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ORIGINAL ARTICLE

Case–control study to identify risk factors for SARS-CoV-2 infection among university students in the northeastern USA

Kevin J. Cummings | **Marin Clarkberg** | **Jefferson Busche** | **Alexander J. Travis** | **Genevive R. Meredith** | **Isaac Weisfuse** | **Casey L. Cazer** | **Gary A. Koretzky** | **Lorin D. Warnick**

Cornell University, Ithaca, New York, USA

Correspondence
Kevin J. Cummings, Department of Public and Ecosystem Health, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA.
Email: kjc39@cornell.edu

Abstract

Curbing the coronavirus disease 2019 (COVID-19) pandemic requires a thorough understanding of risk factors for transmission of SARS-CoV-2, the etiologic agent. Institutions of higher education present unique challenges for controlling disease spread because of features inherent to these settings. Our objective was to determine risk factors for SARS-CoV-2 infection among a university student population in the northeastern USA during the spring and fall 2021 semesters, using the case–control study design. Cases were defined as students with a newly diagnosed SARS-CoV-2 infection detected either through the robust PCR-based surveillance testing program on campus or through healthcare testing if symptoms compatible with COVID-19 were present. Controls were defined as students with negative SARS-CoV-2 status, based on consistently negative PCR results at the time of selection. A comprehensive questionnaire was administered to each student enrolled in the study, covering a broad range of campus life activities. A total of 446 cases and 1,185 controls were included in this study. Multivariable logistic regression analysis showed that recent party attendance (adjusted OR = 2.3, $p < .0001$), recently visiting a bar (aOR = 1.6, $p = .007$), living in a campus residence hall (aOR = 1.6, $p = .001$), fraternity/sorority membership (aOR = 1.8, $p = .002$), and recent travel (aOR = 1.3, $p = .04$) were associated with being a COVID-19 case. Having an on-campus job was negatively associated with being a COVID-19 case (aOR = 0.6, $p = .0003$). Among cases, the most commonly reported symptoms were cough (43.9%), fatigue (38.1%) and sore throat (30.3%). These findings can be used to inform the development of COVID-19 mitigation strategies and public health outreach efforts in university settings, thus reducing SARS-CoV-2 transmission among students and helping to preserve the vital education and research missions of these institutions.

KEYWORDS
case–control study, COVID-19, epidemiology, public health, risk factors, SARS-CoV-2

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has resulted in over 525 million cases and 6.2 million deaths globally, as of May 2022 (JHU Coronavirus Resource Center, 2022). Clinical presentation varies widely, but the most common symptoms are fever, dry cough and dyspnoea (Suleyman et al., 2020; Vahey et al., 2021). Other possible symptoms include fatigue, myalgia, anosmia, ageusia, rhinorrhoea, sore throat, vomiting and diarrhoea (Zeng et al., 2020). Severe clinical manifestations may occur, with hypoxemic respiratory failure being the most frequent reason for ICU admission (Wiersinga et al., 2020). In addition, infection may result in long-term sequelae such as dyspnoea, fatigue and cognitive impairments (Groff et al., 2021). Transmission of SARS-CoV-2, the etiologic agent of COVID-19, most commonly occurs via respiratory droplet spread, such as through coughing, sneezing or talking (Wiersinga et al., 2020). However, SARS-CoV-2 can also be transmitted via fomites and aerosol spread (Wiersinga et al., 2020).

Mitigating the spread of disease requires a comprehensive understanding of risk factors for transmission of SARS-CoV-2. Institutions of higher education (IHEs) present unique challenges for controlling transmission because of features inherent to these settings. College students typically live in residence halls or similar housing; spend considerable time in communal spaces such as classrooms, laboratories and dining halls; participate in campus activities including athletics, clubs and Greek organizations; and take part in various social gatherings.

