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Monitoring SARS-CoV-2 incidence and seroconversion in a university cohort in California, June to August 2020

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1 **Title:** Monitoring SARS-CoV-2 incidence and seroconversion in a university cohort in California,
2 June to August 2020

3
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1
2
3 **27 Abstract**
4

5 **28 Objective:** To inform effective SARS-CoV-2 mitigation strategies in university settings, we
6
7 **29** piloted an integrated symptom and exposure monitoring and testing system among a cohort of
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9 **30** university students and employees.

11 **31 Methods:** We aimed to identify incident SARS-CoV-2 infections in a longitudinal cohort of 2,180
12
13 **32** students and 738 employees of a public university in California from June to August 2020. At
14
15 **33** baseline and endline, we tested participants for active SARS-CoV-2 infection via quantitative
16
17 **34** polymerase chain reaction (qPCR) test and collected blood for antibody testing. Participants
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19 **35** received notifications to complete additional qPCR tests throughout the study if they reported
20
21 **36** symptoms or exposures in daily surveys or were selected for surveillance testing. Viral whole
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23 **37** genome sequencing was performed on positive qPCR samples, and phylogenetic trees were
24
25 **38** constructed with these genomes and external genomes retrieved from GISAID.

28 **39 Results:** Over the study period, 57 students (2.6%) and 3 employees (0.3%) were diagnosed
29
30 **40** with SARS-CoV-2 infection via qPCR test. Phylogenetic analyses revealed that a super-
31
32 **41** spreader event among undergraduates in congregate housing accounted for at least 48% of
33
34 **42** cases but did not spread beyond campus. Test positivity was higher among participants who
35
36 **43** self-reported symptoms (incidence rate ratio [IRR]: 12.4; 95% confidence interval [CI]: 7.3, 21.3)
37
38 **44** or had household exposures (IRR: 12.3; 95% CI: 5.6, 26.9) which triggered notifications to test.
39
40 **45** Most (91%) participants with newly identified antibodies at endline had been diagnosed with
41
42 **46** incident infection via qPCR test during the study.

45 **47 Conclusions:** Our findings suggest that integrated monitoring systems can successfully identify
46
47 **48** and link at-risk students to SARS-CoV-2 testing. Building upon such systems may prove key in
48
49 **49** the next stage of the pandemic, as universities grapple with highly transmissible variants,
50
51 **50** incomplete vaccine coverage and breakthrough infections, and reduced reliance on prevention
52
53 **51** strategies such as masking and remote learning.
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52 **Strengths and limitations of this study**

- 53 ● The study is strengthened by rich longitudinal data including more than 117,000 daily
54 symptom surveys; 17,000 weekly exposure surveys; 7,600 qPCR tests to detect active
55 SARS-CoV-2 infection; and 4,900 antibody tests to detect previous infection collected
56 from 2,918 university students and employees over three months.
- 57 ● Using seroconversion data from serial antibody tests and phylogenetic analyses
58 comparing viral genome sequences to a broader database, we were able to evaluate the
59 extent to which the study system identified incident cases and contained an outbreak
60 among university students. However, our identification of participants who seroconverted
61 between baseline and endline may be incomplete due to loss-to-follow up and imperfect
62 sensitivity of SARS-CoV-2 antibody testing.
- 63 ● A high proportion of identified cases were traced to one outbreak, limiting the
64 generalizability of our exploratory assessment of risk factors for incident infection. While
65 self-referral into the study in the context of the outbreak is likely to induce selection bias,
66 it also illustrates the utility of implementing non-stigmatizing, incentivized testing
67 approaches to increase testing uptake among at-risk students.
- 68 ● As the study took place before the development of highly transmissible variants and
69 vaccine rollout, further research is necessary to adapt and evaluate similar systems in
70 the context of both heightened transmissibility and more prevalent natural and vaccine-
71 induced immunity.

72 **Background**

73 Universities have been identified as hotspots for SARS-CoV-2 transmission in the United
74 States,¹ where SARS-CoV-2 incidence is highest among young adults.² Young adults may be
75 less likely to adhere to social distancing guidelines and more likely to experience workplace
76 exposure (for example, at food service or retail jobs).² Their risk may be heightened in university
77 settings where many live in congregate housing, interact with wide social networks, or attend
78 large gatherings.³ Although young adults are at low risk of serious acute illness or death from
79 COVID-19 (the disease caused by SARS-CoV-2),⁴ the higher likelihood of asymptomatic or
80 mildly symptomatic infection in this age group makes young adults a key population through
81 which SARS-CoV-2 may be spread to other, more vulnerable groups.^{2,5} Indeed, there is
82 evidence that transmission among university students may lead to increased COVID-19-related
83 mortality in the surrounding counties.⁶⁻⁸ Although widespread vaccination has enabled most
84 campuses to return to in-person activities, the elimination of SARS-CoV-2 transmission in
85 campus populations may be stymied by vaccine hesitancy among students and employees and
86 breakthrough infection and subsequent transmission by vaccinated persons, particularly in the
87 context of waning immunity and viral variants which reduce vaccine efficacy.^{9,10} Therefore, rapid
88 and resource-efficient identification of incident cases in university populations is a critical first
89 step of outbreak investigation and control, followed by isolation, case investigation, and contact
90 tracing, to minimize transmission within campus and to the broader community.

91 Universities have adopted a wide range of approaches for testing and outbreak
92 mitigation.¹¹⁻¹³ While a number of well-resourced universities have scaled up testing capacity in
93 order to frequently test all students and employees accessing campus or living in university-
94 affiliated housing,¹³ many other universities do not have well-defined testing strategies or restrict
95 testing to those with symptoms or known exposure.¹² Beyond investing in testing programs,
96 some universities have sought to reduce on-campus transmission by mandating the completion
97 of self-administered symptom screening tools by students and employees. However, such tools

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3 98 have primarily been used to regulate daily access to campus (i.e., deny entry to those who
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5 99 report COVID-19-like symptoms), rather than to detect emergent outbreaks among university
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7 100 populations. As universities resume normal operations and discontinue mitigation strategies
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9 101 such as masking, non-punitive, resource-efficient strategies which can both identify those who
10
11 102 are at highest risk of infection *and* expediently link them to low-barrier testing services may play
12
13 103 a key role in transitioning from a “one-size-fits-all” approach of uniform testing to a sustainable
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15 104 monitoring paradigm.

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17
18 105 In 2020, we piloted an integrated symptom and exposure monitoring and testing system
19
20 106 designed to identify incident SARS-CoV-2 infections among a cohort of university students and
21
22 107 employees.¹⁴ Here we describe the incidence and seroprevalence of SARS-CoV-2 infection
23
24 108 within this cohort to evaluate the extent to which incident infections were successfully detected
25
26 109 and contained over the study period, identify sociodemographic factors associated with incident
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28 110 infection, and ascertain which self-reported symptoms and exposures tracked by the monitoring
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30 111 system were predictive of test positivity, with the ultimate objective of informing monitoring and
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32 112 testing strategies in university settings.

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36 37 114 **Methods**

38 39 115 *Study design and setting*

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41 116 The study comprised three prospective cohorts of University of California, Berkeley
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43 117 affiliates followed from June to August 2020: students, essential workers (i.e., employees
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45 118 working on campus in health, facilities, or key student services), and other employees
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47 119 (hereafter, “faculty/staff”). We report the findings according to the Strengthening the Reporting
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49 120 of Observational Studies in Epidemiology (STROBE) checklist for cohort studies.¹⁵

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51 121 Throughout the study period, UC Berkeley did not offer in-person classes, and on-
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53 122 campus work was restricted to essential workers and a small subset of faculty, staff, and
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55 123 student researchers. Although few students were living in on-campus residence halls, many

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3 124 students continued to live in congregate living settings off campus, such as fraternities,
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5 125 sororities, and co-operative housing.
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9 127 *Participant recruitment and eligibility*

11 128 The study was promoted through targeted messages from university officials to campus
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13 129 email listservs and social media platforms from early June to mid-July 2020. To increase reach
14
15 130 to students expected to be at higher risk of COVID-19, we also placed flyers in congregate living
16
17 131 settings and conducted in-person recruitment for student athletes who had resumed training on
18
19 132 campus. Participants were eligible to enroll in the study if they were at least 18 years of age,
20
21 133 were a current student or employee at UC Berkeley, and planned to live in or near Berkeley
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23 134 during summer 2020. Specific eligibility criteria and enrollment windows varied by cohort
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25 135 (Supplementary Table 1, Supplementary Figure 1).
26
27

28 136 Upon enrollment, participants were linked to an online baseline survey that collected
29
30 137 sociodemographic data and information about their COVID-19-related health history.
31
32 138 Participants were then referred to a baseline testing appointment at University Health Services
33
34 139 (UHS) which included a SARS-CoV-2 quantitative polymerase chain reaction (qPCR) test and
35
36 140 blood collection for antibody testing (procedures described below). To facilitate daily
37
38 141 temperature monitoring, study staff also provided participants with free oral thermometers upon
39
40 142 request at testing appointments. Participants who completed this appointment or a non-study
41
42 143 qPCR test at UHS by July 20th were eligible to remain in the study. We pre-specified a
43
44 144 maximum sample size of 4,000 participants across cohorts but did not reach this limit before the
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46 145 final day of baseline data collection.
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51 147 *Symptom and exposure surveys*

53 148 Participants received daily text messages or emails, depending on their preference
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55 149 specified in the baseline survey, which linked to short symptom surveys through which they
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3 150 reported their daily body temperature and any symptoms of illness. Once per week, the daily
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5 151 survey included a longer exposure module, which asked about recent symptoms of illness
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7 152 among their household member(s), potential exposure(s) to COVID-19, and activities related to
8
9 153 potential COVID-19 risk. All surveys were administered via REDCap.^{16,17}
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13 155 *Endline survey and testing*

15 156 In early August, participants were sent an endline survey which collected updated
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17 157 information on their COVID-19 history to identify any diagnoses outside of the study.

19 158 Participants in the student and essential worker cohorts were also invited to complete endline
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21 159 testing appointments by August 18th, including a final qPCR test and blood collection.
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26 161 *qPCR testing*

28 162 Midturbinate nasal and oral swabs were collected by UHS clinical staff and tested for
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30 163 SARS-CoV-2 by qPCR at the Innovative Genomics Institute (IGI).¹⁸ qPCR tests were performed
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32 164 at baseline for all three cohorts and at endline for the student and essential worker cohorts.
33

34 165 Between baseline and endline testing, additional qPCR tests were performed for the following
35
36 166 reasons:

- 38 167 • **Symptom- or exposure-based tests triggered based on participants' responses in**
40
41 168 **daily surveys:** Participants who reported COVID-19-like signs or symptoms¹ (in
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43 169 themselves or household member(s)) or who reported a suspected or confirmed COVID-
44
45 170 19 case in their household were automatically notified to sign up for a qPCR test.

54
55 ¹ Signs or symptoms which triggered a testing notification when reported were: temperature of $\geq 100.4^{\circ}\text{F}$, dry cough
56 (without mucus), coughing up mucus, feeling feverish, unusual pain or pressure in the chest, difficulty breathing,
57 shortness of breath, unexplained trouble thinking or concentrating, loss of sense of taste, or loss of sense of smell.

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3 171 • **Random surveillance testing:** A subset of participants in the student and faculty/staff
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5 172 cohorts who had not had a qPCR test within a week were randomly selected and
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7 173 emailed notifications to come in for surveillance testing in July.
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9 174 • **Address-based surveillance testing:** Participants who lived at the same address as
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11 175 another participant who tested positive for SARS-CoV-2 were immediately emailed
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13 176 surveillance testing notifications. Following an outbreak among group-housed students
14
15 177 in early July, surveillance testing notifications were also emailed to all participants who
16
17 178 had not been tested within the week and who reported living in fraternities, sororities, or
18
19 179 co-operative housing.
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22 180 • **Participant-initiated testing:** Participants could self-schedule study testing
23
24 181 appointments on demand, with or without consulting a healthcare provider and
25
26 182 regardless of exposure history.

27
28 183 Participants with positive qPCR test results were informed by phone by UHS clinical staff, who
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30 184 provided guidance on isolation and performed case investigation to identify potential contacts.
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32 185 Participants with negative qPCR test results were informed of their results via the UHS online
33
34 186 patient portal.
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38 39 188 *SARS-CoV-2 sequencing and phylogenetic analyses*

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41 189 Viral whole genome sequencing was performed on a set of positive samples at the IGI,
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43 190 using previously described procedures.¹⁹ Briefly, SARS-CoV-2 RNA extracted from swabs was
44
45 191 reverse transcribed using SuperScript IV (Invitrogen), and the viral genome was amplified from
46
47 192 the resulting cDNA in four separate qPCR reactions using distinct primer sets tiling the SARS-
48
49 193 CoV-2 genome. The four qPCR reactions were pooled 1:1:1:1 and diluted 1:50 in H₂O. A
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51 194 second qPCR reaction was set up to add Nextera Unique Dual Indexing (UDI) sequences to
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53 195 either end of the amplicons. The resulting qPCR reaction was cleaned up using 0.7x AMPureXP
54
55 196 beads (Beckman Coulter) and quantified using a Qubit dsDNA HS Assay Kit (Thermo Fisher).

