and increased the speed of our testing pipeline, enabling us to maintain a 24-hour turnaround time on average while increasing scale.

As of March 2021, there were only 4 viruses collected statewide that fall into the Greek outbreak cluster and the last was collected on October 14, 2020. This demonstrates that sustained spread in the surrounding community did not occur in the subset of samples sequenced from the surrounding county/state. This does not fully rule out “spillover” of virus from the Greek outbreak into the outside community, given that a limited subset samples are sequenced.

Other limitations of this study include that our online format of consent, enrollment, and daily attestation surveys increased participant engagement but was a barrier to participation for individuals with limited technological literacy or access. Additionally, study materials were available in English only. Data about participant exposures, including the daily attestation, were based on self-report, and questions about risk-taking behaviors were asked only at enrollment. After report of a positive exposure or attendance at a high risk gathering, participants were offered testing twice, and positive cases could have been missed due to infrequent testing during the incubation period. While on-campus testing through this program was often the most convenient testing option, data included here is not comprehensive in describing on-campus cases since other testing mechanisms were also available. Race and ethnicity representation in the study population was not representative

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of the university community, potentially due to differences in willingness to participate in studies, and this was likely further skewed by a university campaign to enroll and test members of the Greek community. Because our study included fewer underrepresented minorities than the overall university community, our report may represent an underestimate the total number of infections. Our ability to speculate on the patterns related to Greek community transmission dynamics are impacted by the availability of other testing mechanisms and inability to sequence all study genomes.

We report here a strategy for SARS-CoV-2 testing on a large university campus using contactless, rapid enrollment, and self-administered testing during Autumn quarter 2020. Most infections were detected in the Greek community, and this group experienced distinct genomic and epidemiologic dynamics compared to other university communities and the surrounding area. This evidence suggests that testing those engaged in high-risk activities, in combination with testing people experiencing symptoms, may be critical steps in stopping on-campus transmission and potentially prevent community spread in a setting of limited resources. Our data also suggests that interventions to reduce large gatherings and promote mask wearing indoors is likely to reduce campus outbreaks.

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CONFLICT OF INTERESTS

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REFERENCES

1. Malmgren J, Guo B, Kaplan HG. Continued Age Shift of Confirmed Positive COVID-19 Incidence Over Time to Children and Young Adults: Washington State March - August 2020. *medRxiv*. 2020/11/16/ 2020:2020.11.12.20229468. doi:10.1101/2020.11.12.20229468

2. Boehmer TK. Changing Age Distribution of the COVID-19 Pandemic — United States, May–August 2020. *MMWR Morb Mortal Wkly Rep*. 2020 2020;69doi:10.15585/mmwr.mm6939e1

3. Hubler S, Hartocollis A. How Colleges Became the New Covid Hot Spots. *The New York Times*. 2020/09/11/. Accessed 2021/01/28/20:18:39. https://www.nytimes.com/2020/09/11/us/college-campus-outbreak-covid.html

4. O'Donnell C, Brownlee K, Martin E, et al. SARS-CoV-2 Control on a Large Urban College Campus Without Mass Testing. *medRxiv*. 2021/01/25/ 2021:2021.01.21.21249825. doi:10.1101/2021.01.21.21249825

5. Christensen K. Tracking and Treating COVID-19 in Human Waste. *Michigan Technological University*. 2020/05/27/ 2020;

6. Booeshaghi AS, Tan F, Renton B, Berger Z, Pachter L. Markedly heterogeneous COVID-19 testing plans among US colleges and universities. *medRxiv*. 2020/08/11/ 2020:2020.08.09.20171223. doi:10.1101/2020.08.09.20171223

7. Cdc. Communities, Schools, Workplaces, & Events. *Centers for Disease Control and Prevention*. 2020/04/30/ 2020;

8. Discover the University of Washington. *About the UW* blog. https://www.washington.edu/about/

9. University of W. 2020 University of Washington Financial Report. 2020 2020;

10. How the pandemic will affect autumn quarter learning (Message to students from the United States). *Novel coronavirus information* blog. https://www.washington.edu/coronavirus/2020/08/06/autumn-quarter-learning-message-to-students-from-the-united-states/

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Downloaded from https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofab464/6372006 by guest on 20 September 2021

11. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *J Biomed Inform*. 2019/07// 2019;95:103208. doi:10.1016/j.jbi.2019.103208

12. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009/04// 2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010

13. McAloon C, Collins Á, Hunt K, et al. Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. *BMJ Open*. Aug 16 2020;10(8):e039652. doi:10.1136/bmjopen-2020-039652

14. McCulloch DJ, Kim AE, Wilcox NC, et al. Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. *JAMA Netw Open*. 2020/07/22/ 2020;3(7):e2016382. doi:10.1001/jamanetworkopen.2020.16382

15. Chu HY, Boeckh M, Englund JA, et al. The Seattle Flu Study: a multiarm community-based prospective study protocol for assessing influenza prevalence, transmission and genomic epidemiology. *BMJ Open*. 2020/10// 2020;10(10):e037295. doi:10.1136/bmjopen-2020-037295

16. Srivatsan S, Han PD, van Raay K, et al. Preliminary support for a "dry swab, extraction free" protocol for SARS-CoV-2 testing via RT-qPCR. *bioRxiv*. 2020/04/23/ 2020;doi:10.1101/2020.04.22.056283

