Early Introduction and Rise of the Omicron Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Variant in Highly Vaccinated University Populations

Brittany A. Petros,1,2,3,4,5,6 Jacquelyn Turcinovic,5,6,a Nicole L. Welch,2,7 Laura F. White,6 Eric D. Kolaczyk,9,10 Matthew R. Bauer,2,11 Michael Cleary,12 Sabrina T. Dobkins,2 Lynn Doucette-Stamm,13 Mitch Gore,14 Parvathy Nair,15 Tien G. Nguyen,5 Scott Rose,16 Bradford P. Taylor,16 Daniel Tsang,16 Erik Wendlandt,16 Michele Hope,16 Judy T. Platt,15 Karen R. Jacobson,18 Tara Bouton,26 Seyho Yune,19 Jared R. Auclair,20,21,22 Lena Landaverde,13,23 Catherine M. Klaipperich,13,17,24 Davidson H. Hamer,5,18,24,25,26 William P. Hanage,16 Bronwyn L. MacInnis,7 Pardis C. Sabeti,2,15,27,28,29,30,b Erik Wendlandt,16 Michele Hope,16 Judy T. Platt,15 Karen R. Jacobson,18 Tara Bouton,26 Seyho Yune,19 Jared R. Auclair,20,21,22 Lena Landaverde,13,23 Catherine M. Klaipperich,13,17,24 Davidson H. Hamer,5,18,24,25,26 William P. Hanage,16 Bronwyn L. MacInnis,7 Pardis C. Sabeti,2,15,27,28,29,30,b John H. Connor,1,5,9,11,12 and Michael Springer,2,3,5

1Department of Systems Biology, Harvard Medical School, Boston, Massachusetts, USA; 2Broad Institute of Massachusetts Institute of Technology and Harvard, Cambridge, Massachusetts, USA; 3Division of Health Sciences and Technology and Harvard Medical School, Cambridge, Massachusetts, USA; 4Harvard/Massachusetts Institute of Technology, MD-PhD Program, Boston, Massachusetts, USA; 5National Emerging Infectious Diseases Laboratories, Boston, Massachusetts, USA; 6Bioinformatics Program, Boston University, Boston, Massachusetts, USA; 7Harvard Program in Biostatistics, School of Public Health, Boston University, Boston, Massachusetts, USA; 8Department of Mathematics & Statistics, Boston University, Boston, Massachusetts, USA; 9 earm B. Hariri Institute for Computing and Computational Science and Engineering, Boston University, Boston, Massachusetts, USA; 10Harvard Program in Biological and Biomedical Sciences, Division of Medical Sciences, Harvard School of Public Health, Boston, Massachusetts, USA; 11Harvard University Clinical Laboratory, Cambridge, Massachusetts, USA; 12Boston University Clinical Testing Laboratory, Boston University Boston, Massachusetts, USA; 13Integrated DNA Technologies, Inc, Coralville, Iowa, USA; 14Howard Hughes Medical Institute, Chevy Chase, Maryland, USA; 15Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA; 16Department of Chemistry and Chemical Biology, Northeastern University, Boston, Massachusetts, USA; 17Life Sciences Testing Center, Northeastern University, Burlington, Massachusetts, USA; 18Biopharmaceutical Analysis and Training Laboratory, Burlington, Massachusetts, USA; 19Department of Biomedical Engineering, Boston University, Boston, Massachusetts, USA; 20Department of Medical Sciences, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA; 21Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Cambridge, Massachusetts, USA; 22Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, USA; 23Division of Microbiology, Boston University School of Medicine, Boston, Massachusetts, USA; 24Center for Emerging Infectious Disease Research and Policy, Boston University, Boston, Massachusetts, USA; 25Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, Massachusetts, USA; 26Department of Biomedical Engineering, Boston University, Boston, Massachusetts, USA; 27Department of Global Health, Boston University School of Public Health, Boston, Massachusetts, USA; 28Department of Biomedical Analysis and Training Laboratory, Burlington, Massachusetts, USA; 29Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA; 30Center for Emerging Infectious Disease Research and Policy, Boston University, Boston, Massachusetts, USA; 31Department of Microbiology, Boston University School of Medicine, Boston, Massachusetts, USA