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3 197 The libraries were then pooled to an equimolar ratio and sequenced with a 10% PhiX spike in
4
5 198 using a MiSeq v3 kit at 300bp PE reads.
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7 199 Fastq sequencing files were processed through a custom pipeline using publicly
8
9 200 available software. The reads were preprocessed by quality trimming, removing adaptors, and
10
11 201 PhiX cleaning with BBTtools,²⁰ and then aligned to the Wuhan reference sequence
12
13 202 (NC_045512.2) with minimap2 v2.16-r922. ARTICv3 primers were trimmed, and the consensus
14
15 203 sequence was built with iVar v1.3.1, where an 'N' is called if the depth is less than 10 reads at
16
17 204 any nucleotide. The genomes were then processed through the Nextstrain Auger pipeline with
18
19 205 other genomes from GISAID to construct a maximum likelihood tree.^{21,22} Several phylogenies
20
21 206 were constructed for this analysis: a tree of 7,091 genomes subsampled from the worldwide
22
23 207 genomes in GISAID at the time (approximately 200,000 genomes as of October 2020) was used
24
25 208 to place the IGI genomes in the larger tree; a tree with all IGI genomes sequenced at the time of
26
27 209 analysis (356 genomes); and a tree containing 500 genomes (from 1 million genomes as of April
28
29 210 2021) was constructed using USHER.²³
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34 212 *Antibody testing*

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37 213 Up to 10 mL of blood was collected by phlebotomists via venipuncture at baseline from
38
39 214 participants in all three cohorts and again at endline from participants in the student and
40
41 215 essential worker cohorts. Blood was centrifuged and serum was stored at -20°C for 2 to 4
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43 216 months before being tested at Vitalant Research Institute using the VITROS Immunodiagnostic
44
45 217 Products Anti-SARS-CoV-2 Total Reagent Pack, which detects IgA, IgG, and IgM antibodies
46
47 218 and has an estimated clinical specificity of 100% and unreported sensitivity.²⁴
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51 220 *Participant compensation*

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54 221 Participants in the student cohort received a \$50 gift card after completing baseline
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56 222 testing and 10 daily surveys; this incentive was conditional on daily survey completion to
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223 encourage early habit formation.²⁵ Student participants received a second \$50 gift card at their
224 endline testing appointment. To facilitate travel to and from UHS for testing appointments,
225 student participants were also offered pre-paid car rides via a ride-sharing app.

226 Participants in the essential worker cohort received a gift card worth \$1 per daily survey
227 completed (to a maximum of \$70) after the study ended. Participants in the faculty/staff cohort
228 were not compensated.

229

230 *Statistical analyses*

231 To identify sociodemographic factors associated with incident infection, we used Poisson
232 regression to estimate unadjusted incidence rate ratios (IRRs) for SARS-CoV-2 infection by
233 study cohort and within strata of sociodemographic variables self-reported in the baseline
234 survey (e.g., age, gender, housing type), setting person-months of enrollment as an offset term
235 to account for differing lengths of follow-up.

236 We also calculated IRRs comparing test positivity by recent signs/symptoms, exposures,
237 and activities reported in the daily and weekly surveys. We estimated IRRs for several
238 temperature thresholds (i.e., $\geq 100.4^{\circ}\text{F}$, $\geq 100.0^{\circ}\text{F}$, $\geq 99.0^{\circ}\text{F}$) to compare to symptom-specific
239 IRRs; however, continuous associations between temperature and positivity have been
240 previously explored in this cohort.²⁶ We accounted for clustered observations due to repeated
241 tests per participant using a generalized estimating equation approach with Huber-White
242 standard error estimates and an exchangeable working correlation structure.²⁷

243 Finally, to assess the extent to which the testing and monitoring system captured
244 incident infections, we identified participants who seroconverted from having non-reactive (no
245 antibodies detected) to reactive (antibodies detected) blood samples between baseline and
246 endline and calculated the proportion of these participants who were also diagnosed with
247 incident SARS-CoV-2 infection via positive qPCR test during the study period. Analyses were
248 conducted in R version 4.0.4.²⁸

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5 250 *Ethical approvals*

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7 251 All study activities were approved by the University of California, Berkeley Committee for
8
9 252 the Protection of Human Subjects (#2020-06-13349, #2020-05-13261, #2020-04-13238).

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14 254 *Patient and public involvement*

15 255 The study's target population comprised university students and employees. While the
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17 256 study was conducted by faculty, staff, and graduate students from the UC Berkeley School of
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19 257 Public Health, University Health Services, and the Innovative Genomics Institute, the broader
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21 258 student body and university workforce were not involved in designing the study or selecting the
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23 259 research question, outcome measures, or method of disseminating results.

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28 261 **Results**29
30 262 *Participant recruitment and retention*

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32 263 Between June 1 and July 20th, 2020, we enrolled 2,180 students, 268 essential workers,
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34 264 and 470 faculty/staff who completed at least one qPCR test or antibody test (Table 1,
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36 265 Supplementary Figure 1). The student cohort was split between undergraduate (52%) and
37
38 266 graduate (48%) students. Nearly half (44%) of essential workers worked in health services.
39
40 267 While 85% of essential workers were working on campus at the time of enrollment, most (81%)
41
42 268 faculty/staff were working entirely remotely. At the time of enrollment, only 12 (0.4%)
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44 269 participants reported a previous COVID-19 diagnosis.

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46 270 Participants provided a total of 5,545 person-months of follow-up from enrollment to the
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48 271 end of the study (mean person-days per participant: 57, range: 32-78). Participants completed a
49
50 272 mean of 40 daily symptom surveys and 6 weekly exposure surveys over the study period, for a
51
52 273 total of 117,235 symptom and 17,172 exposure surveys. A subset of participants did not
53
54 274 complete any daily symptom surveys (1.7%) or weekly exposure surveys (4.2%).

Table 1. Baseline characteristics of participants in the Berkeley COVID-19 Safe Campus Initiative by study cohort, June-August 2020.

	All	Students	Essential Workers	Faculty/Staff
N (row %)	2,918 (100)	2,180 (74.7)	268 (9.2)	470 (16.1)
Age, mean \pm SD	29.4 \pm 11.6	24.3 \pm 5.4	42.5 \pm 12.3	45.2 \pm 12.3
Gender, n (column %)				
Man	1,177 (40.3)	911 (41.8)	103 (38.4)	163 (34.7)
Woman	1,653 (56.6)	1,187 (54.4)	164 (61.2)	302 (64.3)
Non-binary/other	51 (1.7)	46 (2.1)	1 (0.4)	4 (0.9)
Race/ethnicity, n (column %)*				
American Indian/Alaska Native	39 (1.3)	29 (1.3)	2 (0.7)	8 (1.7)
Asian/Pacific Islander	833 (28.5)	703 (32.2)	66 (24.6)	64 (13.6)
Black/African American	103 (3.5)	83 (3.8)	16 (6.0)	4 (0.9)
Hispanic/Latine/Spanish origin	420 (14.4)	346 (15.9)	39 (14.6)	35 (7.4)
White	1,814 (62.2)	1,261 (57.8)	160 (59.7)	393 (83.6)
Other	280 (9.6)	223 (10.2)	31 (11.6)	26 (5.5)
Program level, n (column %)				
Undergraduate	-	1,114 (51.7)	-	-
Graduate	-	1,039 (48.2)	-	-
Living at fraternity/sorority, n (column %)	-	125 (5.7%)	-	-
Education, n (column %)				
High school diploma/GED	-	-	6 (2.2)	0 (0)
Some college or trade school	-	-	59 (22.0)	13 (2.8)
Bachelor's degree	-	-	78 (29.1)	119 (25.3)
Graduate/professional degree	-	-	121 (45.1)	337 (71.7)
Department, n (column %)				
Health services	-	-	129 (48.1)	-
Facilities/building services	-	-	61 (22.8)	-
Student services/other	-	-	77 (28.7)	-
Job title, n (column %)				
Faculty	-	-	-	110 (23.4)
Staff	-	-	-	311 (66.2)
Postdoctoral scholar/other	-	-	-	49 (10.4)
Currently working outside the home, n (column %)	748 (25.6)	418 (19.2)	228 (85.1)	102 (21.7)
Pre-enrollment COVID-19 diagnosis, n (column %)	12 (0.4)	8 (0.4)	1 (0.4)	3 (0.6)

*Categories not mutually exclusive.

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3 279 *SARS-CoV-2 incidence*
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5 280 During the study period, participants underwent 7,638 qPCR tests for active SARS-CoV-
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7 281 2 infection, with a mean of 2.6 tests per participant (range: 0-9). Almost all (99.9%) participants
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9 282 completed at least one qPCR test. Overall, 60 participants (2.0%) tested positive: 57 students, 2
10
11 283 essential workers, and 1 faculty/staff.
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14 284 Among cohorts, students were at highest risk of incident infection over the study period
15
16 285 (IRR students vs. faculty/staff: 5.83; 95% confidence interval [CI]: 1.28, 102.99). Due to the low
17
18 286 number of cases outside of the student cohort, we examined additional risk factors for infections
19
20 287 among students only (Table 2), finding higher rates of infection among students who were 18-19
21
22 288 years old (IRR vs. students ≥ 22 years: 8.34; 95% CI: 4.17, 17.48) and undergraduates (IRR vs.
23
24 289 graduate students: 4.12; 95% CI: 2.17, 8.66). We also observed a higher incidence among
25
26 290 white students (IRR: 2.80 vs. non-white students; 95% CI: 1.53, 5.54). These associations were
27
28 291 largely driven by an outbreak among participants living in fraternities or sororities. Nearly one-
29
30 292 quarter of participants living in fraternities or sororities were infected with SARS-CoV-2 during
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32 293 the study period (IRR vs. other students: 20.86; 95% CI: 12.27, 35.54), and these participants
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34 294 accounted for 49% of cases observed among student participants.
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Table 2. Bivariate associations between sociodemographic characteristics and SARS-CoV-2 incidence among student participants in the Safe Campus Initiative, June-August 2020.

	Cases, N (row %)	Non-Cases, N (row %)	IRR (95% CI)
Overall*	57 (2.6)	2,120 (97.4)	-
Age			
18-19 years	21 (8.0)	243 (92.0)	8.34 (4.17, 17.48)
20-21 years	24 (3.8)	607 (96.2)	4.15 (2.11, 8.58)
≥22 years	12 (0.9)	1,270 (99.1)	Reference
Gender			
Woman	37 (3.1)	1,147 (96.9)	1.45 (0.85, 2.58)
Man	19 (2.1)	892 (97.9)	Reference
Non-binary/other	0 (0)	46 (100)	-
Race/ethnicity**			
American Indian/Alaska Native	0 (0)	29 (100)	-
Asian/Pacific Islander	11 (1.6)	691 (98.4)	0.49 (0.24, 0.91)
Black/African American	1 (1.2)	82 (98.8)	0.45 (0.03, 2.03)
Hispanic/Latine/Spanish origin	8 (2.3)	337 (97.7)	0.88 (0.39, 1.76)
White	45 (3.6)	1,216 (96.4)	2.80 (1.53, 5.54)
Other	4 (1.8)	217 (98.2)	0.65 (0.20, 1.58)
Program level			
Undergraduate	46 (4.1)	1,067 (95.9)	4.12 (2.17, 8.66)
Graduate	10 (1.0)	1,027 (99.0)	Reference
Living at fraternity/sorority	28 (22.4)	97 (77.6)	20.86 (12.27, 35.54)
Currently working outside the home	6 (1.4)	410 (98.6)	0.51 (0.20, 1.11)

IRR: incidence rate ratio, CI: confidence interval.

*N=2,177 students with at least one qPCR test for SARS-CoV-2 during the study period.

**Not mutually exclusive; all participants not included in specified racial/ethnic category served as reference for each comparison.

Phylogenetic analysis

We retrieved whole viral genome sequences for 35 of the 60 positive cases from this study, 29 (83%) of which were found to be part of a campus super-spreader event involving a total of 57 campus-affiliated individuals with samples sequenced by IGI (Figure 1A). Most (69%) study participants within this cluster lived at one of two residences, with likely a single participant originating the super-spreader event. The cluster of genomes was defined by three mutations (A6360G, C24502A and G110083T), two of which were extremely rare at the time of the outbreak. The combination of the three variants was only found in four genomes outside of

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3 310 this cluster (two in the UK and two in Florida) by October 2020, making it a strong phylogenetic
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5 311 signature.

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7 312 Phylogenetic analysis demonstrated that the cluster remained confined to campus, as
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9 313 this signature was not observed in any genomes from samples in the surrounding communities
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11 314 or California state in the months following the super-spreader event. When the trio of mutations
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13 315 was searched in a phylogeny constructed from over 1.2 million genomes worldwide using
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15 316 USHER in April 2021,²³ no descendent leaves were found in the tree under the cluster (Figure
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17 317 1B), indicating that the lineage died out after the super-spreader event.

