The Clinical and Genomic Epidemiology of Rhinovirus in Homeless Shelters — King County, Washington

Eric J. Chow, MD, MS, MPH*[1] Amanda M. Casto, MD, PhD,[1,2] Pavitra Roychoudhury, PhD,[2,3] Peter D. Han, MS[4,5] Hong Xie,[3] Brian Pfau,[4,5] Tien V. Nguyen,[3] Jaydee Sereewit, MS,[6] Julia H. Rogers, MPH,[1,7] Sarah N. Cox, MSPH,[1,7] Caitlin R. Wolf, BS,[1] Melissa A. Rolfes, PhD, MPH,[8] Emily Mosites, PhD, MPH,[9] Timothy M. Uyeki, MD, MPH,[8] Alexander L. Greninger, MD, PhD,[2,6] James P. Hughes, PhD,[2,10] M. Mia Shim, MD, MPH,[11,12] Nancy Sugg, MD,[12] Jeffrey S. Duchin, MD,[1,11] Lea M. Starita, PhD,[4,5] Janet A. Englund, MD,[13] Helen Y. Chu, MD, MPH**[1]

[1]Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle (98195), Washington, USA

[2]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle (98109), Washington, USA

[3]Virology Division, Department of Laboratory Medicine and Pathology, University of Washington, Seattle (98195), Washington, USA

[4]Brotman Baty Institute for Precision Medicine, Seattle (98195), Washington, USA

[5]Department of Genome Sciences, University of Washington, Seattle (98195), Washington, USA

[6]Department of Laboratory Medicine and Pathology, University of Washington, Seattle (98195), Washington, USA

[7]Department of Epidemiology, University of Washington, Seattle (98195), Washington, USA

[8]Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta (30333), Georgia, USA

[9]Office of the Deputy Director for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta (30333), Georgia, USA

[10]Department of Biostatistics, University of Washington, Seattle (98105), Washington, USA

[11]Public Health – Seattle & King County, Seattle (98104), Washington, USA

[12]Department of Medicine, University of Washington, Seattle (98195), Washington, USA

[13]Division of Pediatric Infectious Diseases, Department of Pediatrics, University of Washington, Seattle Children's Research Institute, Seattle (98105), Washington, USA

Running Title: Rhinovirus in Homeless Shelters

* *Corresponding author: Eric J. Chow, MD, MS, MPH, Division of Allergy and Infectious Diseases, University of Washington, 1959 NE Pacific Street Box 356423, Seattle, Washington 98195, E-mail: ejchow@uw.edu, Ph:206-685-4456, Fax:206-616-3892*

**Alternate Corresponding Author: *Helen Y. Chu, MD, MPH, Division of Allergy and Infectious Diseases, University of Washington, 750 Republican Street, Seattle, Washington 98109, Ph: 206-685-8702, E-mail: helenchu@uw.edu*

Abstract

Background

Rhinovirus (RV) is a common cause of respiratory illness in all people, including those experiencing homelessness. RV epidemiology in homeless shelters is unknown.

Methods

We analyzed data from a cross-sectional homeless shelter study in King County, Washington, October 2019-May 2021. Shelter residents or guardians aged ≥3 months reporting acute respiratory illness completed questionnaires and submitted nasal swabs. After April 1, 2020, enrollment expanded to residents and staff regardless of symptoms. Samples were tested by multiplex RT-PCR for respiratory viruses. A subset of RV-positive samples was sequenced.

Results

There were 1,066 RV-positive samples with RV present every month of the study period. RV was the most common virus before and during the COVID-19 pandemic (43% and 77% of virus-positive samples, respectively). Participants from family shelters had the highest prevalence of RV. Among 131 sequenced samples, 33 RV serotypes were identified with each serotype detected for ≤4 months.

Conclusions

RV infections persisted through community mitigation measures and was most prevalent in shelters housing families. Sequencing showed a diversity of circulating RV serotypes each detected over short periods of time. Community-based surveillance in congregate settings is important to characterize respiratory viral infections during and after the COVID-19 pandemic.

Key Words: Rhinovirus, respiratory viral infection, respiratory pathogen, homeless shelter, people experiencing homelessness, congregate setting, COVID-19 pandemic, epidemiology, genomic analysis

Background

In the United States, almost 600,000 people experienced homelessness nightly in 2020 [1] with approximately 11,751 people experiencing homelessness (PEH) in King County, Washington alone [2]. The ongoing COVID-19 pandemic has highlighted the health risks posed by respiratory viral infections in PEH. PEH have a disproportionate burden of chronic disease, exacerbated by mental illnesses, substance use [3] and social inequities [4] leading to an increased risk of premature mortality [5]. PEH who stay in shelters are at increased risk of infection due to difficulties with limited space for social distancing, isolation of sick individuals, contact tracing, adequate ventilation and sanitation [6, 7]. Despite the public health challenges posed by SARS-CoV-2 in homeless shelters, respiratory virus epidemiology including rhinovirus (RV) in these settings remains poorly understood.