Background. The Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is highly transmissible in vaccinated and unvaccinated populations. The dynamics that govern its establishment and propensity toward fixation (reaching 100% frequency in the SARS-CoV-2 population) in communities remain unknown. Here, we describe the dynamics of Omicron at 3 institutions of higher education (IHEs) in the greater Boston area.

Methods. We use diagnostic and variant-specifying molecular assays and epidemiological analytical approaches to describe the rapid dominance of Omicron following its introduction into 3 IHEs with asymptomatic surveillance programs.

Results. We show that the establishment of Omicron at IHEs precedes that of the state and region and that the time to fixation is shorter at IHEs (9.5–12.5 days) than in the state (14.8 days) or region. We show that the trajectory of Omicron fixation among university employees resembles that of students, with a 2- to 3-day delay. Finally, we compare cycle threshold values in Omicron vs Delta variant cases on college campuses and identify lower viral loads among college affiliates who harbor Omicron infections.

Conclusions. We document the rapid takeover of the Omicron variant at IHEs, reaching near-fixation within the span of 9.5–12.5 days despite lower viral loads, on average, than the previously dominant Delta variant. These findings highlight the transmissibility of Omicron, its propensity to rapidly dominate small populations, and the ability of robust asymptomatic surveillance programs to offer early insights into the dynamics of pathogen arrival and spread.

Keywords. SARS-CoV-2; epidemiology; infectious disease surveillance.
among both vaccinated and unvaccinated individuals [3], although the relative rates of transmission from each remain unclear. Evidence suggests that Omicron can partially evade immunity acquired from prior COVID-19 infection [4] and from a 2-dose messenger RNA (mRNA) vaccine regimen [5], though a third dose improves Omicron neutralization efficiency, at least in the short term [6].

To mitigate the risks of congregate living, institutes of higher education (IHEs) use a combination of vaccination requirements [7, 8], high-frequency testing [8, 9], and behavioral interventions such as masking and social distancing to control viral spread. An analysis [10] suggests that in the setting of masking and frequent testing, case counts are not correlated with dorm occupancy or in-person instruction; this is consistent with the evidence that cases have been predominantly acquired in off-campus settings [11]. Moreover, detailed genomic analyses of an IHE and its nearby communities suggested that transmission dynamics within the IHE did not result in spread to the greater community [12]. Thus, many IHEs successfully controlled the spread of COVID-19 through the Delta surge. However, in December 2021, COVID-19 case counts rose rapidly in college communities [13] and in New England (NE) as a whole, with viral genomic sequencing confirming Omicron as the cause. While some institutions responded by converting to distance learning or requiring booster shots [14–18], the feasibility of maintaining residential college life without another spike in cases was in question.

Here, we capitalize on asymptomatic testing programs at 3 Boston-based IHEs, Boston University (BU), Harvard University (HU), and Northeastern University (NU), to document the rapid takeover of the Omicron variant, reaching near-fixation within the span of 9.5–12.5 days despite lower viral loads, on average, than the previously dominant Delta (B.1.627.2) variant.