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21 319 *Factors associated with test positivity*

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23 320 At least one symptom survey was completed in the 7 days before sample collection for
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25 321 90% of tests (n=6,864), including 72% of tests (n=5,469) that had symptom data from the day of
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27 322 sample collection. Of the 54 cases who completed at least one survey during the week before
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29 323 their positive sample was collected (mean: 4 surveys), 23 cases (43%) had reported at least
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31 324 one of the nine COVID-19 symptoms that triggered a notification for them to test. Test positivity
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33 325 was 12.4 times higher among participants who had a recent symptom-triggered notification
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35 326 (95% CI: 7.3, 21.3) (Table 3). Notification-triggering symptoms most strongly associated with
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37 327 test positivity included loss of sense of taste or smell and feeling feverish. Weakness, sweats or
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39 328 chills, and swollen glands were the non-triggering symptoms most strongly associated with test
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41 329 positivity.

Table 3. Bivariate associations between prospectively monitored symptoms and exposures and SARS-CoV-2 qPCR test positivity among participants in the Safe Campus Initiative, June-August 2020.

	Test Positivity, % (+ Tests / All Tests)	IRR (95% CI)
Overall*	0.8 (60 / 7,629)	-
Signs/symptoms within 7 days of test		
No	0.4 (21 / 5,704)	Reference
Yes (any)	3.2 (31 / 971)	8.6 (5.0, 14.9)
- Temperature $\geq 100.4^{\circ}\text{F}$ †	0.0 (0 / 8)	0.0 (0.0, 0.0)
- Temperature $\geq 100.0^{\circ}\text{F}$	11.8 (2 / 17)	15.6 (4.1, 60.4)
- Temperature $\geq 99.0^{\circ}\text{F}$	2.6 (9 / 346)	4.1 (1.9, 8.7)
- Feeling feverish †	14.9 (11 / 74)	23.7 (12.7, 44.3)
- Dry cough †	5.5 (7 / 128)	7.9 (3.6, 17.2)
- Coughing up mucus †	5.5 (5 / 91)	7.6 (3.1, 18.8)
- Unusual chest pain or pressure †	9.7 (6 / 62)	13.8 (6.1, 31.1)
- Difficulty breathing †	5.6 (1 / 18)	7.2 (1.1, 48.7)
- Shortness of breath †	8.7 (4 / 46)	11.9 (4.4, 31.9)
- Trouble thinking/concentrating †	7.6 (5 / 66)	10.6 (4.3, 25.7)
- Loss of sense of taste †	42.9 (3 / 7)	57.6 (23.5, 141)
- Loss of sense of smell †	33.3 (4 / 12)	45.8 (19.0, 110)
- Any notification-triggering symptom †	5.8 (23 / 397)	12.4 (7.3, 21.3)
- Loss of appetite	10.0 (6 / 60)	14.3 (6.3, 32.5)
- Fatigue	3.5 (13 / 373)	5.6 (3.0, 10.4)
- Trouble sleeping	5.1 (7 / 137)	7.4 (3.4, 16.1)
- Headache	4.6 (14 / 302)	7.7 (4.2, 14.1)
- Runny, blocked, or painful sinuses	5.2 (14 / 268)	8.8 (4.8, 16.0)
- Sneezing	1.9 (2 / 104)	2.5 (0.6, 10.0)
- Swollen, red, or painful eyes	8.6 (5 / 53)	12.1 (4.9, 29.7)
- Sore throat	3.1 (8 / 259)	4.5 (2.1, 9.4)
- Stomach pain	5.8 (5 / 86)	8.1 (3.3, 19.8)
- Diarrhea	4.8 (4 / 83)	6.6 (2.4, 17.8)
- Nausea or vomiting	3.3 (3 / 92)	4.4 (1.4, 13.6)
- Body aches or muscle pain	8.1 (12 / 149)	13.0 (7.0, 24.4)
- Sweats or chills	11.3 (10 / 89)	17.5 (9.0, 34.0)
- Swollen glands	11.9 (5 / 42)	16.6 (7.0, 39.7)
- Weakness	13.2 (10 / 76)	20.5 (10.6, 39.4)
Exposures within 14 days before test		
No	0.3 (14 / 4,179)	Reference
Yes (any)	3.4 (17 / 499)	10.1 (5.0, 20.4)
- Suspected or confirmed COVID-19 case in household †	6.7 (6 / 89)	14.7 (6.0, 35.9)
- Close contact with suspected or confirmed case outside household	2.9 (4 / 138)	6.3 (2.2, 18.2)
- Household member with new COVID-19-like symptoms †	4.4 (5 / 114)	7.6 (3.0, 19.6)
- Household member with any new symptoms of illness	2.4 (8 / 336)	4.7 (2.1, 10.4)

- Any notification-triggering exposure †	5.2 (9 / 173)	12.3 (5.6, 26.9)
Activities within 14 days before test		
No	0.5 (3 / 630)	Reference
Yes (any)	0.7 (29 / 4,142)	1.5 (0.5, 4.8)
- Spent time at another residence	1.1 (26 / 2,330)	4.6 (1.9, 11.1)
- Had visitors at own residence	1.0 (22 / 2,203)	2.5 (1.2, 5.4)
- Attended gathering >10 people	2.8 (19 / 672)	9.0 (4.4, 18.1)
- Worked outside of home	0.5 (10 / 2,132)	0.6 (0.3, 1.2)
- Used public restroom	0.7 (12 / 1,830)	1.0 (0.5, 2.0)
- Used public transportation	0.6 (5 / 695)	0.8 (0.3, 2.3)
- Participated in group sports	1.6 (4 / 255)	2.6 (0.9, 7.3)

qPCR: quantitative polymerase chain reaction, IRR: incidence rate ratio, CI: confidence interval.

*Excluding resamples and repeated positives; includes N=2,914 participants with at least one qPCR test for SARS-CoV-2 during the study period.

† Reporting triggered notification to test.

Participants completed at least one weekly exposure survey in the 14 days before sample collection for 61% of tests (n=4,678). Of the 31 cases who had recently completed an exposure survey at the time of sample collection, 9 (29%) reported a potential household exposure that triggered a notification for them to test (Table 3). Test positivity was 12.3 times higher among participants who had a recent exposure-triggered notification (95% CI: 5.6, 26.9). Test positivity was also significantly higher among participants who reported recent engagement in 'higher risk' social activities, most notably attending a gathering of more than 10 people (IRR: 9.0; 95% CI: 4.4, 18.1).

SARS-CoV-2 seroprevalence

Only 18 (0.6%) of 2,877 participants who provided blood samples at baseline had SARS-CoV-2 antibodies (Table 4), all but one of them students. Most participants with antibodies at baseline either suspected past infection (28%), had been previously diagnosed (22%), or had a positive qPCR test the day blood was drawn (11%). Most (85%) participants in the student and essential worker cohorts provided blood samples at both baseline and endline (mean interval between samples: 48 days). Among 2,076 participants with baseline and endline blood samples, 33 (1.6%) seroconverted from non-reactive at baseline to reactive at endline, 30

355 of whom (91%) were also diagnosed via qPCR test during the study. Of the three participants
 356 who seroconverted without a positive qPCR test, two self-reported suspected past infection (one
 357 before baseline, one during the study period), while the third did not suspect past infection and
 358 had four negative qPCR tests over 40 days of study participation.

359 Of the 60 participants with incident SARS-CoV-2 infection during the study period, 41
 360 (68%) provided an endline blood sample at least one week after the date of their first positive
 361 qPCR test (mean time between positive qPCR test and blood sample: 36 days; range 13-52
 362 days). Of these, 34 (83%) were reactive (Table 4).

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364 **Table 4.** Seroprevalence of SARS-CoV-2 antibodies among participants in the Safe Campus
 365 Initiative, June-August 2020.

	Baseline, N (%)	Endline, N (%)	Both, N (%)
Serostatus – Cross-sectional*			
Reactive	18 (0.6)	48 (2.3)	-
Non-reactive	2,859 (99.4)	2,039 (97.7)	-
Serostatus – Longitudinal**			
Non-Reactive → Non-Reactive	-	-	2,029 (97.7)
Non-Reactive → Reactive	-	-	33 (1.6)
Reactive → Non-Reactive	-	-	0 (0)
Reactive → Reactive	-	-	14 (0.7)
Serostatus – Previous qPCR Positive†			
Reactive	-	34 (82.9)	-
Non-reactive	-	7 (17.1)	-

366 qPCR: quantitative polymerase chain reaction.

367 *N=2,888 participants who provided at least one blood sample.

368 **N=2,076 participants who provided blood samples at baseline and endline.

369 †N=41 participants who provided an endline blood sample ≥7 days *after* infection with SARS-CoV-2 identified via
 370 positive qPCR test.

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372 Discussion

373 This study provides a model of a voluntary, incentivized system to identify and link at-risk
 374 students to SARS-CoV-2 testing. While the incidence and seroprevalence of SARS-CoV-2 were
 375 generally low in this cohort of university students and employees in the summer of 2020, we

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3 376 observed the highest incidence among undergraduate students living in congregate settings,
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5 377 with nearly half of cases found to be associated with a super-spreader event.
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7 378 Within this cohort, we previously demonstrated the acceptability of our low-barrier
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9 379 SARS-CoV-2 mitigation approach and the limitations of temperature monitoring as a tool for
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11 380 case identification.^{14,26} The present analysis builds upon these contributions by triangulating
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13 381 prospective qPCR testing data with phylogenetic analyses of positive samples and serial
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15 382 antibody testing to evaluate whether case identification and containment were achieved. In
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17 383 doing so, we found evidence that the system successfully identified a high proportion of incident
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19 384 SARS-CoV-2 cases among participants and may have mitigated community transmission after
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21 385 an outbreak. Specifically, 91% of participants with newly-identified antibodies for SARS-CoV-2
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23 386 at the end of the study had also been diagnosed with incident infection via qPCR test during the
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25 387 study period. While a sizeable cluster of cases among participants was traced to a single super-
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27 388 spreader event, the associated cluster lineage was successfully contained without spreading
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29 389 beyond campus. As the outbreak unfolded, the system also allowed for rapid real-time response
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31 390 (i.e., surveillance testing notifications to students living in congregate housing) and offered a
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33 391 readily accessible, incentivized entry point for testing for students concerned about potential
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35 392 exposure.
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39 393 Although some universities have adopted punitive measures intended to prevent
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41 394 transmission by controlling student behavior (for example, suspending students for hosting
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43 395 gatherings),^{29–31} this approach has been criticized for its potential to reduce students' trust and
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45 396 cooperation.^{32–34} Instead of punishing or shaming students who fail to adhere to public health
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47 397 guidance, some epidemiologists have called for a harm-reduction approach which supports and
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49 398 engages students as part of the solution.^{32–34} The present study reinforces the potential to
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51 399 integrate voluntary testing and risk monitoring systems to support targeted case identification,
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53 400 as evidenced by the significantly higher positivity rates found among participants whose self-
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55 401 reported symptoms and exposures triggered notifications to test. Our findings also support
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3 402 increased outreach to groups of students at highest risk, particularly younger students in
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5 403 congregate housing.
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7 404 This study is strengthened by rich longitudinal data, including symptom and exposure
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9 405 tracking, qPCR testing, and seroprevalence data from more than 2,000 participants. The study
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11 406 population comprised of a broad sample of university affiliates, both students and employees,
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13 407 with strong representation of university subpopulations perceived to be at higher risk of infection
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15 408 (e.g., undergraduates, essential healthcare workers). As on-campus activities were severely
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17 409 restricted throughout the study period (all classes were held online, and few students were living
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19 410 in residence halls), this study cannot provide insight into SARS-CoV-2 transmission risks related
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21 411 to on-campus student activities. Nevertheless, as 73% of UC Berkeley undergraduate students
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23 412 lived off campus *before* the pandemic,³⁵ systems to detect off-campus (i.e., community and
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25 413 household) transmission remain important for SARS-CoV-2 monitoring efforts among students.
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27 414 Additionally, all participants in the essential workers cohort and a subset of participants in the
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29 415 faculty/cohort were working on campus during the study period, further motivating efforts to
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31 416 monitor incidence in this population.
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34 417 There remain several limitations. We observed relatively few SARS-CoV-2 cases during
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36 418 the study period, which took place before the development of highly transmissible variants, such
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38 419 as Delta and Omicron, and before vaccine rollout. Further research is necessary to adapt and
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40 420 evaluate similar systems in the context of both heightened transmissibility and more prevalent
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42 421 natural and vaccine-induced immunity. Observed associations between symptoms and positivity
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44 422 may also differ among those who have been infected by more recent variants and/or
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46 423 vaccinated. Additionally, a high proportion of identified cases were traced to one outbreak,
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48 424 limiting the generalizability of our exploratory assessment of risk factors for incident infection.
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50 425 There was also anecdotal evidence that the outbreak prompted exposed students to enroll as
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52 426 study participants.¹⁴ While this self-referral into the study is likely to increase selection bias, it
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54 427 also illustrates the utility of implementing non-stigmatizing, incentivized testing approaches to
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3 428 increase testing uptake among at-risk students. Finally, our identification of participants who
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5 429 seroconverted between baseline and endline may be incomplete due to loss-to-follow up and
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7 430 imperfect sensitivity of SARS-CoV-2 antibody testing.
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9 431 By integrating symptom and exposure monitoring systems with low-barrier testing, we
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11 432 identified incident SARS-CoV-2 infections to reduce transmission within a university setting.
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13 433 While there have been seismic shifts in the SARS-CoV-2 pandemic since 2020, universities
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15 434 continue to grapple with how best to mitigate on-campus spread in the face of emerging
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17 435 variants, incomplete vaccination coverage, breakthrough infections, and decreased reliance on
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19 436 other mitigation strategies (e.g., masking, remote learning).^{36,37} The lessons learned through this
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21 437 study may inform the design of future adaptive strategies, ideally building beyond
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23 438 symptom/exposure monitoring and qPCR testing to integrate complementary interventions such
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25 439 as rapid antigen self-testing and vaccination promotion.
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3 440 **Keywords:** COVID-19, SARS-CoV-2, United States, young adults, students, universities,
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5 441 essential workers, seroprevalence
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18