17. Weil AA, Newman KL, Ong TD, et al. Cross-Sectional Prevalence of SARS-CoV-2 Among Skilled Nursing Facility Employees and Residents Across Facilities in Seattle. *J Gen Intern Med*. 2020/09/01/ 2020:1-6. doi:10.1007/s11606-020-06165-7

18. Bedford T, Greninger AL, Roychoudhury P, et al. Cryptic transmission of SARS-CoV-2 in Washington state. *Science*. 2020/10/30/ 2020;370(6516):571-575. doi:10.1126/science.abc0523

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Downloaded from https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofab464/6372006 by guest on 20 September 2021

19. *seattleflu/assembly*. Seattle Flu Study; 2021. Accessed 2021/02/01/23:06:36. https://github.com/seattleflu/assembly

20. Hadfield J, Megill C, Bell SM, et al. Nextstrain: real-time tracking of pathogen evolution. *Bioinformatics*. 2018/12/01/ 2018;34(23):4121-4123. doi:10.1093/bioinformatics/bty407

21. Shu Y, McCauley J. GISAID: Global initiative on sharing all influenza data – from vision to reality. *Eurosurveillance*. 2017/03/30/ 2017;22(13)doi:10.2807/1560-7917.ES.2017.22.13.30494

22. Office of Enrollment Information Services: Data M. Quick Stats: Bothell Enrollment Autumn 2020. *University of Washington*.

23. Office of Enrollment Information Services: Data M. Quick Stats: Tacoma Enrollment Autumn 2020. *University of Washington*. 2020 2020;

24. Office of Enrollment Information Services: Data M. Quick Stats: Seattle Enrollment Autumn 2020. *University of Washington*. 2020 2020;

25. University of Washington COVID-19 Case Tracking Dashboard. *University of Washington*.

26. COVID-19 Data Dashboard. *Washington Department of Health*.

27. Vang KE. Participation in Fraternity and Sorority Activities and the Spread of COVID-19 Among Residential University Communities — Arkansas, August 21–September 5, 2020. *MMWR Morb Mortal Wkly Rep*. 2021 2021;70doi:10.15585/mmwr.mm7001a5

28. Rubin D, Eisen M, Collins S, Pennington JW, Wang X, Coffin S. SARS-CoV-2 Infection in Public School District Employees Following a District-Wide Vaccination Program - Philadelphia County, Pennsylvania, March 21-April 23, 2021. *MMWR Morb Mortal Wkly Rep*. Jul 30 2021;70(30):1040-1043. doi:10.15585/mmwr.mm7030e1

29. Pray IW. Trends in Outbreak-Associated Cases of COVID-19 — Wisconsin, March–November 2020. *MMWR Morb Mortal Wkly Rep*. 2021 2021;70doi:10.15585/mmwr.mm7004a2

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30. Richmond CS, Sabin AP, Jobe DA, Lovrich SD, Kenny PA. SARS-CoV-2 sequencing reveals rapid transmission from college student clusters resulting in morbidity and deaths in vulnerable populations. *medRxiv*. 2020/10/14/ 2020:2020.10.12.20210294. doi:10.1101/2020.10.12.20210294

31. Losina E, Leifer V, Millham L, et al. College Campuses and COVID-19 Mitigation: Clinical and Economic Value. *Ann Intern Med*. 2020/12/21/ 2020;doi:10.7326/M20-6558

32. *SCAN Data Results and Technical Report #3*. 2020. *Greater Seattle Coronavirus Assessment Network*. 2020/08/03/. Accessed 2021/02/14/. https://publichealthinsider.com/wp-content/uploads/2020/08/8.3-SCAN-Technical-Report-3_FINAL_CLEAN.pdf