The objective of this study was to determine risk factors for SARS-CoV-2 infection among students at Cornell University (Ithaca, New York, USA), using the case–control study design. Identification of factors that are driving transmission on campus can help inform the development of COVID-19 intervention strategies and public health outreach campaigns in university settings.

2 | MATERIALS AND METHODS

2.1 | Source population

Cornell University had a student population of 25,582 on the Ithaca campus in the fall 2021 semester. This included 15,503 undergraduate students, 7,101 graduate students, and 2,978 professional students. For the study described here, cases and controls were drawn from the student population during the spring and fall 2021 semesters. In April 2021, university administration announced that all students would be required to be fully vaccinated against COVID-19 by the start of the fall semester to maintain an enrolled status, unless they had an approved medical or religion exemption. However, the proportion of vaccinated students had already exceeded 80% by the end of April 2021.

The university had developed an online tool (called Daily Check) that required Cornell community members to confirm that they were symptom free and had not had close contact with a SARS-CoV-2-positive or symptomatic individual, prior to coming to campus each day. Through this online tool, all students were asked if they were willing to be contacted regarding COVID-19 research participation. A total of 56% of students agreed to be contacted.

2.2 | COVID-19 testing

The SARS-CoV-2 surveillance testing program required twice weekly asymptomatic testing for undergraduate and professional students and weekly testing for graduate students (as well as faculty and staff). Testing schedules were adjusted somewhat over the course of the program to meet changing conditions. All nine surveillance testing locations on campus (open 8:00 AM to 4:00 PM, 7 days a week) operated under the same protocol for supervised self-collection of anterior nares samples. Students with symptoms compatible with COVID-19 were tested at Cornell Health, the healthcare provider for students on the Ithaca campus, through collection of anterior nares samples. All samples were sent to the Cornell COVID-19 Testing Laboratory (based in the College of Veterinary Medicine and operating in collaboration with Cayuga Health Systems) for processing via real-time PCR using the EZ-SARS-CoV-2 Real-Time RT-PCR assay (Tetracore, Inc., Rockville, MD). The estimated sensitivity of this assay ranges between 94% and 96%, while specificity is estimated to be 94%, as compared to other real-time PCR analysis of nasopharyngeal samples (Laverack et al., 2021).

2.3 | Cases and controls

Cases were defined as students with a newly diagnosed SARS-CoV-2 infection, that is, initial diagnosis must have occurred at least 14 days beyond the start of the semester to be considered an incident case. Cases were detected through surveillance testing or testing for cause. Eligible cases included those individuals with a confirmed positive test result, with or without compatible symptoms. All confirmed positive test results were logged in a database in REDCap (Research Electronic Data Capture), a secure web-based tool for data management and survey administration (Harris et al., 2009, 2019). Via REDCap, we provided the study description to SARS-CoV-2-positive students who had previously agreed to be contacted regarding COVID-19 research participation, at the time of isolation. Interested students were then able to link directly to the study consent form and subsequent questionnaire. Eligible cases were enrolled if informed consent was provided.

Controls were defined as students with negative SARS-CoV-2 status, defined as consistently negative real-time PCR results at the time of selection. The study description was provided to SARS-CoV-2-negative students who had previously agreed to be contacted regarding COVID-19 research participation. Three potential controls per case, selected randomly at the time each case was identified, were sent the study description via REDCap. Interested students were again able to link directly to the study consent form and subsequent questionnaire. Eligible controls were enrolled if informed consent was provided. In instances of low response, additional potential controls

were randomly selected to receive the study description, to reach our desired target of three controls per case. Individuals were excluded if there was a history of positive SARS-CoV-2 status.

Overall, the proportion of invited students who participated in the study was 26%. Response was 33% among potential cases and 24% among potential controls. This study was approved by the Cornell University Institutional Review Board.