**METHODS**

**Patient Samples and Ethics Statement**

We gathered de-identified sample information from 3 institutions with campus testing programs [11] (Table 1). We received the following information for every positive test collected between 2 December 2021 and 21 December 2021: sample collection date, cycle threshold (Ct) for 1 or more genes, and variant designation. From BU, we also received affiliate status (student vs employee, where employees include faculty, staff, and contractual employees). For HU, SARS-CoV-2 samples were collected from consented individuals under the Harvard Longwood Campus institutional review board (IRB) 20-1877 and covered by an exempt determination (EX-7295) at the Broad Institute. For BU, SARS-CoV-2 samples and data access were covered by an exemption determination under BU IRB 102 from HU) with missing variant information (ie, due to assay technical limitations) from all subsequent analyses. We removed 53 of the 22 211 (0.2%) MA sequences from GISAID that had a variant classification other than Delta or Omicron. We removed 22 211 of the 30 796 (72.1%) NE sequences from GISAID [29–31] that were in MA (ie, NE curve fits do not include MA) and 29 of the remaining 8585 (0.3%) sequences that had a variant classification other than Delta or Omicron. We removed 20 gene-specific data points with Ct >40 or Ct <5 due to possible technical errors. For Ct comparisons, samples with missing data due to failed amplification of a specific gene were removed solely from the analysis of that gene. For the per-affiliation analyses, we removed 6 of 524 (1.1%) BU cases with missing student or employee designations.

**Logistic Regression and Inference**

We fit logistic models on binary variant calls as a function of the date, estimating the proportion of cases that were Omicron over time for each university individually (with data from 2 December–21 December), for MA and NE (with data from 1 December–1 January) and for BU by affiliation (student vs employee; with data from 2 December–21 December). We documented 95% confidence intervals (CIs) for our model’s parameters, the overdispersion ratio, and McFadden’s pseudo-\(R^2\) (Supplementary Methods).

We estimated the date at which the Omicron fraction reached 10%, 50%, and 90%, hereafter defined as \(O_{10}\), \(O_{50}\), and \(O_{90}\). We used the notation \(\Delta O_{x, \text{A} \rightarrow \text{B}} = O_x, \text{Population A} – O_x, \text{Population B}\) 102.
represent the difference in the date at which the Omicron fraction reached x% between 2 populations, and we used the notation ΔO_{90−10} = O_{90−10} to represent the number of days it took a particular population’s Omicron fraction to rise from 10% to 90%.

We derived point estimates for Ox by inverting our regression model, such that:

\[ O_x = \frac{\text{logit}^{-1}(\frac{x}{100}) - B_0}{B_1}, \]

where \(B_0\) is the intercept and \(B_1\) is the slope. To generate a standard error for \(O_x\), we used the delta method [32, 33] with the transformation function \(O_x(x)\) (as above) and with the mean and covariance of \(x\) determined by the coefficients and covariance matrix of our regression model, respectively.

We generated 95% CIs for \(O_x\) and compared \(O_x\) values between populations by approximating the distribution of \(O_x\) via the family of Student t distributions (Supplementary Methods).

**Case Counts**

For MA and NE, we summed confirmed and probable daily cases into the metric total daily cases. We noted weekly variation in case reporting (ie, no MA cases were reported on the weekends; Supplementary Figure 1) and thus calculated 7-day rolling averages. We noted smaller-scale variation in case count (ie, slope of cases vs time) in MA and NE during the same period (note: testing rates were lower in these populations), followed by a striking regional surge in late December (Figure 1A). The Omicron surge at IHEs in mid-December was accompanied by a more modest rise in case counts (ie, slope of cases vs time) in MA and NE during the same period (note: testing rates were lower in these populations), followed by a striking regional surge in late December (Figure 1A, Supplementary Figure 1). A total of 1606 SARS-CoV-2 cases were identified across the 3 institutions (BU, HU, and NU) between 2 December (0% Omicron) and 21 December (91% Omicron). The fraction of cases that were Omicron across the IHEs, MA, and NE displayed a classic sigmoid-shaped curve consistent with logistic growth (Figure 1B, Supplementary Table 2), moving toward Omicron fixation. Delta diminished in frequency as well as total case count. By 5 January, the Harvard University Clinical Laboratory found that 100% of 159 samples tested were Omicron.