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FIGURES

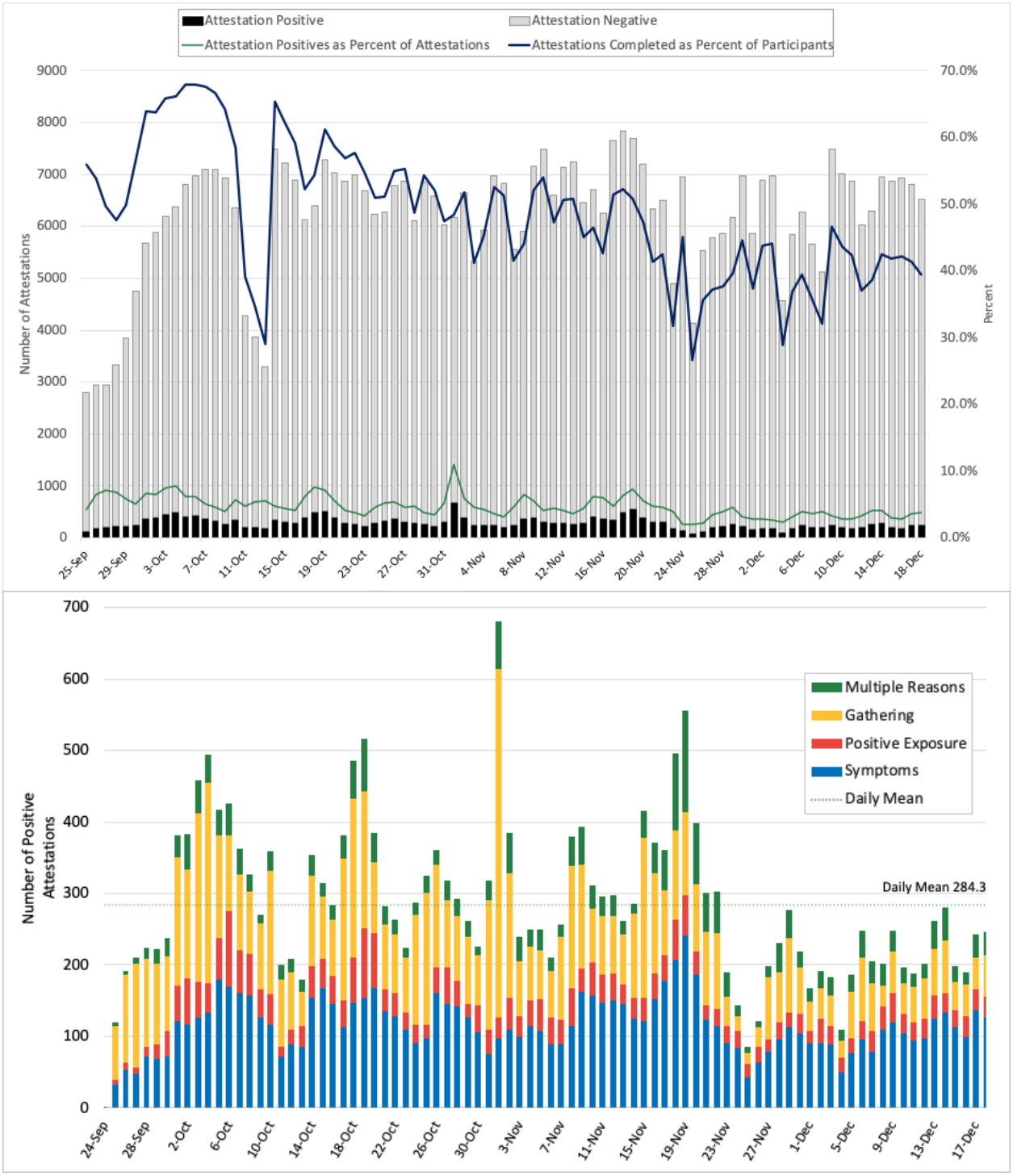

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Figure 1. Daily attestation survey engagement over time. (A) Number of daily attestations completed daily during the study period. Between October 11-13, 2020 we experienced an outage of the text messaging service used to send daily attestation survey invites and this resulted in a reduced response rate. (B) Positive daily attestations stratified by reason for positive attestation. A marked increase in positive attestations was observed the day after Halloween, when 487 reported gathering, a 4.7-fold increase from the mean daily gathering attestation positive of 105.

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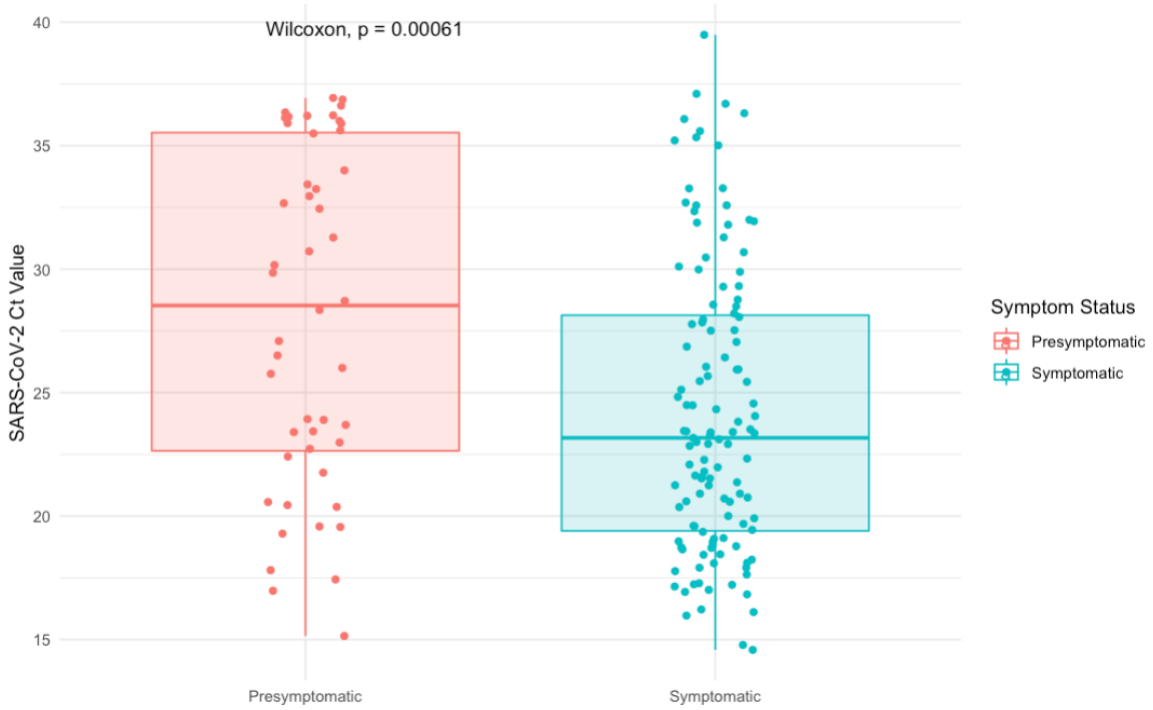

Figure 2. Comparison of viral load in symptomatic (n=124) vs. presymptomatic (n=48) positive and inconclusive samples. Cycle threshold (Ct) for samples (each represented by one dot) tested using our protocol with nucleic acid extraction (before November 18) are shown here. Complete data is shown in Supplemental Figure 6. Box plots show the median values and 25th and 75th percentiles, with vertical lines demonstrating the range of values.