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22
23

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25
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28 477 <https://github.com/lauren-hunter/bcsci>
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31 478 **Ethical approvals:** All study activities were approved by the University of California, Berkeley
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33 479 Committee for the Protection of Human Subjects (#2020-06-13349, #2020-05-13261, #2020-04-
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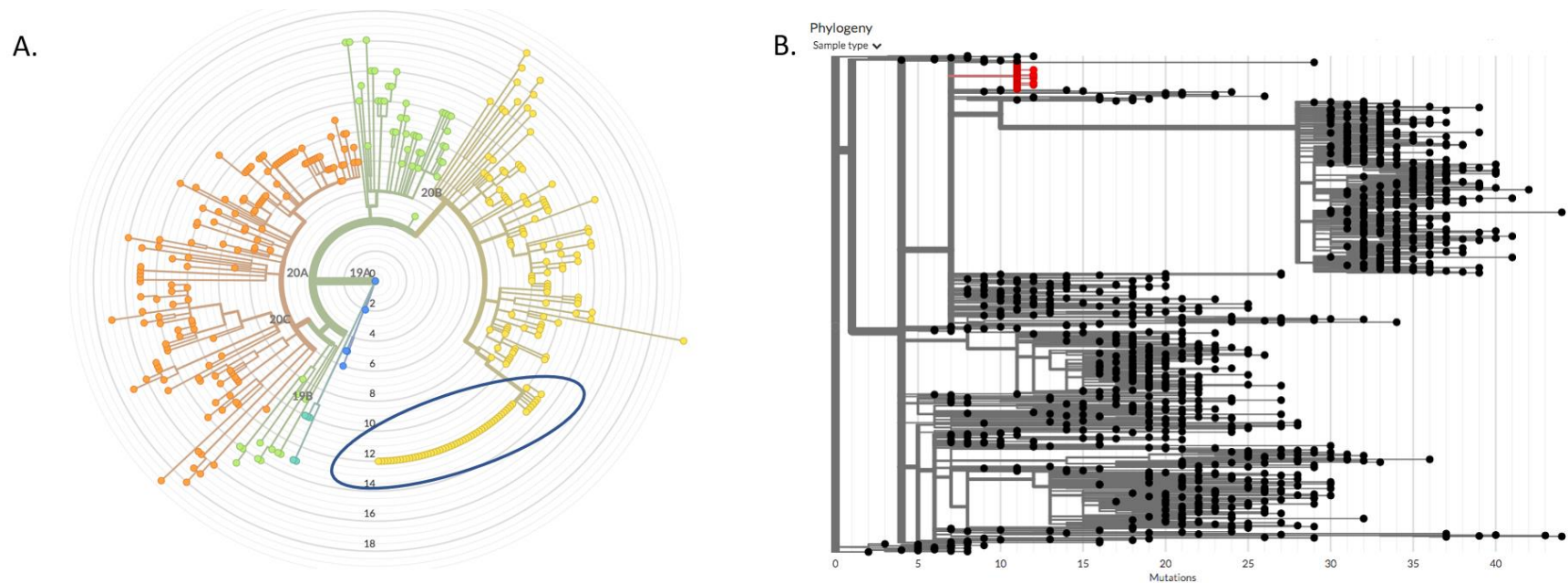
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Figure 1. Phylogeny of outbreak-associated strain of SARS-CoV-2 among participants in the Safe Campus Initiative.



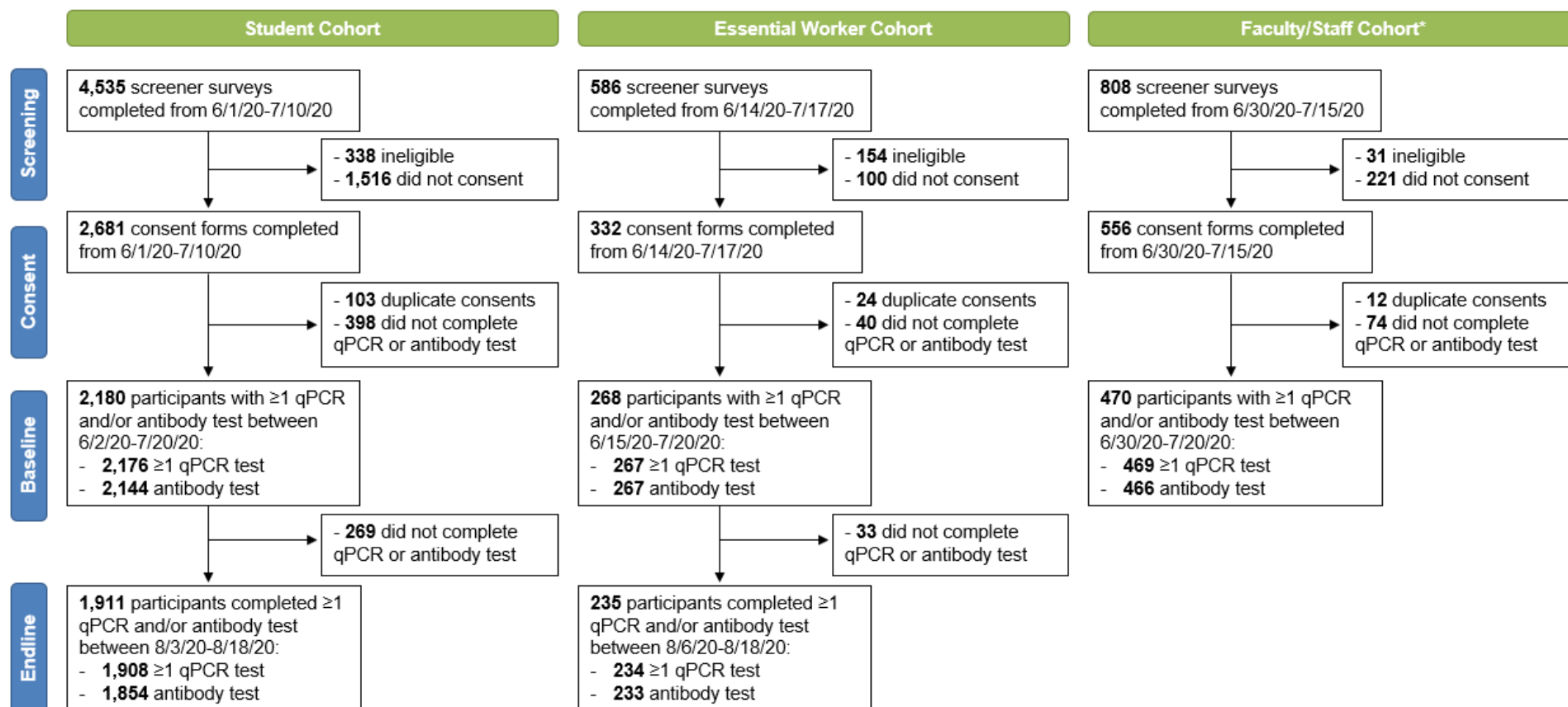
A. A maximum likelihood phylogeny constructed from 357 genomes sequenced by the Innovative Genomics Institute between May and July 2020 constructed using Nextstrain. Branch lengths represent divergence from Wuhan reference genome at center. Blue circle marks cluster of identical genomes from a campus super-spreader event.

B. A 1,057 node subtree of a neighbor-joining tree constructed with all SARS-CoV-2 sequences to date (constructed using UShER with over 1 million genomes in April 2021), showing the most similar genomes to the super-spreader event cluster (in red). There are no descendant branches from the cluster, demonstrating that the outbreak was contained and the lineage died out.

Supplementary Table 1. Eligibility criteria across Berkeley COVID-19 Safe Campus Study cohorts.

	Student Cohort	Essential Worker Cohort	Faculty/Staff Cohort
Eligibility Criteria	- At least 18 years of age	- At least 18 years of age	- At least 18 years of age
	- Currently enrolled as an undergraduate or graduate student at UC Berkeley (i.e., not graduated in Spring 2020 or incoming for Fall 2020)	- Currently employed in one of the following departments at UC Berkeley: health services, police, facility services or other building management, environmental health and safety, laboratory animal care, athletics, dining, childcare, other residential or student services - Currently working on campus at UC Berkeley or expected to return to work during June 2020	- Currently employed as a faculty member, staff member, or postdoctoral scholar at UC Berkeley - Not already enrolled in the essential workers cohort
	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20	N/A	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20
	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records

Supplementary Figure 1. Flow diagram for Berkeley COVID-19 Safe Campus Study cohorts.



qPCR: quantitative polymerase chain reaction.

*Faculty/staff cohort not invited for endline testing appointments but could complete follow-up qPCR tests through 8/18/20.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-9, Supplementary Figure 1
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-9, Supplementary Table 1
		(b) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-10
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	N/A
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, explain how loss to follow-up was addressed	N/A
		(e) Describe any sensitivity analyses	N/A

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Supplementary Figure 1
		(b) Give reasons for non-participation at each stage	Supplementary Figure 1
		(c) Consider use of a flow diagram	Supplementary Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	11-13
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14, Tables 2-3
		(b) Report category boundaries when continuous variables were categorized	10, Table 3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

BMJ Open

Monitoring SARS-CoV-2 incidence and seroconversion among university students and employees: a longitudinal cohort study in California, June to August 2020

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2
3 1 **Title:** Monitoring SARS-CoV-2 incidence and seroconversion among university students and
4 employees: a longitudinal cohort study in California, June to August 2020
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8 3
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27 **Abstract**

28 **Objectives:** To identify incident SARS-CoV-2 infections and inform effective mitigation
29 strategies in university settings, we piloted an integrated symptom and exposure monitoring and
30 testing system among a cohort of university students and employees.

31 **Design:** Prospective cohort study.

32 **Setting:** A public university in California from June to August 2020.

33 **Participants:** 2,180 university students and 738 university employees.

34 **Primary outcome measures:** At baseline and endline, we tested participants for active SARS-
35 CoV-2 infection via quantitative polymerase chain reaction (qPCR) test and collected blood
36 samples for antibody testing. Participants received notifications to complete additional qPCR
37 tests throughout the study if they reported symptoms or exposures in daily surveys or were
38 selected for surveillance testing. Viral whole genome sequencing was performed on positive
39 qPCR samples, and phylogenetic trees were constructed with these genomes and external
40 genomes.

41 **Results:** Over the study period, 57 students (2.6%) and 3 employees (0.4%) were diagnosed
42 with SARS-CoV-2 infection via qPCR test. Phylogenetic analyses revealed that a super-
43 spreader event among undergraduates in congregate housing accounted for at least 48% of
44 cases but did not spread beyond campus. Test positivity was higher among participants who
45 self-reported symptoms (incidence rate ratio [IRR]: 12.7; 95% confidence interval [CI]: 7.4, 21.8)
46 or had household exposures (IRR: 10.3; 95% CI: 4.8, 22.0) that triggered notifications to test.
47 Most (91%) participants with newly identified antibodies at endline had been diagnosed with
48 incident infection via qPCR test during the study.

49 **Conclusions:** Our findings suggest that integrated monitoring systems can successfully identify
50 and link at-risk students to SARS-CoV-2 testing. As the study took place before the evolution of
51 highly transmissible variants and widespread availability of vaccines and rapid antigen tests,
52 further research is necessary to adapt and evaluate similar systems in the present context.

53 **Strengths and limitations of this study**

- 54 • The study is strengthened by rich longitudinal data including more than 117,000 daily
55 symptom surveys; 17,000 weekly exposure surveys; 7,600 qPCR tests to detect active
56 SARS-CoV-2 infection; and 4,900 antibody tests to detect previous infection collected
57 from 2,918 university students and employees over three months.
- 58 • We used seroconversion data from serial antibody tests and phylogenetic analyses
59 comparing viral genome sequences to a broader database to evaluate the extent to
60 which the study system identified incident cases and contained an outbreak among
61 university students.
- 62 • Our identification of participants who seroconverted between baseline and endline may
63 be incomplete due to loss-to-follow up and imperfect sensitivity of SARS-CoV-2 antibody
64 testing.
- 65 • A high proportion of identified cases were traced to one outbreak, limiting the
66 generalizability of our exploratory assessment of risk factors for incident infection. .