2.4 | Questionnaire

A standardized, pilot-tested questionnaire was administered to each case and control, focusing on putative behavioural risk factors for SARS-CoV-2 infection that are especially relevant to a university setting. Collected data included demographic information, symptoms, habits and beliefs regarding public health measures, and exposure history during the previous 14 days. Exposure data included academic activities, residence information, campus life activities, dining habits, social activities, employment information, local transportation use and travel history. To strictly maintain confidentiality, no identifiable information was collected; the questionnaire data were kept separate from the online consent forms, and the two were not connected.

2.5 | Statistical analysis

Data were imported into a statistical software program (SAS, version 9.4; SAS Institute Inc., Cary, NC, USA) for variable coding and analysis. Descriptive analysis was performed on all variables, and chi-squared testing was used to establish whether each variable was independently associated with case or control status. A multivariable logistic regression model was then used to identify and quantify risk factors for SARS-CoV-2 infection, with case/control status as the dichotomous outcome variable. Initial selection of variables was based on the bivariable analysis screening ($p < .25$), and a backward elimination approach was used to determine a final multivariable model. Values of $p < .05$ were considered statistically significant.

3 | RESULTS

A total of 446 cases and 1,185 controls from the spring and fall 2021 semesters were included in this study (46 cases and 140 controls from spring; 400 cases and 1,045 controls from fall). Among cases who reported their gender (97.1%), 57.3% (248/433) were female, 41.8% (181/433) were male and 0.9% (4/433) identified as nonbinary (Table 1). The median age among cases who reported their age (86.5%) was 20.0 years. Among controls who reported their gender (94.7%), 57.3% (643/1,122) were female, 40.7% (457/1,122) were male and 2.0% (22/1,122) identified as nonbinary. The median age among controls who reported their age (87.2%) was 22.0 years.

Bivariable analysis revealed that more cases than controls reported a history of party attendance (49.1% vs. 26.3%, $p < .0001$), visiting a bar (17.3% vs. 9.0%, $p < .0001$) and concert/play attendance (8.7% vs. 5.0%, $p = .004$) during the previous 14 days. More cases than controls also reported a history of sport participation (15.4% vs. 11.1%, $p = .03$) and fraternity/sorority membership (17.4% vs. 8.2%, $p < .0001$). Living in a campus residence hall was more common ($p = .03$) among cases (34.0%) than controls (28.0%), and more cases (26.2%) than controls (21.3%) reported a history of recent travel outside of Ithaca ($p = .04$). Current use of a vaping device was more common ($p = .02$) among cases (8.9%) than controls (5.6%), and more cases (23.7%) than controls (18.7%) reported never or rarely wearing a mask when off campus and indoors ($p = .03$). Fewer cases (20.4%) than controls (28.9%) reported a history of having an on-campus job ($p = .0005$).

TABLE 1 Demographic variables reported by cases (with a newly diagnosed SARS-CoV-2 infection) and controls among a university student population in the northeastern USA during the spring and fall 2021 semesters

Variable	Cases, % (*n*)	Controls, % (*n*)
Gender		
Female	57.3 (248)	57.3 (643)
Male	41.8 (181)	40.7 (457)
Nonbinary	0.9 (4)	2.0 (22)
Racial or ethnic identity[a]		
American Indian or Alaska Native	0.4 (2)	0.8 (9)
Asian	24.2 (108)	31.9 (378)
Black or African American	9.4 (42)	3.5 (42)
Hispanic or Latina/Latino	11.2 (50)	11.9 (141)
Native Hawaiian or other Pacific Islander	0.2 (1)	0.8 (9)
White	57.8 (258)	53.6 (635)
Arab or Middle Eastern	2.7 (12)	1.9 (23)
Age (median)	20.0 years	22.0 years

[a]Totals exceed 100% because some students indicated more than one racial or ethnic identity.