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Figure 3A.

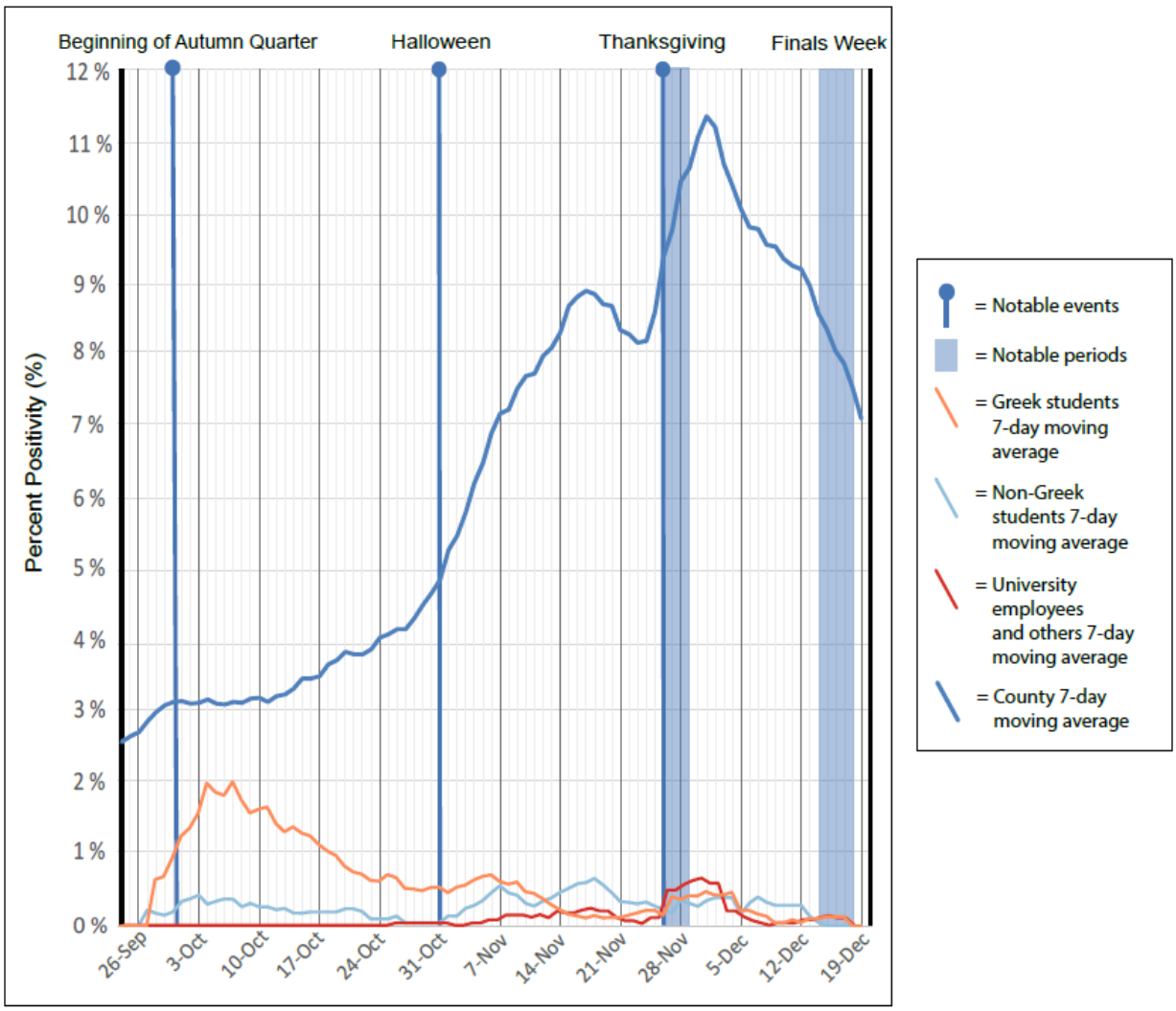

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Figure 3B.