67 **Background**

68 Universities have been identified as hotspots for SARS-CoV-2 transmission in the United
69 States,[1] where SARS-CoV-2 incidence is highest among young adults.[2] Young adults may
70 be less likely to adhere to social distancing guidelines and more likely to experience workplace
71 exposure (for example, at food service or retail jobs).[2] Their risk may be heightened in
72 university settings where many live in congregate housing, interact with wide social networks, or
73 attend large gatherings.[3] Although young adults are at low risk of serious acute illness or
74 death from COVID-19 (the disease caused by SARS-CoV-2),[4] the higher likelihood of
75 asymptomatic or mildly symptomatic infection in this age group makes young adults a key
76 population through which SARS-CoV-2 may spread to other, more vulnerable groups.[2,5]
77 Indeed, there is evidence that transmission among university students may lead to increased
78 COVID-19-related mortality in the surrounding counties.[6–8] Although widespread vaccination
79 has enabled campuses to return to in-person activities, the elimination of SARS-CoV-2
80 transmission in campus populations may be stymied by vaccine hesitancy among students and
81 employees and breakthrough infection and subsequent transmission by vaccinated persons,
82 particularly in the context of waning immunity and viral variants which reduce vaccine
83 efficacy.[9,10] Therefore, rapid and resource-efficient identification of incident cases in
84 university populations is a critical first step of outbreak investigation and control, followed by
85 isolation, case investigation, and contact tracing, to minimize transmission within campus and to
86 the broader community.

87 Universities have adopted a wide range of approaches for testing and outbreak
88 mitigation.[11–13] While a number of well-resourced universities have scaled up testing capacity
89 in order to frequently test all students and employees accessing campus or living in university-
90 affiliated housing,[13] many other universities do not have well-defined testing strategies or
91 restrict testing to those with symptoms or known exposure.[12] Beyond investing in testing
92 programs, some universities have sought to reduce on-campus transmission by mandating the

1
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3 93 completion of self-administered symptom screening tools by students and employees. However,
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5 94 such tools have primarily been used to regulate daily access to campus (i.e., deny entry to
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7 95 those who report COVID-19-like symptoms), rather than to detect emergent outbreaks among
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9 96 university populations. As universities resume normal operations and discontinue mitigation
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11 97 strategies such as masking, non-punitive, resource-efficient strategies which can both identify
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13 98 those who are at highest risk of infection *and* expediently link them to low-barrier testing
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15 99 services may play a key role in transitioning from a “one-size-fits-all” approach of uniform testing
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18 100 to a sustainable monitoring paradigm.

19
20 101 In 2020, we piloted an integrated symptom and exposure monitoring and testing system
21
22 102 designed to identify incident SARS-CoV-2 infections among a cohort of university students and
23
24 103 employees.[14] Here we describe the incidence and seroprevalence of SARS-CoV-2 infection
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26 104 within this cohort to evaluate the extent to which incident infections were successfully detected
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28 105 and contained over the study period, identify sociodemographic factors associated with incident
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30 106 infection, and ascertain which self-reported symptoms and exposures tracked by the monitoring
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32 107 system were predictive of test positivity, with the ultimate objective of informing monitoring and
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34 108 testing strategies in university settings.
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38 39 110 **Methods**

40 41 111 *Study design and setting*

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43 112 The study comprised three prospective cohorts of University of California, Berkeley
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45 113 affiliates followed from June to August 2020: students, essential workers (i.e., employees
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47 114 working on campus in health, facilities, or student services), and other employees (hereafter,
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49 115 “faculty/staff”). We report the findings according to the Strengthening the Reporting of
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51 116 Observational Studies in Epidemiology (STROBE) checklist for cohort studies.[15]
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54 117 Throughout the study period, public health orders mandated the use of face coverings in
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56 118 public and upheld many restrictions set forth by earlier shelter-in-place orders, while allowing
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3 119 phased reopening of certain businesses and activities.[16] UC Berkeley did not offer in-person
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5 120 classes, and on-campus work was restricted to essential workers and a small subset of faculty,
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7 121 staff, and student researchers. Although few students were living in on-campus residence halls,
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9 122 many students continued to live in congregate living settings off campus, such as fraternities,
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11 123 sororities, and co-operative housing. From June to August 2020, daily case counts in Alameda
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13 124 County ranged from approximately 50 to 350 (0 to 17 within the city of Berkeley).[17]
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17 18 126 *Participant recruitment and eligibility*

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20 127 The study was promoted through targeted messages from university officials to campus
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22 128 email listservs and social media platforms from early June to mid-July 2020. To increase reach
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24 129 to students expected to be at higher risk of COVID-19, we also placed flyers in congregate living
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26 130 settings and conducted in-person recruitment for student athletes who had resumed training on
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28 131 campus. Participants were eligible to enroll in the study if they were at least 18 years of age,
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30 132 were a current student or employee at UC Berkeley, and planned to live in or near Berkeley
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32 133 during the summer of 2020. Specific eligibility criteria and enrollment windows varied by cohort
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34 134 (Supplementary Table 1, Supplementary Figure 1).
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36

37 135 Upon enrollment, participants were linked to an online baseline survey that collected
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39 136 sociodemographic data and information about their COVID-19-related health history.
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41 137 Participants were then referred to a baseline testing appointment at University Health Services
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43 138 (UHS) which included a SARS-CoV-2 quantitative polymerase chain reaction (qPCR) test and
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45 139 blood collection for antibody testing (procedures described below). To facilitate daily
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47 140 temperature monitoring, study staff also provided participants with free oral thermometers upon
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49 141 request at testing appointments. Participants who completed this appointment or a non-study
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51 142 qPCR test at UHS by July 20 were eligible to remain in the study. We pre-specified a maximum
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53 143 sample size of 4,000 participants across cohorts but did not reach this limit before the final day
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55 144 of baseline data collection.
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5 146 *Symptom and exposure surveys*

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7 147 Participants received daily text messages or emails, depending on their preference
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9 148 specified in the baseline survey, which linked to short symptom surveys through which they
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11 149 reported their body temperature and any symptoms of illness. Once per week, the daily survey
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13 150 included a longer exposure module, which asked about recent symptoms of illness among their
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15 151 household member(s), potential exposure(s) to COVID-19, and activities related to potential
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17 152 COVID-19 risk. All surveys were administered via REDCap.[18,19]

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22 154 *Endline survey and testing*

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24 155 In early August, participants were sent an endline survey which collected updated
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26 156 information on their COVID-19 history to identify any diagnoses outside of the study.
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28 157 Participants in the student and essential worker cohorts were also invited to complete endline
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30 158 testing appointments by August 18, including a final qPCR test and blood collection.

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32 15933
34 160 *qPCR testing*

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36 161 Midturbinate nasal and oral swabs were collected by UHS clinical staff and tested for
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38 162 SARS-CoV-2 by qPCR at the Innovative Genomics Institute (IGI).[20] qPCR tests were
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40 163 performed at baseline for all three cohorts and at endline for the student and essential worker
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42 164 cohorts. Between baseline and endline testing, additional qPCR tests were performed for the
43
44 165 following reasons:

- 45
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47 166 • **Symptom- or exposure-based tests triggered based on participants' responses in**
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49 167 **daily surveys:** Participants who reported COVID-19-like signs or symptoms¹ (in

54
55 ¹ Signs or symptoms which triggered a testing notification when reported were: temperature of $\geq 100.4^{\circ}\text{F}$, dry cough
56 (without mucus), coughing up mucus, feeling feverish, unusual pain or pressure in the chest, difficulty breathing,
57 shortness of breath, unexplained trouble thinking or concentrating, loss of sense of taste, or loss of sense of smell.

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2
3 168 themselves or household member(s)) or who reported a suspected or confirmed COVID-
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5 169 19 case in their household were automatically notified to sign up for a qPCR test.
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7 170 • **Random surveillance testing:** A subset of participants in the student and faculty/staff
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9 171 cohorts who had not had a qPCR test within a week were randomly selected and
10
11 172 emailed notifications to come in for surveillance testing in July.
12
13 173 • **Address-based surveillance testing:** Participants who lived at the same address as
14
15 174 another participant who tested positive for SARS-CoV-2 were immediately emailed
16
17 175 surveillance testing notifications. Following an outbreak among group-housed students
18
19 176 in early July, surveillance testing notifications were also emailed to all participants who
20
21 177 had not been tested within the week and who reported living in fraternities, sororities, or
22
23 178 co-operative housing.
24
25 179 • **Participant-initiated testing:** Participants could self-schedule study testing
26
27 180 appointments on demand, with or without consulting a healthcare provider and
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29 181 regardless of exposure history.
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32 182 Participants with positive qPCR test results were informed by phone by UHS clinical staff, who
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34 183 provided guidance on isolation and performed case investigation to identify potential contacts.
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36 184 Participants with negative qPCR test results were informed of their results via the UHS online
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38 185 patient portal.
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43 187 *SARS-CoV-2 sequencing and phylogenetic analyses*

45 188 Viral whole genome sequencing was performed on a set of positive samples at the IGI,
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47 189 using previously described procedures.[21] Briefly, SARS-CoV-2 RNA extracted from swabs
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49 190 was reverse transcribed using SuperScript IV (Invitrogen), and the viral genome was amplified
50
51 191 from the resulting cDNA in four separate qPCR reactions using distinct primer sets tiling the
52
53 192 SARS-CoV-2 genome. The four qPCR reactions were pooled 1:1:1:1 and diluted 1:50 in H₂O. A
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55 193 second qPCR reaction was set up to add Nextera Unique Dual Indexing (UDI) sequences to
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3 194 either end of the amplicons. The resulting qPCR reaction was cleaned up using 0.7x AMPureXP
4
5 195 beads (Beckman Coulter) and quantified using a Qubit dsDNA HS Assay Kit (Thermo Fisher).
6
7 196 The libraries were then pooled to an equimolar ratio and sequenced with a 10% PhiX spike in
8
9 197 using a MiSeq v3 kit at 300bp PE reads.

11 198 Fastq sequencing files were processed through a custom pipeline using publicly
12
13 199 available software. The reads were preprocessed by quality trimming, removing adaptors, and
14
15 200 PhiX cleaning with BBTtools,[22] and then aligned to the Wuhan reference sequence
16
17 201 (NC_045512.2) with minimap2 v2.16-r922. ARTICv3 primers were trimmed, and the consensus
18
19 202 sequence was built with iVar v1.3.1, where an 'N' is called if the depth is less than 10 reads at
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21 203 any nucleotide. The genomes were then processed through the Nextstrain Auger pipeline with
22
23 204 other genomes from GISAID to construct a maximum likelihood tree.[23,24] Several
24
25 205 phylogenies were constructed for this analysis: a tree of 7,091 genomes subsampled from the
26
27 206 worldwide genomes in GISAID at the time (approximately 200,000 genomes as of October
28
29 207 2020) was used to place the IGI genomes in the larger tree; a tree with all IGI genomes
30
31 208 sequenced at the time of analysis (356 genomes); and a tree containing 500 genomes (from 1
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33 209 million genomes as of April 2021) was constructed using UShER.[25]
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39 211 *Antibody testing*

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41 212 Up to 10 mL of blood was collected by phlebotomists via venipuncture at baseline from
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43 213 participants in all three cohorts and again at endline from participants in the student and
44
45 214 essential worker cohorts. Blood was centrifuged and serum was stored at -20°C for 2 to 4
46
47 215 months before being tested at Vitalant Research Institute using the VITROS Immunodiagnostic
48
49 216 Products Anti-SARS-CoV-2 Total Reagent Pack, which detects IgA, IgG, and IgM antibodies
50
51 217 against the SARS-CoV-2 spike protein S1 antigen and has an estimated clinical specificity of
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53 218 100% and unreported sensitivity.[26]
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220 *Participant compensation*

221 Participants in the student cohort received a \$50 gift card after completing baseline
222 testing and 10 daily surveys; this incentive was conditional on daily survey completion to
223 encourage early habit formation.[27] Student participants received a second \$50 gift card at
224 their endline testing appointment. To facilitate travel to and from UHS for testing appointments,
225 student participants were also offered pre-paid car rides via a ride-sharing app.

226 Participants in the essential worker cohort received a gift card worth \$1 per daily survey
227 completed (to a maximum of \$70) after the study ended. Participants in the faculty/staff cohort
228 were not compensated.

230 *Statistical analyses*

231 To identify sociodemographic factors associated with incident infection, we used Poisson
232 regression to estimate unadjusted incidence rate ratios (IRRs) for SARS-CoV-2 infection by
233 study cohort and within strata of sociodemographic variables self-reported in the baseline
234 survey (e.g., age, gender, housing type), setting person-months of enrollment as an offset term
235 to account for differing lengths of follow-up.