**Ct Value Comparisons**

We compared Ct values for Delta and Omicron cases per institution and per target, as each university had a unique testing protocol. We compared Ct values for the N1 (BU, HU), N2 (BU, NU), and ORF1ab (NU) genes. We also compared Ct values at BU per affiliation. We used the Wilcoxon rank sum test with Benjamini-Hochberg correction [35] to assess the relationship between SARS-CoV-2 variant and Ct.

**RESULTS**

There was a rapid increase in both daily case count and the Omicron fraction at IHEs in December 2021. In early December, Delta was circulating across MA and at IHEs, though case rates were higher per capita in the community outside of IHEs (Figure 1A). The Omicron surge at IHEs in mid-December was accompanied by a more modest rise in case counts (ie, slope of cases vs time) in MA and NE during the same period (note: testing rates were lower in these populations), followed by a striking regional surge in late December (Figure 1A, Supplementary Figure 1). A total of 1606 SARS-CoV-2 cases were identified across the 3 institutions (BU, HU, and NU) between 2 December (0% Omicron) and 21 December (91% Omicron). The fraction of cases that were Omicron across the IHEs, MA, and NE displayed a classic sigmoid-shaped curve consistent with logistic growth (Figure 1B, Supplementary Table 2), moving toward Omicron fixation. Delta diminished in frequency as well as total case count. By 5 January, the Harvard University Clinical Laboratory found that 100% of 159 samples tested were Omicron.

Omicron was established earlier and rose to fixation faster at IHEs than in MA as a whole (Figure 1B). We noted that MA
and NE (without MA) had visually indistinguishable curves and fitted parameters with highly overlapping CIs (Supplementary Table 2). Thus, we compared the timing of Omicron’s trajectory between IHEs and MA, with results generalizable to NE. To compare the timing of Omicron establishment across populations, we generated a metric \( O_{10} \); see the Methods section) that estimates the date range at which 10% of the cases were Omicron. \( O_{10} \) occurred significantly earlier at IHEs than in MA, by an average of 2.4 days (BU), 3.8 days (NU), and 9.2 days (HU) (Table 2, Supplementary Table 3). To compare the duration at which Omicron fixated across populations, we generated the metric \( \Delta O_{90–10} \), the duration (in days) during which Omicron rose from 10% to 90% of cases (see the Methods section). \( \Delta O_{90–10} \) was 9.5 at NU (95% CI, 9.2–9.8), 10.8 at BU (95% CI, 10.4–11.1), 12.5 at NU (95% CI, 12.1–12.9), and 14.8 in MA (95% CI, 14.8–14.9), indicating that the trajectory to Omicron fixation occurred more rapidly at IHEs (Table 2). Taken together, these data point toward Omicron’s earlier establishment and faster rise to fixation at IHEs compared with MA or NE.

Next, we found that BU employees displayed Omicron dynamics similar to those of BU students, with a 2–3 day delay in onset. We found no significant association between affiliation (student vs employee) and variant (Figure 2A; Fisher exact test, \( P = .12, \) odds ratio = 0.7 with 95% CI, .5–1.1), with employees accounting for 28.7% (74 Delta, 73 Omicron) of cases (1.13 per 100 employees) and students accounting for 71.3% (157 Delta, 214 Omicron; Figure 2B) of cases (1.20 per 100 students). We again used \( O_{10} \) (see the Methods section) to compare the timing of Omicron establishment between populations. \( O_{10} \) occurred significantly earlier among BU students relative to BU employees (by an average of 2.8 days).
DISCUSSION

Here, we document Omicron’s swift spread through Boston-based IHEs in December 2021, which led to unprecedented increases in case counts. Though the IHEs and the urban environment in which they are located were experiencing Delta transmission at the time of Omicron introduction, Omicron rapidly became the dominant variant. Over an 9- to 13-day period, variant proportions converted from >90% Delta to >90% Omicron. Importantly, the rapid increase in Omicron case counts was identified in highly vaccinated populations in which Omicron’s viral load, as inferred from anterior nares diagnostic Ct, was comparable to or lower than that of Delta. This is consistent with other reports that used throat or oropharyngeal swabs [36, 37], suggesting that the difference in viral loads is not specific to the anterior nares. This highlights that Omicron’s fitness is neither driven by a higher viral load nor reliant on an immunologically naive population.