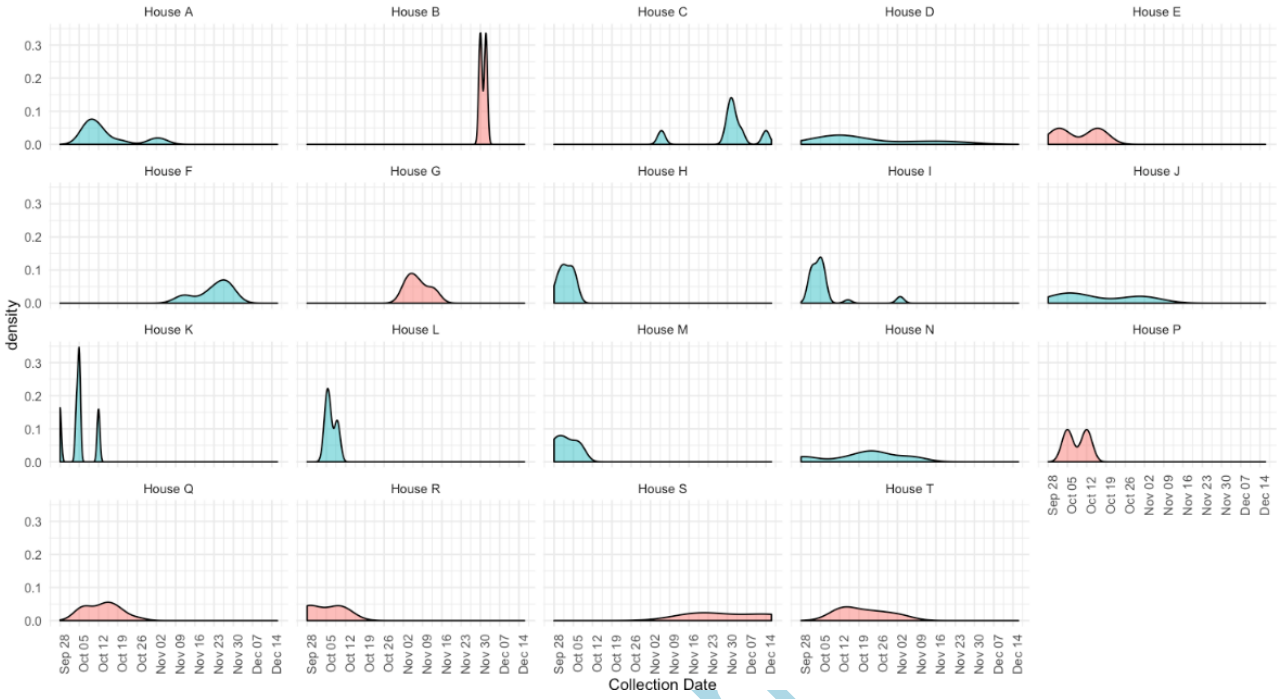

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Figure 3C.

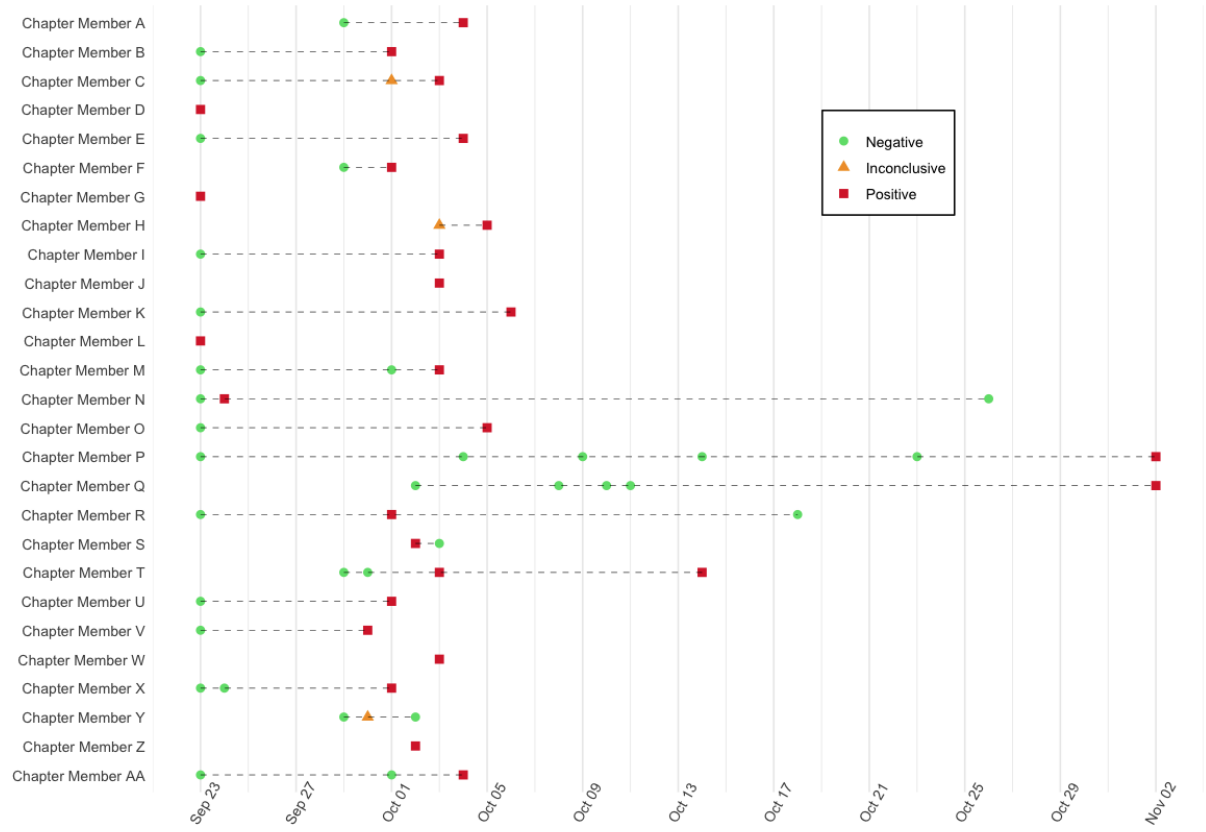

Figure 3. Dynamics of a Greek community outbreak. (A) Percent positivity over time of university groups and the surrounding county. The employee category includes university staff and faculty, and the Greek-affiliated students category includes all Greek-affiliated students including those living in Greek houses, Greek off-campus housing, and Greek-affiliated dorm residents. (B) Greek Chapter-level SARS-CoV-2 outbreak dynamics. Counts of cases identified by chapter during Autumn quarter. Sororities are shown in blue and the fraternities in red. Chapters with no infections detected (n=20) or <=2 infections detected (n=5) are not shown. (C) Example of chapter-level individual SARS-CoV-2 outbreak dynamics within one Greek chapter (ending on November 2nd). Lines represent individual study participants tested multiple times, and dots signify a single test.