Multivariable logistic regression analysis (Table 2) showed that recent party attendance (adjusted OR = 2.3, $p < .0001$), recently visiting a bar (aOR = 1.6, $p = .007$), living in a campus residence hall (aOR = 1.6, $p = .001$), fraternity/sorority membership (aOR = 1.8, $p = .002$) and recent travel outside of Ithaca (aOR = 1.3, $p = .04$) were associated with being a COVID-19 case. Having an on-campus job was negatively associated with being a COVID-19 case (aOR = 0.6, $p = .0003$).

Among cases, the most commonly noted symptoms were cough (43.9%), fatigue (38.1%) and sore throat (30.3%). Body aches (23.3%), fever (15.7%), loss of taste or smell (12.6%), dyspnoea (5.4%) and vomiting or diarrhoea (5.4%) were reported less frequently. A total of 38.3% of cases reported having no symptoms.

4 | DISCUSSION

Recent party attendance and visiting a bar were risk factors for SARS-CoV-2 infection among Cornell University students. These activities

TABLE 2 Association between status as a case (newly diagnosed SARS-CoV-2 infection) and campus life activities among a university student population in the northeastern USA during the spring and fall 2021 semesters, as estimated by a logistic regression model

Variable	Adjusted odds ratio	95% Confidence interval	*p*
Recent party attendance (last 14 days)	2.3	(1.8, 3.0)	< .0001
Recently visiting a bar (last 14 days)	1.6	(1.1, 2.3)	.007
Living in a campus residence hall	1.6	(1.2, 2.0)	.001
Fraternity/sorority membership	1.8	(1.2, 2.6)	.002
Recent travel (last 14 days)	1.3	(1.1, 1.8)	.04
Having an on-campus job	0.6	(0.5, 0.8)	.0003

typically involve a high density of people in an indoor setting, presumably with individuals in proximity and perhaps raising their voices to be heard. Alcohol consumption is also likely to be a factor, with the potential for concomitant lapses in judgment and reduced adherence to public health guidelines related to COVID-19. In a previous study among college students in Indiana (Kianersi et al., 2021), socializing in groups larger than five people while drinking alcohol increased the likelihood of SARS-CoV-2 seropositive status. Similarly, participation in social events and frequent alcohol consumption were associated with SARS-CoV-2 PCR-positive status among students at a Wisconsin university (Segaloff et al., 2021). In another study (Hobbs et al., 2020), attending a social gathering with persons outside the household was associated with greater risk of SARS-CoV-2 infection among individuals under 18 years of age, as confirmed by PCR. There are several potential strategies for mitigating this risk at universities. Campus parties could be curtailed during certain time frames based on COVID-19 benchmarks such as rising case numbers within the university or surrounding community. Social gatherings could be modified in various ways, such as holding them outside, limiting the number of attendees, or enforcing masking and social distancing guidelines. Universities could also offer and promote alternative types of events that provide students with a necessary social outlet while still safeguarding public health.

Living in a campus residence hall was also a risk factor for SARS-CoV-2 infection among Cornell students. This type of living arrangement greatly increases the potential for close contact among students, both in terms of density of people and available time for social interactions. Residence halls generally include rooms with two or more occupants, shared bathrooms and communal areas for gathering. Having a roommate or socializing in rooms or common areas would provide ample opportunity for transmission. In a study focused on the effect of housing status on COVID-19 risk at a Wisconsin university (Bigouette et al., 2021), students residing in a shared living space (bedroom or suite) were more likely to test positive than students living alone, based on either antigen or PCR testing. Evidence of transmission among students within shared university housing was also found in England, using a genomic epidemiologic approach (Aggarwal et al., 2022). Our findings are also consistent with the recognized role of household transmission in COVID-19 epidemiology (Burke et al., 2021; Madewell et al., 2021). If feasible, reducing the number of students living in campus residence halls would help decrease the risk of SARS-CoV-2 transmission at universities. Group housing may also help explain why membership in a fraternity or sorority increased the risk of SARS-CoV-2 infection among students in the present study, in addition to a presumably greater likelihood of attending parties sponsored by Greek organizations.