Though the date of establishment differed at the 3 IHEs, the dynamics of Omicron takeover were strikingly similar. The rapid rise in the Omicron fraction was offset by 1–4 days between universities, though we cannot rule out differences in testing cadence as the cause of the lag. The dynamics of Omicron dominance were similar across campuses despite differences in testing programs, on-campus vs off-campus housing, and variant designation technologies. Additionally, the time to fixation for BU employees was more comparable to that of BU students than that of the state, supporting a transmission mode that is independent of the residential nature of college campuses.

In contrast to the early establishment and dominance in the IHEs in our study, Omicron’s procession toward fixation in MA occurred more slowly. While the difference in introduction time could be accounted for by earlier detection of cases in asymptomatic testing programs, the differences in slope and time to fixation cannot be explained by this factor. These dynamics are consistent with overdispersion in transmission, in which clusters of cases are responsible for the majority of spread, and the early stages of establishment within a community are stochastic and scale with the number of introductions [38, 39]. Overdispersion in SARS-CoV-2 transmission is well documented [38, 40–42], and our work is consistent with the continuation of this phenomenon with Omicron. IHEs are not siloed in their interaction networks; however, the proportion of interactions within an IHE’s network is greater than the proportion of interactions that exit into the community; as a result, clusters of transmission are readily detected via robust screening. The ability of Omicron to rapidly spread...
through a vaccinated population means that even communities that escape the initial peak of Omicron in the United States require continued monitoring. For example, rural communities may experience late introductions of Omicron and may not notice its arrival until a significant proportion of the population has become infected. This is of particular concern in areas with low vaccination rates, where a rapid rise in case counts can overwhelm healthcare systems.

There are technical limitations to the generalizability of this study. SGTF, caused by the deletion of amino acids 69–70, was one method we used for variant designation. While SGTF occurs in multiple SARS-CoV-2 variants, the Delta variant, which lacks this deletion, was the predominant circulating variant before Omicron’s arrival. Thus, SGTF was sensitive and specific (94.6% and 99.5%, respectively, inferred from GISAID data [29–31]) for Omicron in MA during the study period. Moreover, while it is possible that differences in viral loads are confounded by differences in timing of viral incubation or clearance, longitudinal sampling of infected individuals suggests that Omicron samples have lower peak viral loads than

Figure 2. A, Total number of cases at Boston University (BU) stratified by variant and stacked from 2 December–21 December. Gray, Delta; red, Omicron. B, Total number of cases at BU stratified by affiliation status and stacked from 2 December–21 December. Light green, employees; green, students. C, Proportion of cases that were Omicron from 2 December–21 December (BU students and employees) and 1 December 1–1 January (MA). Data were modeled using logistic regression. Massachusetts data from Global Initiative on Sharing All Influenza Data. Abbreviations: MA, Massachusetts; NE, New England; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
Delta samples [36]. Finally, there are multiple potential models for the relationship between student and employee dynamics, including student–employee transmissions and transmissions that cycle between students, the community, and employees. However, we lack the viral genomic sequencing, contact tracing, and community testing data necessary to distinguish these possibilities.