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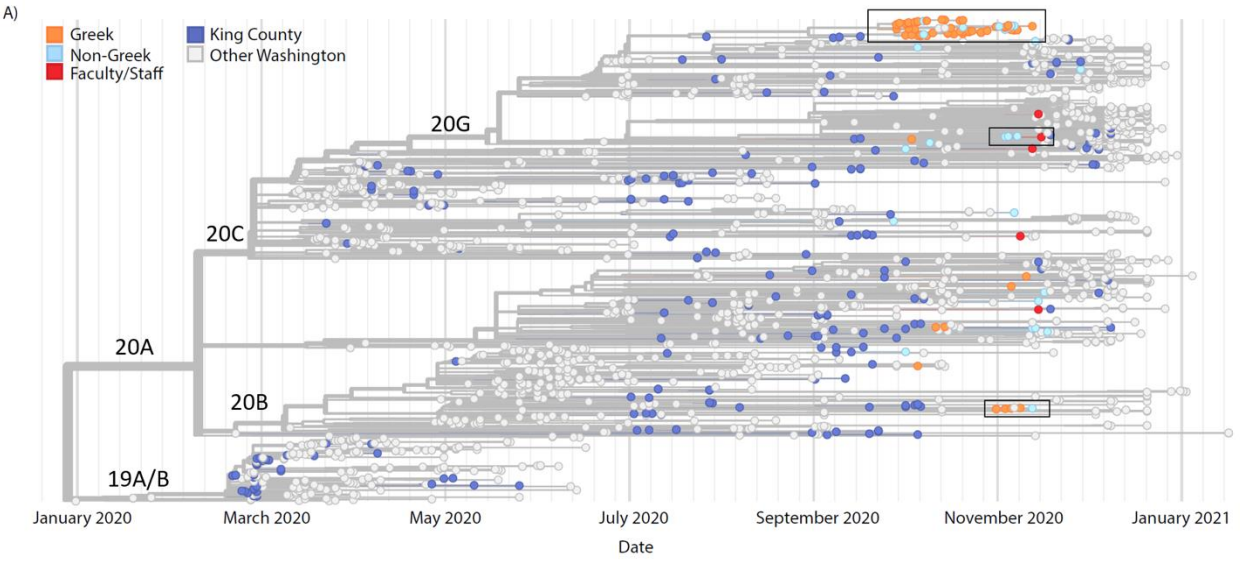