236 We also calculated IRRs comparing test positivity by recent signs/symptoms, exposures,
237 and activities reported in the daily and weekly surveys. We estimated IRRs for several
238 temperature thresholds (i.e., $\geq 100.4^{\circ}\text{F}$, $\geq 100.0^{\circ}\text{F}$, $\geq 99.0^{\circ}\text{F}$) to compare to symptom-specific
239 IRRs; however, continuous associations between temperature and positivity have been
240 previously explored in this cohort, finding that temperature screening has low sensitivity to
241 SARS-CoV-2 infection and, thus, limited efficacy as a primary means of detection.[28] While it
242 was not possible to isolate participants' specific reason(s) for testing over the study period (e.g.,
243 participants could receive symptom- and/or exposure-triggered testing notifications over the
244 same time window in which they completed baseline or endline testing), we linked qPCR test
245 results to recently-completed symptom and exposure surveys to identify testing appointments

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3 246 that took place in the days or weeks following symptom- and exposure-triggered testing
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5 247 notifications (Supplementary Figure 2). We accounted for clustered observations due to
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7 248 repeated tests per participant using a generalized estimating equation approach with Huber-
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9 249 White standard error estimates and an exchangeable working correlation structure.[29]

11 250 Finally, to assess the extent to which the testing and monitoring system captured
12
13 251 incident infections, we identified participants who seroconverted from having non-reactive (no
14
15 252 antibodies detected) to reactive (antibodies detected) blood samples between baseline and
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17 253 endline and calculated the proportion of these participants who were also diagnosed with
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19 254 incident SARS-CoV-2 infection via positive qPCR test during the study period. Analyses were
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21 255 conducted in R version 4.2.1.[30]
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26 257 *Ethical approvals*

28 258 All study activities were approved by the University of California, Berkeley Committee for
29
30 259 the Protection of Human Subjects (#2020-06-13349, #2020-05-13261, #2020-04-13238).
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33 260

35 261 *Patient and public involvement*

37 262 The study's target population comprised university students and employees. While the
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39 263 study was conducted by faculty, staff, and graduate students from the UC Berkeley School of
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41 264 Public Health, University Health Services, and the Innovative Genomics Institute, the broader
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43 265 student body and university workforce were not involved in designing the study or selecting the
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45 266 research question, outcome measures, or method of disseminating results.
46

47 267

50 268 **Results**

52 269 *Participant recruitment and retention*

54 270 Between June 1 and July 20, 2020, we enrolled 2,180 students, 268 essential workers,
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56 271 and 470 faculty/staff who completed at least one qPCR test or antibody test (Table 1,
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272 Supplementary Figure 1). The student cohort was split between undergraduate (52%) and
 273 graduate (48%) students. Nearly half (44%) of essential workers worked in health services.
 274 While 85% of essential workers were working on campus at the time of enrollment, most (81%)
 275 faculty/staff were working entirely remotely. At the time of enrollment, only 12 (0.4%)
 276 participants reported a previous COVID-19 diagnosis.

277 Participants provided a total of 5,545 person-months of follow-up from enrollment to the
 278 end of the study (mean person-days per participant: 57, range: 32-78). Participants completed a
 279 mean of 40 daily symptom surveys and 6 weekly exposure surveys over the study period, for a
 280 total of 117,239 symptom and 17,162 exposure surveys. A subset of participants did not
 281 complete any daily symptom surveys (1.7%) or weekly exposure surveys (4.2%).

282 **Table 1.** Baseline characteristics of participants in the Berkeley COVID-19 Safe Campus
 283 Initiative by study cohort, June-August 2020.

	All	Students	Essential Workers	Faculty/Staff
N (row %)	2,918 (100)	2,180 (74.7)	268 (9.2)	470 (16.1)
Age, mean \pm SD	29.4 \pm 11.6	24.3 \pm 5.4	42.5 \pm 12.3	45.2 \pm 12.3
Gender, n (column %)				
Man	1,177 (40.3)	911 (41.8)	103 (38.4)	163 (34.7)
Woman	1,653 (56.6)	1,187 (54.4)	164 (61.2)	302 (64.3)
Non-binary/other	51 (1.7)	46 (2.1)	1 (0.4)	4 (0.9)
Race/ethnicity, n (column %)*				
American Indian/Alaska Native	39 (1.3)	29 (1.3)	2 (0.7)	8 (1.7)
Asian/Pacific Islander	833 (28.5)	703 (32.2)	66 (24.6)	64 (13.6)
Black/African American	103 (3.5)	83 (3.8)	16 (6.0)	4 (0.9)
Hispanic/Latine/Spanish origin	420 (14.4)	346 (15.9)	39 (14.6)	35 (7.4)
White	1,814 (62.2)	1,261 (57.8)	160 (59.7)	393 (83.6)
Other	280 (9.6)	223 (10.2)	31 (11.6)	26 (5.5)
Program level, n (column %)				
Undergraduate	-	1,114 (51.7)	-	-
Graduate	-	1,039 (48.2)	-	-
Living at fraternity/sorority, n (column %)	-	125 (5.7%)	-	-
Education, n (column %)				
High school diploma/GED	-	-	6 (2.2)	0 (0)
Some college or trade school	-	-	59 (22.0)	13 (2.8)
Bachelor's degree	-	-	78 (29.1)	119 (25.3)
Graduate/professional degree	-	-	121 (45.1)	337 (71.7)

Department, n (column %)				
Health services	-	-	129 (48.1)	-
Facilities/building services	-	-	61 (22.8)	-
Student services/other	-	-	77 (28.7)	-
Job title, n (column %)				
Faculty	-	-	-	110 (23.4)
Staff	-	-	-	311 (66.2)
Postdoctoral scholar/other	-	-	-	49 (10.4)
Currently working outside the home, n (column %)	748 (25.6)	418 (19.2)	228 (85.1)	102 (21.7)
Pre-enrollment COVID-19 diagnosis, n (column %)	12 (0.4)	8 (0.4)	1 (0.4)	3 (0.6)

*Categories not mutually exclusive.

SARS-CoV-2 incidence

During the study period, participants underwent 7,638 qPCR tests for active SARS-CoV-2 infection, with a mean of 2.6 tests per participant (range: 0-9). Almost all (99.9%) participants completed at least one qPCR test. Overall, 60 participants (2.0%) tested positive: 57 students, 2 essential workers, and 1 faculty/staff.

Among cohorts, students were at highest risk of incident infection over the study period (IRR students vs. faculty/staff: 5.8; 95% confidence interval [CI]: 1.3, 103.0). Due to the low number of cases outside of the student cohort, we examined additional risk factors for infections among students only (Table 2), finding higher rates of infection among students who were 18-19 years old (IRR vs. students ≥ 22 years: 8.3; 95% CI: 4.2, 17.5) and undergraduates (IRR vs. graduate students: 4.1; 95% CI: 2.2, 8.7). We also observed a higher incidence among white students (IRR: 2.8 vs. non-white students; 95% CI: 1.5, 5.5). These associations were largely driven by an outbreak among participants living in fraternities or sororities. Nearly one-quarter of participants living in fraternities or sororities were infected with SARS-CoV-2 during the study period (IRR vs. other students: 20.9; 95% CI: 12.3, 35.5), and these participants accounted for 49% of cases observed among student participants.

Table 2. Bivariate associations between sociodemographic characteristics and SARS-CoV-2 incidence among student participants in the Safe Campus Initiative, June-August 2020.

	Cases, N (row %)	Non-Cases, N (row %)	IRR (95% CI)
Overall*	57 (2.6)	2,120 (97.4)	-
Age			
18-19 years	21 (8.0)	243 (92.0)	8.3 (4.2, 17.5)
20-21 years	24 (3.8)	607 (96.2)	4.2 (2.1, 8.6)
≥22 years	12 (0.9)	1,270 (99.1)	Reference
Gender			
Woman	37 (3.1)	1,147 (96.9)	1.5 (0.9, 2.6)
Man	19 (2.1)	892 (97.9)	Reference
Non-binary/other	0 (0)	46 (100)	-
Race/ethnicity**			
American Indian/Alaska Native	0 (0)	29 (100)	-
Asian/Pacific Islander	11 (1.6)	691 (98.4)	0.5 (0.2, 0.9)
Black/African American	1 (1.2)	82 (98.8)	0.5 (0.03, 2.0)
Hispanic/Latine/Spanish origin	8 (2.3)	337 (97.7)	0.9 (0.4, 1.8)
White	45 (3.6)	1,216 (96.4)	2.8 (1.5, 5.5)
Other	4 (1.8)	217 (98.2)	0.7 (0.2, 1.6)
Program level			
Undergraduate	46 (4.1)	1,067 (95.9)	4.1 (2.2, 8.7)
Graduate	10 (1.0)	1,027 (99.0)	Reference
Living at fraternity/sorority	28 (22.4)	97 (77.6)	20.9 (12.3, 35.5)
Currently working outside the home	6 (1.4)	410 (98.6)	0.5 (0.2, 1.1)

IRR: incidence rate ratio, CI: confidence interval.

*N=2,177 students with at least one qPCR test for SARS-CoV-2 during the study period.

**Not mutually exclusive; all participants not included in specified racial/ethnic category served as reference for each comparison.

Phylogenetic analysis

We retrieved whole viral genome sequences for 35 of the 60 positive cases from this study, 29 (83%) of which were found to be part of a campus super-spreader event involving a total of 57 campus-affiliated individuals with samples sequenced by IGI (Figure 1A). Most (69%) study participants within this cluster lived at one of two residences, with likely a single participant originating the super-spreader event. The cluster of genomes was defined by three mutations (A6360G, C24502A and G110083T), two of which were extremely rare at the time of the outbreak. The combination of the three variants was only found in four genomes outside of

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3 317 this cluster (two in the UK and two in Florida) by October 2020, making it a strong phylogenetic
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5 318 signature.

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7 319 Phylogenetic analysis demonstrated that the cluster remained confined to campus, as
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9 320 this signature was not observed in any genomes from samples in the surrounding communities
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11 321 or California state in the months following the super-spreader event. When the trio of mutations
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13 322 was searched in a phylogeny constructed from over 1.2 million genomes worldwide using
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15 323 USHER in April 2021,[25] no descendent leaves were found in the tree under the cluster (Figure
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17 324 1B), indicating that the lineage died out after the super-spreader event.

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21 326 *Factors associated with test positivity*

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23 327 At least one symptom survey was completed in the 7 days before sample collection for
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25 328 88% of tests (n=6,668), including 72% of tests (n=5,465) that had symptom data from the day of
26
27 329 sample collection. Of the 52 cases who completed at least one survey during the week before
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29 330 their positive sample was collected (mean: 4 surveys), 23 cases (44%) had reported at least
30
31 331 one of the nine COVID-19 symptoms that triggered a notification for them to test. Test positivity
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33 332 was 12.7 times higher among participants who had a recent symptom-triggered notification
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35 333 (95% CI: 7.4, 21.8) (Table 3). Notification-triggering symptoms most strongly associated with
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37 334 test positivity included loss of sense of taste or smell and feeling feverish. Weakness, sweats or
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39 335 chills, and swollen glands were the non-triggering symptoms most strongly associated with test
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41 336 positivity.
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Table 3. Bivariate associations between prospectively monitored symptoms and exposures and SARS-CoV-2 qPCR test positivity among participants in the Safe Campus Initiative, June-August 2020.