Moreover, IHEs differ from MA in social structure and demographics, which may play a role in Omicron dynamics. Though universities include individuals from different communities, the age distribution, residential life, and extracurricular activities could influence Omicron dynamics. Furthermore, the degree to which potential superspreader events could be important for the initial seeding of Omicron and its continued spread is not captured here. It is possible that the spread of Omicron in non-IHEs may be slower if the structure of the social network differs [43], resulting in fewer opportunities for clustered transmission. We cannot separate

### Table 3. Affiliation-Specific Point Estimates and 95% Confidence Intervals for $O_x$ and for $\Delta O_{90-10}$

| Affiliation                  | $O_{10}$  | $O_{10}$ 95% CI | $O_{50}$ | $O_{50}$ 95% CI | $O_{90}$ | $O_{90}$ 95% CI | $\Delta O_{90-10}$ days | $\Delta O_{90-10}$ 95% CI (days) |
|-----------------------------|-----------|-----------------|----------|-----------------|----------|-----------------|--------------------------|---------------------------------|
| Boston University employees | 12 December | 10–14 December  | 16 December | 15–17 December  | 20 December | 19–22 December  | 8.5                      | (7.9–9.1)                      |
| Boston University students  | 9 December | 7–10 December  | 14 December | 13–14 December  | 18 December | 17–20 December  | 9.5                      | (9.1–9.9)                      |
| Massachusetts               | 12 December | 12 December  | 19 December | 19–20 December  | 27 December | 27 December  | 14.8                    | (14.8–14.9)                    |

$O_x$, the date at which the Omicron fraction equals $x$ percent. $\Delta O_{90-10}$, the duration of time that it takes the Omicron fraction to rise from 10% to 90%. CIs were generated via the Student $t$ distribution, with estimation of the standard errors via the delta method (see the Methods section).

Abbreviation: CI, confidence interval.

### Figure 3.

N1 cycle threshold for Delta vs Omicron cases at BU (A) and HU (B). N2 cycle threshold for Delta vs Omicron cases at BU (C) and NU (D). Gray, Delta; red, Omicron. The first, second, and third quartiles are within the box, with the median line bolded. The whisker length is 1.5 times the interquartile range (IQR), unless the furthest point is less than 1.5*(IQR) from the quartile. Outliers are displayed as points. $P$ values via the Wilcoxon rank sum test and corrected via the Benjamini-Hochberg method (across the 4 comparisons in Figure 3 and the 1 comparison in Supplementary Figure 2). Abbreviations: BU, Boston University; HU, Harvard University; NU, Northeastern University.
possible sociobehavioral factors, such as an increase in indoor gatherings prior to the start of final examinations or in anticipation of the winter holidays, from properties intrinsic to the virus that may affect dispersal. Finally, lower vaccination rates in MA may contribute to the relative fitness of Delta vs Omicron, and testing in MA may be biased if symptomatic testing occurs more frequently with Delta than with Omicron.

What can we learn from the spread of Omicron through universities that could help us mitigate future waves of SARS-CoV-2 or other pathogens? First, sites that have characteristics like IHEs can be informative early detection sites. We note 2 of many reasons. First, IHEs include individuals from a variety of backgrounds who intermix at the university and in the larger community, and IHEs have implemented university-wide asymptomatic screening programs. Screening programs like these can catch and categorize infections well before trends are noted in the larger community and have the potential to forecast testing needs and hospital admissions. Second, it is extremely difficult to stop the spread of a highly transmissible virus once it has become established in a community. BU, HU, and NU controlled the spread of previous variants of SARS-CoV-2 via a combination of high-cadence testing, isolation of positive individuals, contract tracing, quarantining of close contacts, social distancing, masking, vaccination requirements, and ventilation improvements. These measures were not sufficient to stop the spread of Omicron, and both BU and HU mitigated further spread via remote learning during the January term. This emphasizes the need for continued surveillance programs to rapidly identify and mitigate outbreaks before they become pandemics.