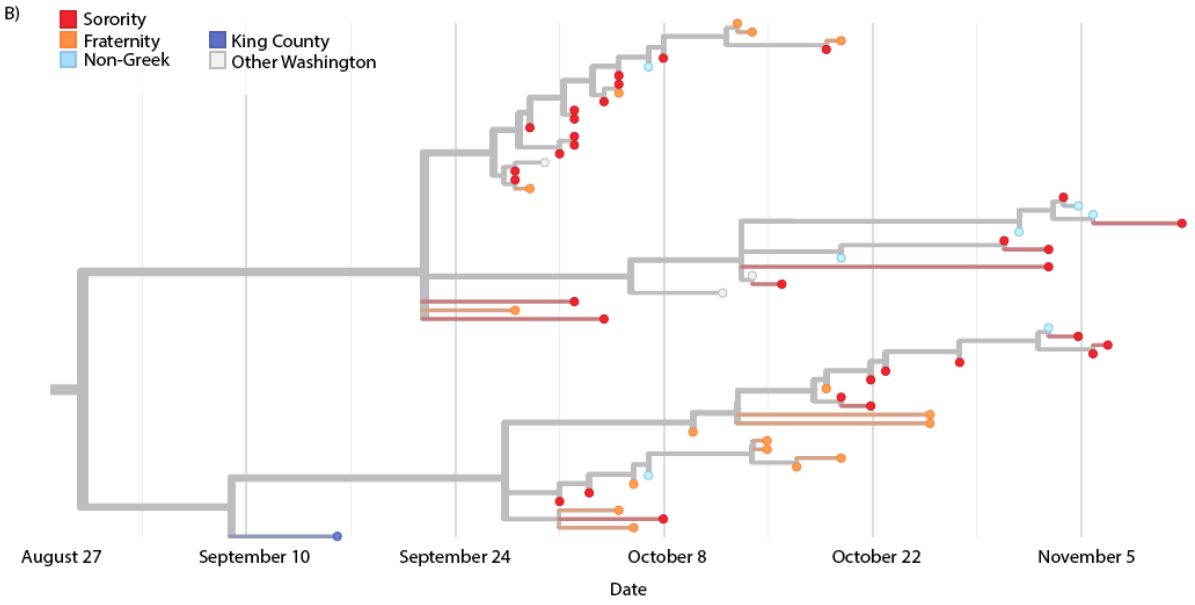

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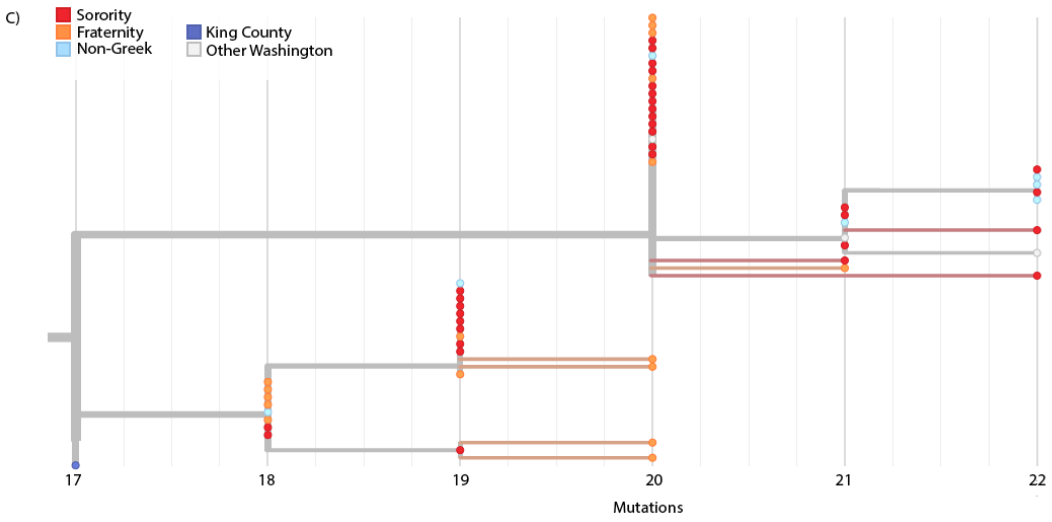

Figure 4: Molecular Epidemiology of a university outbreak. A) Phylogenetic tree of SARS-CoV-2 samples from Washington, including 88 samples from this study. Included here are all SARS-CoV-2 genomes from Washington collected on or after September 25, 2020, a random subsample of 1000 Washington samples collected prior to September 25, and the Wuhan/Hu-1 reference genome. Samples are positioned on the X axis by date of collection. B) Detail of a cluster of university genomes organized horizontally by collection date, and C) by divergence, or the number of genetic changes relative to SARS-CoV-2 reference genome.

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TABLE

Table 1A. Sociodemographic Characteristics of Study Participants

	Students (N=11027)	Staff (N=3898)	Faculty (N=1426)	Other* (N=125)	Overall (N=16476)
Age (years)					
Median [Min, Max]	20 [16, 78]	40 [20, 81]	45 [21, 83]	31 [19, 77]	23 [16, 83]
Age Group					
16-17	52 (0.5%)	0 (0%)	0 (0%)	0 (0%)	52 (0.3%)
18-49	10921 (99.0%)	2709 (69.5%)	870 (61.0%)	105 (84.0%)	14605 (88.6%)
50-64	38 (0.3%)	1051 (27.0%)	387 (27.1%)	12 (9.6%)	1488 (9.0%)
65+	16 (0.1%)	136 (3.5%)	168 (11.8%)	8 (6.4%)	328 (2.0%)
Sex assigned at birth[†]					
Female	6769 (61.4%)	2473 (63.4%)	765 (53.6%)	75 (60.0%)	10082 (61.2%)
Male	4211 (38.2%)	1411 (36.2%)	658 (46.1%)	50 (40.0%)	6330 (38.4%)
Race[‡]					

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American Indian or Alaska Native	45 (0.4%)	17 (0.4%)	6 (0.4%)	0 (0%)	68 (0.4%)
Asian	2736 (24.8%)	486 (12.5%)	189 (13.3%)	21 (16.8%)	3432 (20.8%)
Black or African American	220 (2.0%)	127 (3.3%)	34 (2.4%)	2 (1.6%)	383 (2.3%)
Multiple Races	1099 (10.0%)	229 (5.9%)	44 (3.1%)	8 (6.4%)	1380 (8.4%)
Native Hawaiian or other Pacific Islander	30 (0.3%)	26 (0.7%)	1 (0.1%)	0 (0%)	57 (0.3%)
Other	333 (3.0%)	109 (2.8%)	38 (2.7%)	3 (2.4%)	483 (2.9%)
White	6353 (57.6%)	2805 (72.0%)	1073 (75.2%)	83 (66.4%)	10314 (62.6%)
Missing	211 (1.9%)	99 (2.5%)	41 (2.9%)	8 (6.4%)	359 (2.2%)
Hispanic/Latinx Ethnicity	896 (8.1%)	265 (6.8%)	79 (5.5%)	12 (9.6%)	1252 (7.6%)
UW Greek Member	2672 (24.2%)				
Housing [§]					
Greek (Chapter House and Live Out)	1763 (16.0%)	0 (0%)	1 (0.1%)	1 (0.8%)	1765 (10.7%)
Off-Campus Housing	7116	3863	1423	124	12526

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	(64.5%)	(99.1%)	(99.8%)	(99.2%)	(76.0%)
On-Campus Housing	2101 (19.1%)	11 (0.3%)	0 (0%)	0 (0%)	2112 (12.8%)
Shelter, transitional housing, or other	47 (0.4%)	24 (0.6%)	2 (0.1%)	0 (0%)	73 (0.4%)
On-campus frequency this quarter ¶					
Do not come to campus	3345 (30.3%)	916 (23.5%)	252 (17.7%)	17 (13.6%)	4530 (27.5%)
One day a week or less	3301 (29.9%)	1161 (29.8%)	583 (40.9%)	41 (32.8%)	5086 (30.9%)
Two days a week or more	4381 (39.7%)	1820 (46.7%)	591 (41.4%)	67 (53.6%)	6859 (41.6%)
Registered for In-Person Classes	1712 (15.5%)				
Tested for SARS-CoV-2 prior to enrollment	6556 (59.5%)	1625 (41.7%)	632 (44.3%)	67 (53.6%)	8880 (53.9%)
Campus					
Main Campus	10539 (95.6%)	3650 (93.6%)	1285 (90.1%)	124 (99.2%)	15598 (94.7%)
Satellite Campus A	191 (1.7%)	95 (2.4%)	60 (4.2%)	0 (0%)	346 (2.1%)