	Test Positivity, % (+ Tests / All Tests)	IRR (95% CI)
Overall*	0.8 (60 / 7,615)	-
Signs/symptoms within 7 days of test		
No	0.3 (18 / 5,489)	Reference**
Yes (any)	2.9 (34 / 1,179)	8.8 (5.0, 15.5)
- Temperature $\geq 100.4^{\circ}\text{F}$ †	0.0 (0 / 10)	0.0 (0.0, 0.0)
- Temperature $\geq 100.0^{\circ}\text{F}$	10.5 (2 / 19)	13.2 (3.4, 50.9)
- Temperature $\geq 99.0^{\circ}\text{F}$	2.9 (12 / 417)	4.3 (2.2, 8.2)
- Feeling feverish †	15.3 (11 / 72)	24.6 (13.2, 45.8)
- Dry cough †	5.6 (7 / 126)	8.1 (3.7, 17.7)
- Coughing up mucus †	5.5 (5 / 91)	7.7 (3.1, 19.0)
- Unusual chest pain or pressure †	9.7 (6 / 62)	13.9 (6.1, 31.6)
- Difficulty breathing †	5.6 (1 / 18)	7.2 (1.0, 49.8)
- Shortness of breath †	8.9 (4 / 45)	12.3 (4.6, 32.9)
- Trouble thinking/concentrating †	7.6 (5 / 66)	10.7 (4.4, 26.1)
- Loss of sense of taste †	42.9 (3 / 7)	58.3 (23.7, 143)
- Loss of sense of smell †	33.3 (4 / 12)	46.2 (19.2, 111)
- Any notification-triggering symptom †	5.9 (23 / 393)	12.7 (7.4, 21.8)
- Loss of appetite	10.3 (6 / 58)	14.8 (6.5, 33.9)
- Fatigue	3.5 (13 / 371)	5.4 (3.0, 10.6)
- Trouble sleeping	5.1 (7 / 136)	7.5 (3.4, 16.4)
- Headache	4.7 (14 / 300)	7.8 (4.3, 14.3)
- Runny, blocked, or painful sinuses	5.2 (14 / 267)	8.8 (4.8, 16.2)
- Sneezing	1.9 (2 / 106)	2.5 (0.6, 10.1)
- Swollen, red, or painful eyes	8.6 (5 / 58)	12.1 (4.9, 30.0)
- Sore throat	3.1 (8 / 258)	4.5 (2.1, 9.5)
- Stomach pain	5.8 (5 / 86)	8.1 (3.3, 20.1)
- Diarrhea	4.9 (4 / 82)	6.7 (2.5, 18.2)
- Nausea or vomiting	3.3 (3 / 90)	4.5 (1.4, 14.2)
- Body aches or muscle pain	8.2 (12 / 146)	13.4 (7.2, 25.2)
- Sweats or chills	11.5 (10 / 87)	18.0 (9.2, 35.2)
- Swollen glands	12.2 (5 / 41)	17.3 (7.2, 41.2)
- Weakness	13.5 (10 / 74)	21.2 (11.0, 40.9)
Exposures within 14 days before test		
No	0.3 (15 / 4,319)	Reference**
Yes (any)	3.4 (17 / 506)	9.6 (4.8, 19.2)
- Suspected or confirmed COVID-19 case in household †	7.4 (7 / 95)	13.9 (6.1, 31.8)
- Close contact with suspected or confirmed case outside household	3.5 (5 / 144)	6.0 (2.3, 15.4)
- Household member with new COVID-19-like symptoms †	4.4 (5 / 114)	7.6 (3.0, 19.6)
- Household member with any new symptoms of illness	2.6 (9 / 347)	5.0 (2.3, 10.8)

- Any notification-triggering exposure †	5.1 (9 / 177)	10.3 (4.8, 22.09)
Activities within 14 days before test		
No	0.4 (3 / 678)	Reference**
Yes (any)	0.7 (29 / 4,145)	1.6 (0.5, 5.1)
- Spent time at another residence	1.1 (26 / 2,327)	4.6 (1.9, 11.3)
- Had visitors at own residence	1.0 (22 / 2,205)	2.6 (1.2, 5.5)
- Attended gathering >10 people	2.8 (19 / 672)	9.0 (4.5, 18.1)
- Worked outside of home	0.5 (10 / 2,152)	0.6 (0.3, 1.2)
- Used public restroom	0.7 (12 / 1,821)	1.0 (0.5, 2.0)
- Used public transportation	0.6 (4 / 699)	0.8 (0.3, 2.4)
- Participated in group sports	1.6 (4 / 257)	2.5 (0.9, 7.2)

qPCR: quantitative polymerase chain reaction, IRR: incidence rate ratio, CI: confidence interval.

*Excluding resamples, same-day re-tests, and repeated positives; includes N=2,914 participants with at least one qPCR test for SARS-CoV-2 during the study period.

**Reference group for "Yes (any)" comparisons; reference groups for specific symptoms/exposures/activities were those who did not report that symptom/exposure/activity.

† Reporting triggered notification to test.

Participants completed at least one weekly exposure survey in the 14 days before sample collection for 63% of tests (n=4,825). Of the 32 cases who had recently completed an exposure survey at the time of sample collection, 9 (29%) reported a potential household exposure that triggered a notification for them to test (Table 3). Test positivity was 10.3 times higher among participants who had a recent exposure-triggered notification (95% CI: 4.8, 22.0). Test positivity was also significantly higher among participants who reported recent engagement in 'higher risk' social activities, most notably attending a gathering of more than 10 people (IRR: 9.0; 95% CI: 4.5, 18.1).

SARS-CoV-2 seroprevalence

Only 18 (0.6%) of 2,877 participants who provided blood samples at baseline had SARS-CoV-2 antibodies (Table 4), all but one of them students. Most participants with antibodies at baseline either suspected past infection (28%), had been previously diagnosed (22%), or had a positive qPCR test the day blood was drawn (11%). Most (85%) participants in the student and essential worker cohorts provided blood samples at both baseline and endline (mean interval between samples: 48 days). Among 2,076 participants with baseline and endline

363 blood samples, 33 (1.6%) seroconverted from non-reactive at baseline to reactive at endline, 30
 364 of whom (91%) were also diagnosed via qPCR test during the study. Of the three participants
 365 who seroconverted without a positive qPCR test, two self-reported suspected past infection (one
 366 before baseline, one during the study period), while the third did not suspect past infection and
 367 had four negative qPCR tests over 40 days of study participation.

368 Of the 60 participants with incident SARS-CoV-2 infection during the study period, 41
 369 (68%) provided an endline blood sample at least one week after the date of their first positive
 370 qPCR test (mean time between positive qPCR test and blood sample: 36 days; range 13-52
 371 days). Of these, 34 (83%) were reactive (Table 4).

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373 **Table 4.** Seroprevalence of SARS-CoV-2 antibodies among participants in the Safe Campus
 374 Initiative, June-August 2020.

	Baseline, N (%)	Endline, N (%)	Both, N (%)
Serostatus – Cross-sectional*			
Reactive	18 (0.6)	48 (2.3)	-
Non-reactive	2,859 (99.4)	2,039 (97.7)	-
Serostatus – Longitudinal**			
Non-Reactive → Non-Reactive	-	-	2,029 (97.7)
Non-Reactive → Reactive	-	-	33 (1.6)
Reactive → Non-Reactive	-	-	0 (0)
Reactive → Reactive	-	-	14 (0.7)
Serostatus – Previous qPCR Positive†			
Reactive	-	34 (82.9)	-
Non-reactive	-	7 (17.1)	-

375 qPCR: quantitative polymerase chain reaction.

376 *N=2,888 participants who provided at least one blood sample.

377 **N=2,076 participants who provided blood samples at baseline and endline.

378 †N=41 participants who provided an endline blood sample ≥7 days *after* infection with SARS-CoV-2 identified via
 379 positive qPCR test.

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381 Discussion

382 This study provides a model of a voluntary, incentivized system to identify and link at-risk
 383 students to SARS-CoV-2 testing. While the incidence and seroprevalence of SARS-CoV-2 were

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3 384 generally low in this cohort of university students and employees in the summer of 2020, we
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5 385 observed the highest incidence among undergraduate students living in congregate settings,
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7 386 with nearly half of cases found to be associated with a super-spreader event.
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9 387 At the time of the study, many infection control strategies centered on symptomatic
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11 388 testing, reducing the likelihood of identifying asymptomatic, mildly symptomatic, and pre-
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13 389 symptomatic infections. Our approach sought to integrate symptom-based monitoring with
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15 390 exposure monitoring, random surveillance testing, and targeted surveillance testing in the
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17 391 context of an outbreak. Within this cohort, we previously demonstrated the acceptability of our
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19 392 low-barrier SARS-CoV-2 mitigation approach and the limitations of temperature monitoring as a
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21 393 tool for case identification.[14,28] The present analysis builds upon these contributions by
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23 394 triangulating prospective qPCR testing data with phylogenetic analyses of positive samples and
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25 395 serial antibody testing to evaluate whether case identification and containment were achieved.
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27 396 In doing so, we found evidence that the system successfully identified a high proportion of
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29 397 incident SARS-CoV-2 cases among participants and may have mitigated community
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31 398 transmission after an outbreak. Specifically, 91% of participants with newly-identified antibodies
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33 399 for SARS-CoV-2 at the end of the study had also been diagnosed with incident infection via
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35 400 qPCR test during the study period. While a sizeable cluster of cases among participants was
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37 401 traced to a single super-spreader event, the associated cluster lineage was successfully
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39 402 contained without spreading beyond campus. As the outbreak unfolded, the system also
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41 403 allowed for rapid real-time response (i.e., surveillance testing notifications to students living in
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43 404 congregate housing) and offered a readily accessible, incentivized entry point for testing for
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45 405 students concerned about potential exposure.
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49 406 Although some universities have adopted punitive measures intended to prevent
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51 407 transmission by controlling student behavior (for example, suspending students for hosting
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53 408 gatherings),[31–33] this approach has been criticized for its potential to reduce students' trust
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55 409 and cooperation.[34–36] Instead of punishing or shaming students who fail to adhere to public
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3 410 health guidance, some epidemiologists have called for a harm-reduction approach which
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5 411 supports and engages students as part of the solution.[34–36] The present study reinforces the
6
7 412 potential to integrate voluntary testing and risk monitoring systems to support targeted case
8
9 413 identification, as evidenced by the significantly higher positivity rates found among participants
10
11 414 whose self-reported symptoms and exposures triggered notifications to test. Our findings also
12
13 415 support increased outreach to groups of students at highest risk, particularly younger students
14
15 416 in congregate housing.

17
18 417 This study is strengthened by rich longitudinal data, including symptom and exposure
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20 418 tracking, qPCR testing, and seroprevalence data from more than 2,000 participants. The study
21
22 419 population comprised of a broad sample of university affiliates, both students and employees,
23
24 420 with strong representation of university subpopulations perceived to be at higher risk of infection
25
26 421 (e.g., undergraduates, essential healthcare workers). As on-campus activities were severely
27
28 422 restricted throughout the study period (all classes were held online, and few students were living
29
30 423 in residence halls), this study cannot provide insight into SARS-CoV-2 transmission risks related
31
32 424 to on-campus student activities. Nevertheless, as 73% of UC Berkeley undergraduate students
33
34 425 lived off campus *before* the pandemic,[37] systems to detect off-campus (i.e., community and
35
36 426 household) transmission remain important for SARS-CoV-2 monitoring efforts among students.
37
38 427 Additionally, all participants in the essential workers cohort and a subset of participants in the
39
40 428 faculty/cohort were working on campus during the study period, further motivating efforts to
41
42 429 monitor incidence in this population.

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44
45 430 There remain several limitations. We observed relatively few SARS-CoV-2 cases during
46
47 431 the study period. Accordingly, although many associations are statistically significant, our
48
49 432 estimates are imprecise (i.e., have wide confidence intervals) and must be interpreted with
50
51 433 caution. This study took place before the development of highly transmissible variants, such as
52
53 434 Delta and Omicron, and before vaccine rollout. Observed associations between symptoms and
54
55 435 positivity may also differ among those who have been infected by more recent variants and/or

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2
3 436 vaccinated. Further research is necessary to adapt and evaluate similar systems in the context
4
5 437 of both heightened transmissibility and more prevalent natural and vaccine-induced immunity.
6
7 438 Additionally, a high proportion of identified cases were traced to one outbreak, limiting the
8
9 439 generalizability of our exploratory assessment of risk factors for incident infection. There was
10
11 440 also anecdotal evidence that the outbreak prompted exposed students to enroll as study
12
13 441 participants.[14] While this self-referral into the study is likely to increase selection bias, it also
14
15 442 illustrates the utility of implementing non-stigmatizing, incentivized testing approaches to
16
17 443 increase testing uptake among at-risk students. Finally, our identification of participants who
18
19 444 seroconverted between baseline and endline may be incomplete due to loss-to-follow up and
20
21 445 imperfect sensitivity of SARS-CoV-2 antibody testing.