Lastly, travel outside the Ithaca area was identified as a risk factor for SARS-CoV-2 infection among students in this study. There are geographic discrepancies in COVID-19 prevalence (CDC COVID-19 Response Team, 2020), based on numerous factors including population structure and density, community mitigation strategies, local vaccination uptake and compliance with public health guidelines. In addition, travel increases the number of possible contacts and thus the potential for transmission. Travel may also involve forms of transportation such as airplanes, which might increase the risk of infection (Toyokawa et al., 2022), and it may be associated with attending events, visiting family and friends, and other risk factors.

Having an on-campus job was negatively associated with SARS-CoV-2 infection. The reasons for this are unclear, but perhaps the time demands of employment above and beyond academic responsibilities precluded participation in other activities associated with elevated disease risk. Subsequent analysis revealed that students with an on-campus job were significantly less likely to report a history of party attendance during the previous 14 days versus students who did not have an on-campus job (data not shown).

Some factors were independently associated with being a COVID-19 case but failed to demonstrate a statistically significant association in the multivariable model (current use of a vaping device, participation in a sport, recent concert/play attendance and a reported history of never or rarely wearing a mask when off campus and indoors). Other plausible risk factors were not associated with case status, including current history of cigarette smoking, participation in a campus club, recent use of public or other shared transportation, and recently visiting any of the following: fitness centres or gyms, restaurants, grocery stores, other retail stores, salons or barbershops, movie theatres, or sporting venues. In a case–control study based in Denmark, visiting a fitness centre was a risk factor for SARS-CoV-2 infection, but participation in a sport, public transportation use, and visiting various public places (restaurants, grocery stores and sporting venues) were not associated with infection status (Munch et al., 2021). Similarly, public transportation use and visiting public places (restaurants, grocery stores and salons) were not risk factors for SARS-CoV-2 infection in a case–control study conducted in Portugal (Leite et al., 2021). Dining at a restaurant was a risk factor for SARS-CoV-2 infection in a case–control study based in the United States, but shopping and using public transportation were not associated with infection status (Fisher et al., 2020). Restaurant dining was also a risk factor for SARS-CoV-2

infection in a French case–control study, as was participation in a sport (Galmiche et al., 2021). Use of a vaping device has previously been associated with COVID-19 diagnosis among adolescents and young adults in the United States (Gaiha et al., 2020).

Coughing has been reported as one of the most common symptoms of SARS-CoV-2 infection (Suleyman et al., 2020; Vahey et al., 2021), and it was the most frequently noted symptom among positive students in this study. Fever and dyspnoea are other commonly reported symptoms but were infrequently noted by students. Thirty-eight percent of cases stated having no symptoms, a finding similar to that reported by seropositive students at a California university (Tilley et al., 2020).

To our knowledge, this is the first study to investigate risk factors for SARS-CoV-2 infection among university students in the eastern United States. Case–control studies are ideal for evaluating association with a large number of exposures, and this study benefited from a robust sample size. A comprehensive questionnaire was administered to enrolled students, covering a broad range of campus life activities. SARS-CoV-2-positive students completed the questionnaire shortly after diagnosis (at the time of isolation), thus helping to minimize recall bias. As causal pathways among exposure variables are unclear, it is possible that not all odds ratios can be interpreted as total causal effects. It is also possible that our results cannot be generalized to institutions of higher education elsewhere in the United States, although it seems likely that the risk factors identified here will be relevant to other university populations. Our findings can be used to inform the development of COVID-19 mitigation strategies and public health outreach efforts in university settings, thus reducing SARS-CoV-2 transmission among students and helping to preserve the vital education and research missions of these institutions.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

The authors confirm adherence to the ethical policies of the journal. This study was approved by the Cornell University Institutional Review Board.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Kevin J. Cummings https://orcid.org/0000-0003-3327-596X

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