Supplementary Data

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

Notes

Author contributions. B. A. P. and J. T. accessed and verified the underlying data reported in the article. B. A. P. conducted statistical analyses, and L. F. W. and E. D. K. provided guidance for the analyses. B. A. P. and J. T. produced software and visualizations. J. T. collected and curated Boston University (BU) data, and L. D.-S., J. T. P., K. R. J., B. L., L. L., C. M. K., and D. H. H. provided assistance. N. L. W. collected and curated mCARMEN data with help from M. R. B., S. T. D., and T. G. N. Variant-specific polymerase chain reaction assay was collected and curated by M. C. and M. H. using custom primers and probes designed by M. S., M. G., D. T., and E. W. Project administration was aided by P. N. B. P. curates the Centers for Disease Control and Prevention (CDC) and Global Initiative on Sharing All Influenza Data (GISAID) data. J. R. A. and S. Y. collected and curated Northeastern University (NU) data. B. A. P. wrote the original draft of the manuscript with feedback provided by W. P. H., P. C. S., J. H. C., and M. S. The manuscript was reviewed and edited by N. L. W., P. N. B. P., J. T. B., W. P. H., P. C. S., J. H. C., and M. S. Authors W. P. H., P. C. S., J. H. C., and M. S. conceptualized and supervised the study and reviewed and edited the final manuscript.

Acknowledgments. We gratefully acknowledge the students and employees at each participating university, and the staff at the BU, HU, and NU clinical testing laboratories. We gratefully acknowledge the authors from the originating laboratories responsible for obtaining the specimens and the submitting laboratories where genetic sequence data were generated and shared via GISAID, on which this research is based.

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of General Medical Sciences (NIGMS) or the National Institutes of Health (NIH).

Data sharing. All submitters of data may be contacted directly (www.gisaid.org). Access to patient sample metadata was facilitated by the Massachusetts Consortium on Pathogen Readiness (MassCPR). R analyses are available at https://github.com/bpetros95/omi-uni.

Financial support. This work was supported by the National Institute of General Medical Sciences grant T32GM070773 to B. A. P. and grant R35GM141821 to L. F. W.; BU for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) surveillance to J. H. C.; MassCPR to J. H. C., W. P. H., T. P. B., and K. R. J.; the China Evergrande Group to J. H. C.; the NIH grant NIAID K23 and grant AI152903-01A1 to T. B.; the CDC SARS-CoV-2 Baseline Genomic Surveillance contract (grant 75D30121C0501 to the Broad Institute via the Clinical Research Sequencing Platform, LLC) to B. L. M.; a CDC Broad Agency Announcement grant 75D30120C09605 to B. L. M.; the Rockefeller Foundation grant 2021 HTH 013 to B. L. M. and P. C. S.; the National Institute of Allergy and Infectious Diseases grant U01AI151812 to P. C. S.; the Howard Hughes Medical Institute Investigator award to P. C. S.; and the NIH grant SR01GM120122 to M. S. D. H. H. reports funding support for SARS-CoV-2 research from BU. C. M. K. reports support for this work from BU internal funding. D. T. reports support for this work paid to author from Integrated DNA Technologies. This work is made possible by support from Flu Lab and a cohort of donors through the Audacious Project, a collaborative funding initiative housed at TED, including The ELMA Foundation, MacKenzie Scott, the Skoll Foundation, and Open Philanthropy.