24 446 By integrating symptom and exposure monitoring systems with low-barrier testing, we
25
26 447 identified incident SARS-CoV-2 infections to reduce transmission within a university setting. Our
27
28 448 study contributes to a growing body of literature on novel, integrated SARS-CoV-2 surveillance
29
30 449 strategies in university settings.[38–44] While there have been seismic shifts in the SARS-CoV-
31
32 450 2 pandemic since 2020, universities continue to grapple with how best to mitigate on-campus
33
34 451 spread in the face of emerging variants, incomplete vaccination coverage, breakthrough
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36 452 infections, and decreased reliance on other mitigation strategies (e.g., masking, remote
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38 453 learning).[45,46] In light of universities' resource constraints and persistently high case counts,
39
40 454 incentivized approaches may not be feasible or sustainable in many settings. Thus, further
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42 455 research is needed to identify and test non-monetary incentives and other behavioral nudge
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44 456 strategies that encourage students and other campus community members to actively
45
46 457 participate in public health efforts to combat the pandemic. The lessons learned through this
47
48 458 study may inform the design of future adaptive strategies, ideally building beyond
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50 459 symptom/exposure monitoring and qPCR testing to integrate complementary interventions such
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52 460 as rapid antigen self-testing and vaccination promotion.
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2
3 461 **Keywords:** COVID-19, SARS-CoV-2, United States, young adults, students, universities,
4
5 462 essential workers, seroprevalence
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52
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7 489 to submit for publication.
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9

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11
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15
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18

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22
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27
28 498 <https://github.com/lauren-hunter/bcsci>
29
30

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32
33 500 Committee for the Protection of Human Subjects (#2020-06-13349, #2020-05-13261, #2020-04-
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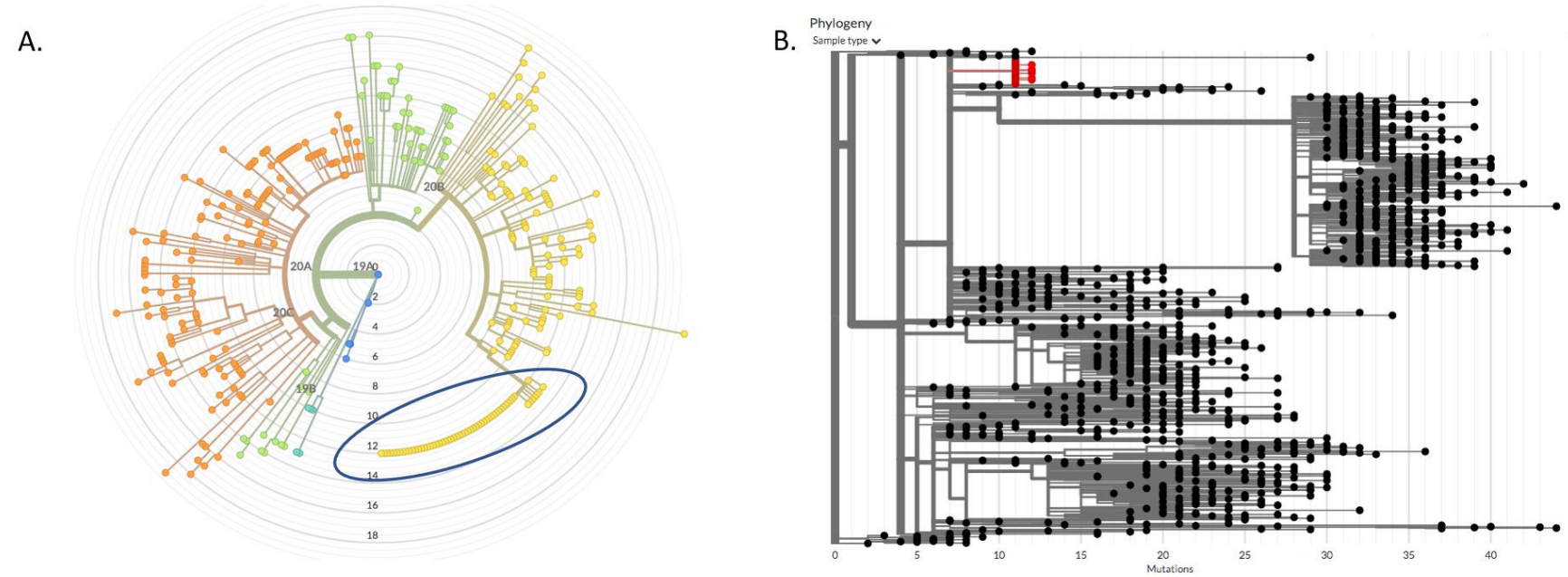
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Figure 1. Phylogeny of outbreak-associated strain of SARS-CoV-2 among participants in the Safe Campus Initiative.



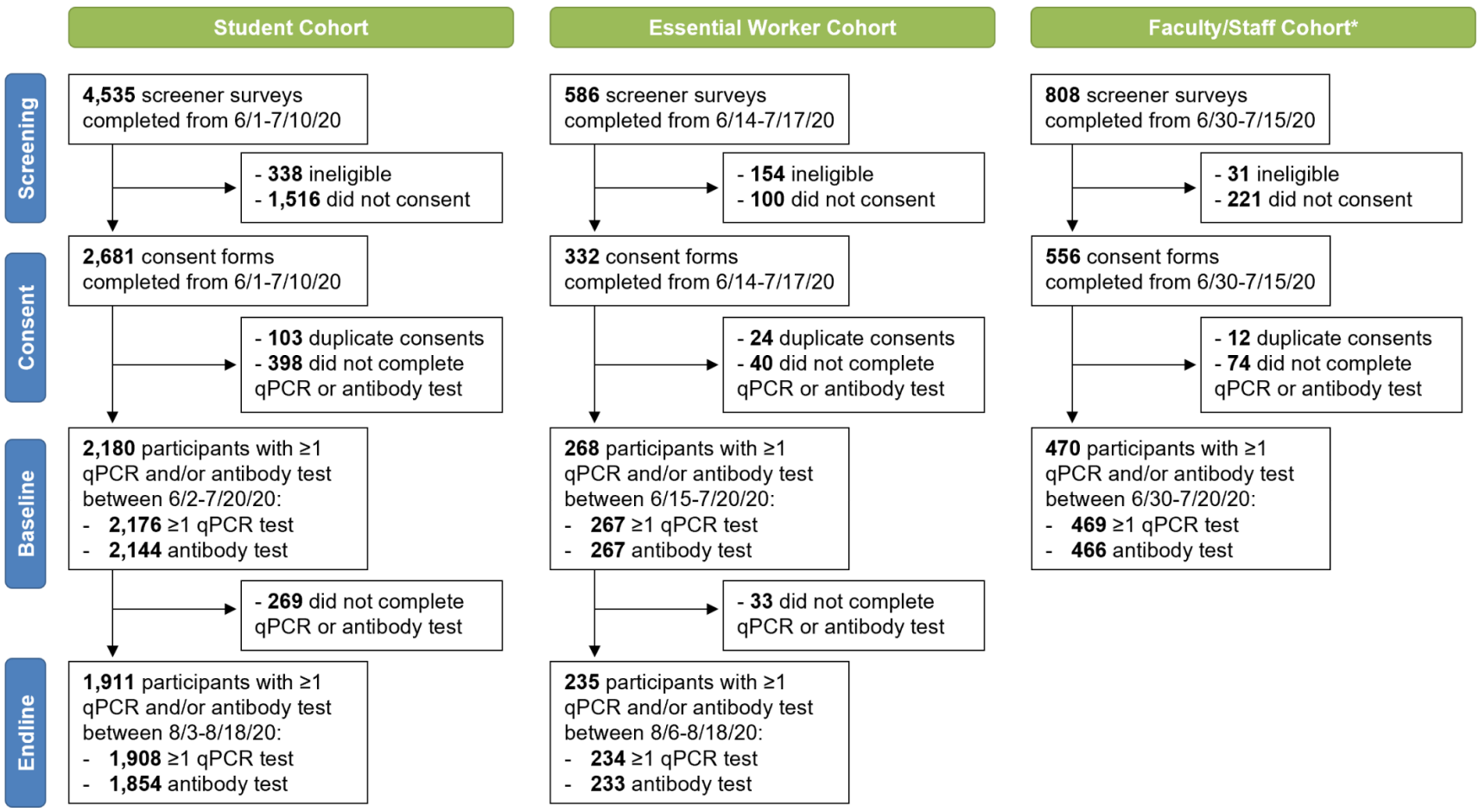
A. A maximum likelihood phylogeny constructed from 357 genomes sequenced by the Innovative Genomics Institute between May and July 2020 constructed using Nextstrain. Branch lengths represent divergence from Wuhan reference genome at center. Blue circle marks cluster of identical genomes from a campus super-spreader event.

B. A 1,057 node subtree of a neighbor-joining tree constructed with all SARS-CoV-2 sequences to date (constructed using UShER with over 1 million genomes in April 2021), showing the most similar genomes to the super-spreader event cluster (in red). There are no descendant branches from the cluster, demonstrating that the outbreak was contained and the lineage died out.

Supplementary Table 1. Eligibility criteria across the Berkeley COVID-19 Safe Campus Study cohorts.

	Student Cohort	Essential Worker Cohort	Faculty/Staff Cohort
Eligibility Criteria	- At least 18 years of age	- At least 18 years of age	- At least 18 years of age
	- Currently enrolled as an undergraduate or graduate student at UC Berkeley (i.e., not graduated in Spring 2020 or incoming for Fall 2020)	- Currently employed in one of the following departments at UC Berkeley: health services, police, facility services or other building management, environmental health and safety, laboratory animal care, athletics, dining, childcare, other residential or student services - Currently working on campus at UC Berkeley or expected to return to work during June 2020	- Currently employed as a faculty member, staff member, or postdoctoral scholar at UC Berkeley - Not already enrolled in the essential workers cohort
	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20	N/A	- Primarily residing in Alameda County or Contra Costa Country between 6/1/20-8/31/20
	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records	- Willing to sign release of information for COVID-19-related medical records

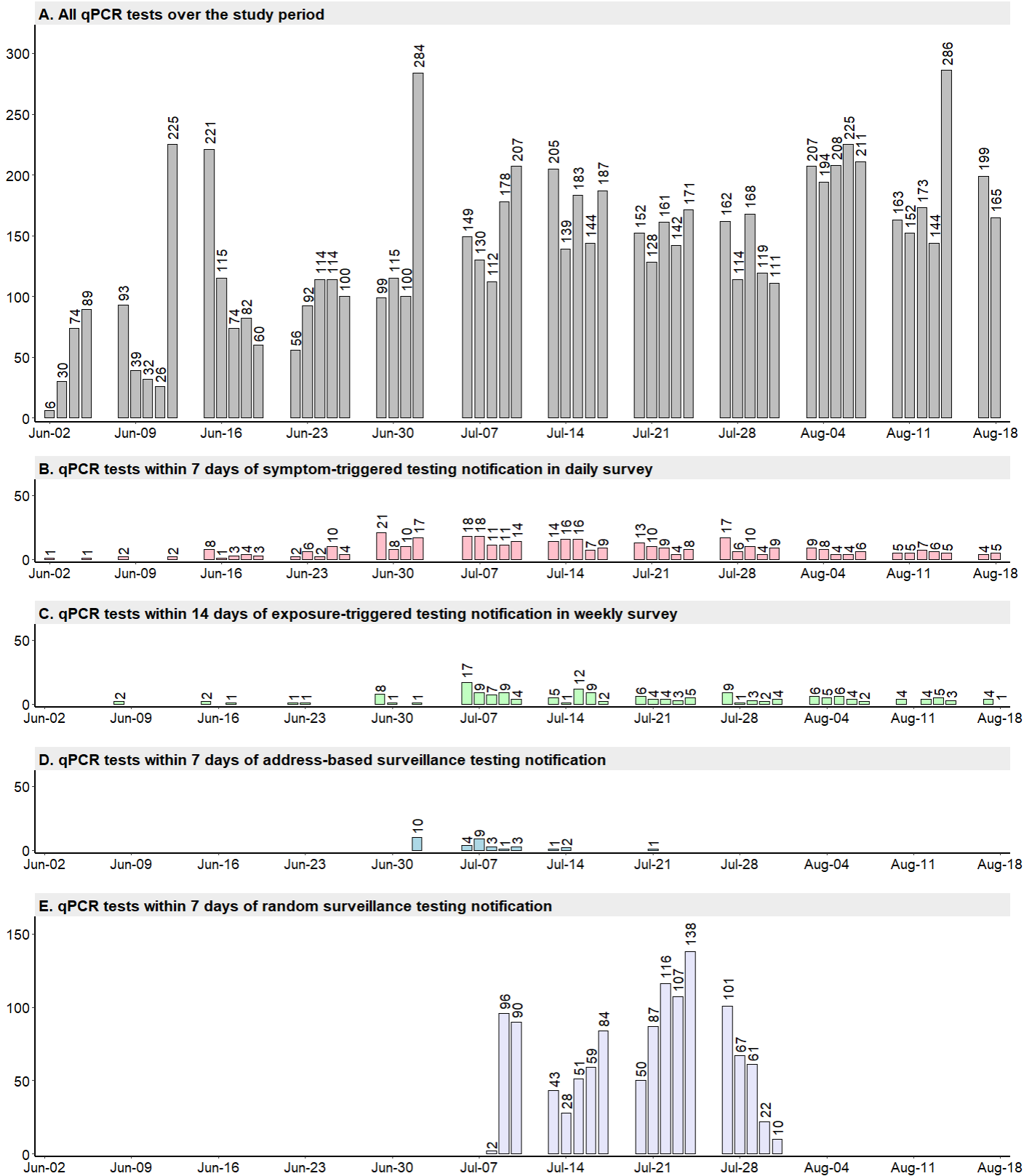
Supplementary Figure 1. Flow diagram for the Berkeley COVID-19 Safe Campus Study cohorts.



qPCR: quantitative polymerase chain reaction.

*Faculty/staff cohort not invited for endline testing appointments but could complete follow-up qPCR tests through 8/18/20.

Supplementary Figure 2. qPCR testing over time across the Berkeley COVID-19 Safe Campus Study cohorts.



qPCR: quantitative polymerase chain reaction.

Note: Panels are not mutually exclusive.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1-2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-9, Supplementary Figure 1
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-9, Supplementary Table 1
		(b) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-10
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	10
		(b) Describe any methods used to examine subgroups and interactions	N/A
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, explain how loss to follow-up was addressed	N/A
		(e) Describe any sensitivity analyses	N/A

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Supplementary Figure 1
		(b) Give reasons for non-participation at each stage	Supplementary Figure 1
		(c) Consider use of a flow diagram	Supplementary Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	11-13
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14, Tables 2-3
		(b) Report category boundaries when continuous variables were categorized	10, Table 3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.