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Satellite Campus B	297 (2.7%)	153 (3.9%)	81 (5.7%)	1 (0.8%)	532 (3.2%)
In the past 7 days, how often did you wear a face mask in public to protect others from getting sick? [#]					
Always	10719 (97.2%)	3800 (97.5%)	1373 (96.3%)	122 (97.6%)	16014 (97.2%)
Sometimes	297 (2.7%)	95 (2.4%)	50 (3.5%)	3 (2.4%)	445 (2.7%)
Never	2 (0.0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.0%)
In the past 7 days, how often did you try to stay 6 feet away from people who don't live with you?**					
Always	7552 (68.5%)	3161 (81.1%)	1211 (84.9%)	98 (78.4%)	12022 (73.0%)
Sometimes	3418 (31.0%)	728 (18.7%)	214 (15.0%)	27 (21.6%)	4387 (26.6%)
Never	42 (0.4%)	5 (0.1%)	1 (0.1%)	0 (0%)	48 (0.3%)

**Those in the 'Other' affiliation category included postdoctoral fellows, externs, volunteers, and other university affiliates*

[†] 4 participants reported "Other" for sex, and 60 had missing sex

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‡*359 participants had missing race and 145 participants chose "Prefer not to say" for Hispanic/Latinx Ethnicity*

§ *A Greek 'Live Out' is a private house or apartment that is shared by members of the same Greek chapter. On-campus housing was defined as dormitories, apartments, and family units.*

¶*1 participant had missing 'Frequency on-campus'*

#*15 participants did not answer 'In the past 7 days, how often did you wear a face mask in public to protect others from getting sick?'*

***19 participants did not answer 'In the past 7 days, how often did you try to stay 6 feet away from people who don't live with you?'*

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Table 1B. Characteristics of Testing Instances by SARS-CoV-2 Result

	Positive	Overall*	Percent Positivity (95% CI†)
	(n=265)	(n=29783)	
Any symptoms	161	11116	1.4% (1.2 - 1.7)
Attended large indoor gathering	57	6996	0.8% (0.6 - 1.1)
Close contact with known positive	92	3877	2.4% (1.9 - 2.9)
Baseline test	35	5700	0.6% (0.4 - 0.9)
Outbreak test	83	5257	1.6% (1.3 - 2)
Holiday test	3	1244	0.2% (0 - 0.7)
Walk-in (no invite)	18	1788	1.0% (0.6 - 1.6)
Risk tier			
Tier 1	220	19239	1.1% (1 - 1.3)
Tier 2	12	4291	0.3% (0.1 - 0.5)
Tier 3	33	6253	0.5% (0.4 - 0.7)

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Affiliation‡			
Student	240	23802	1.0% (0.9 - 1.1)
Staff	19	4417	0.4% (0.3 - 0.7)
Faculty	4	1467	0.3% (0.1 - 0.7)
Age group			
13-17	2	153	1.3% (0.2 - 4.6)
18-49	254	27783	0.9% (0.8 - 1)
50-64	8	1548	0.5% (0.2 - 1)
65+	1	299	0.3% (0 - 1.8)
Sex assigned at birth			
Female	180	19234	0.9% (0.8 - 1.1)
Male	84	10474	0.8% (0.6 - 1)
House members			
Lives alone	16	2708	0.6% (0.3 - 1)
2 people	63	8051	0.8% (0.6 - 1)
3-5 people	34	7468	0.5% (0.3 - 0.6)
6+ people	152	11556	1.3% (1.1 - 1.5)
UW Greek Member	176	12045	1.5% (1.3 - 1.7)

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Race			
American Indian or Alaska Native	0	144	0.0% (0 - 2.5)
Asian	32	4672	0.7% (0.5 - 1)
Black or African American	2	460	0.4% (0.1 - 1.6)
Native Hawaiian or other Pacific Islander	0	59	0.0% (0 - 6.1)
White	191	20464	0.9% (0.8 - 1.1)
Multiple Races	26	2808	0.9% (0.6 - 1.4)
Other	10	707	1.4% (0.7 - 2.6)
Latinx/Hispanic	35	2000	1.8% (1.2 - 2.4)
Housing type			
Apartment (off campus)	32	7403	0.4% (0.3 - 0.6)
Dormitory/Residence Hall (on campus)	43	3507	1.2% (0.9 - 1.6)
House/condo/townhouse (off campus)	62	10433	0.6% (0.5 - 0.8)
Permanent supportive/ transitional housing (off campus)	0	6	0.0% (0 - 45.9)
Homeless Shelter (off campus)	0	5	0.0% (0 - 52.2)
UW Greek Chapter House (off campus)	104	6145	1.7% (1.4 - 2)
UW Greek Live Out (off campus)	24	2168	1.1% (0.7 - 1.6)

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Other	0	116	0.0% (0 - 3.1)
Overall	265	29783	0.9% (0.8 - 1)

**Overall' includes 60 samples that were never tested*

†*Confidence intervals generated using Clopper-Pearson exact methods*

‡*86 'Other' and 15 'Volunteer' affiliation*

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