Potential conflicts of interest. M. S. is cofounder of, shareholder in, and advisor to Rhinostics, Inc and reports a patent for an anterior nares swab (US provisional patent application 63/008,571). M. G., D. T., S. R., and E. W. are employed by Integrated DNA Technologies. D. T. reports stock or stock options from Danaher Corporation (payments to author). S. R. reports stock or stock options from Danaher Corporation. C. M. K. is cofounder of Biosens8, Inc and reports grants or contracts unrelated to this work from the NIH National Institute of General Medical Sciences, Defense Advanced Research Projects Agency, Uniformed Services University, and BU; reports consulting fees paid to author from Adventus Research + Consulting, Inc; is a member of the Biomedical Engineering Society Board; and has a leadership or fiduciary role with the American Institute for Medical and Biological Engineering. J. H. C. is a paid consultant for Cell Signaling Technologies and reports funding unrelated to this work from Mass CPR/Evergrande. W. P. H. serves on scientific advisory boards for Biobot Analytics, Inc and Merck; received consulting fees from Biobot Analytics; contributed expert witness testimony on the expected course of the pandemic for Analysis Group; and reports stock or stock options from Biobot Analytics. P. C. S. is a founder of and shareholder in Sherlock Biosciences, reports consulting fees from Sherlock Biosciences, reports patents for CRISPR technology (PCT/US2018/022764 and PCT/US2019/061577), and is on the board and serves as shareholder for the Danaher Corporation. B. A. P. reports lecture honoraria from the Harvard Secondary School Program and a patent for CRISPR technology (WO 2022/051667). D. H. H. reports funding from an institution unrelated to this work (CDK 1 U01CK00632-01-00 GeoSentinel); consultancy payments to the author from Major League Soccer, the Professional Golf Association of America, Equinox, and Xenophon Strategies, Inc; and participation as chair of a data and safety monitoring board for COVEDZ. M. T. G. reports stock or stock options from Danaher Corporation. T. B. reports grants or contracts unrelated to this work from Gilead Sciences, Inc and Fujifilm Pharmaceuticals U.S.A., Inc. M. H. reports consulting fees as an independent researcher for IHEs.
laboratory consultant for Nichols Management Group, LLC. All remaining authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. World Health Organization. Coronavirus (COVID-19) dashboard. Available at: https://covid19.who.int. Accessed 10 January 2022.
2. Centers for Disease Control and Prevention. COVID data tracker. 2020. Available at: https://covid.cdc.gov/covid-data-tracker/. Accessed 10 January 2022.
3. Pulliam JRC, van Schalkwyk C, Govender N, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. bioRxiv 2021.
4. Valesano AL, Fitzsimmons WJ, Blair CN, et al. SARS-CoV-2 genomic surveillance on an urban university campus during a second wave of the pandemic. JAMA Netw Open 2020; 3:e2016818.
5. Frazier PI, Cashore JM, Duan N, et al. Modeling for COVID-19 college reopening decisions: Cornell, a case study. Proc Natl Acad Sci U S A 2022; 119.
6. Nemet I, Kliker L, Lustig Y, et al. Third BNT162b2 vaccination neutralization of SARS-CoV-2 Omicron infection. N Engl J Med 2021; 386(5):492–4.
7. Hernandez J. Some colleges and universities will start the new year online as staff in the US. Available at: https://covid.cdc.gov/covid-data-tracker/. Accessed 10 January 2022.
8. Stubbs CW, Springer M, Thomas TS. The impacts of testing cadence, mode of in-person classes in the fall. The New York Times. 2021; Available at: https://www.nytimes.com/2021/04/29/us/colleges-vaccinations-enrollment.html. Accessed 10 January 2022.
9. Boyer C, Rumpler E, Kissler S, Lipsitch M. Infectious disease dynamics and restrictions on social gathering size. bioRxiv 2021.
10. Lee EC, Wada NI, Grabowski MK, Gurley ES, Lessler J. The engines of individual variation on disease emergence. Nature 2005; 438:355–9.
11. Lee EC, Wada NI, Grabowski MK, Gurley ES, Lessler J. The engines of individual variation on disease emergence. Nature 2005; 438:355–9.
12. Daily COVID-19 dashboard. 2021. Available at: https://news.northeastern.edu/coronavirus/reopening/testing-dashboard/. Accessed 24 January 2022.
13. Daily COVID-19 dashboard. 2021. Available at: https://news.northeastern.edu/coronavirus/reopening/testing-dashboard/. Accessed 24 January 2022.
14. Brigade COVID-19 data dashboard. Available at: https://www.harvard.edu/coronavirus/covid-vaccine-booster-requirement/. Accessed 10 January 2022.