RV co-circulates with other respiratory viruses contributing to the global burden of respiratory diseases [8]. Pre-pandemic surveillance in the US demonstrated year-round RV circulation with seasonal peaks in the spring and fall [9]. Although referred to as a cause of the "common cold" [10], RV infections in both children and adults can result in lower respiratory tract infections and exacerbations of underlying conditions, including asthma or chronic obstructive pulmonary disease (COPD) [11]. RV includes three major viral species (RV-A, RV-B, RV-C) with 160 known types, hindering efforts to develop viable vaccine candidates [12]. Thus, the focus remains on non-pharmaceutical measures to reduce RV burden. During the COVID-19 pandemic, RV continued circulating despite mitigation measures that have interrupted circulation of influenza, respiratory syncytial virus (RSV), and many other viruses [13]. In this study, we describe the epidemiology of RV infections in homeless shelters in King County, Washington

before and during the first year of the COVID-19 pandemic. We use genomic sequencing to characterize the molecular RV diversity to understand the nuanced complexities of RV epidemiology in shelter sites.

Methods

Study Design, Setting and Population

We retrospectively analyzed cross-sectional data from two studies: (i) a randomized control trial (RCT) of influenza testing and treatment (NCT04141917) occurring between October 2019-March 31, 2020 and October 2020-March 31, 2021, and (ii) a SARS-CoV-2 surveillance study from April 1, 2020 onward. Details of the methods of these studies have been previously described [14, 15]. Participants were enrolled at staffed kiosks from 23 homeless shelter sites within King County, Washington from October 2019-May 2021 and data from the enrollment questionnaire and respiratory samples were used for this study. Briefly, between October 2019-March 31, 2020, eligible participants were shelter residents aged ≥3 months with the following symptoms in the last seven days: new or worsening cough or at least two symptoms including subjective fever, headache, sore throat, runny nose or congestion, shortness of breath, and muscle or body aches; for participants <18 years, diarrhea, rash and ear pain or discharge were also included. Once a month, asymptomatic participants were permitted to enroll. With the community spread of SARS-CoV-2, participant enrollment eligibility expanded to include shelter residents and staff regardless of symptoms from April 1, 2020, onward for all studies. As part of Public Health – Seattle & King County contact tracing efforts, one-day large-scale (surge) testing events were implemented within shelter sites with a SARS-CoV-2-positive case.

Consent was obtained from participants aged ≥18 years or from a guardian for those aged <18 years; assent was obtained from participants aged 13-17 years. At enrollment, participants submitted questionnaires and a respiratory sample for respiratory virus testing. Study enrollment was limited to weekly participation except in cases where new or worsening symptoms developed. Multiple enrollments from the same participant were linked by participant name and birthdate. Encounters refer to each time the participant enrolled in the study. This manuscript was prepared using de-identified study data. The study was approved by the University of Washington Institutional Review Board (Study 00007800).

Questionnaire, Variables and Shelter Site Data

After study consent, the study team administered an enrollment questionnaire via electronic tablet. Questionnaire data including shelter site, birthdate, sex, race, ethnicity, symptoms, pregnancy status, underlying medical conditions, and current tobacco use (including e-cigarettes) were stored through Research Electronic Data Capture (REDCap). Underlying medical conditions collected by self-report included neurological disease, cardiovascular disease, asthma, bronchitis, COPD, hepatic disease, diabetes mellitus, immunosuppression, cancer or another condition that was not listed. New or worsening illness course symptoms over the last seven days were collected in the questionnaire: runny nose or congestion, cough, sore throat, fatigue, myalgias, headaches, subjective fevers, shortness of breath, sweats, nausea or vomiting, chills, diarrhea, rash, ear pain or discharge, and loss of taste and smell (added after April 1, 2020). Encounters where no new or worsening symptoms were reported were classified as asymptomatic. We defined influenza-like illness (ILI) as reported fever and either cough or sore throat and COVID-19-like-illness (CLI) was defined as reported fever and either cough or

shortness of breath. We obtained resident demographics that the shelter served from shelter management staff.

Specimen Collection and Respiratory Virus Testing

Respiratory samples were collected at enrollment. From the start of the study to July 22, 2020, and then from November 1, 2020, through study end, samples were obtained via mid-turbinate (MTB) sterile nylon flocked swabs. Anterior nares swabs (ANS) were used from July 22, 2020, through November 1, 2020, due to supply chain limitations. Specimens were initially collected by study staff, but staff supervised self-collected swabs were used from March 6, 2020, with the community spread of SARS-CoV-2 necessitating heightened safety measures for staff. Respiratory viruses were detected using a custom arrayed RT-PCR platform (Thermo Fisher Open Array) including: influenza virus (A, B and C), respiratory syncytial virus (A and B), human parainfluenza (1-4), human coronaviruses (HCoV-OC43, HCoV-NL63, HCoV-HKU1, HCoV-229E), RV, enterovirus, human bocavirus (excluded after May 29, 2020), human parechovirus (excluded after November 23, 2020), human metapneumovirus and adenovirus. Due to the potential for cross-reactivity between RV and enterovirus, we used a custom review process to differentiate between these viruses (Supplemental methods). Specimens from January 1, 2020 onward were tested for SARS-CoV-2. Details of SARS-CoV-2 testing has previously been published [15]. RV co-detection was defined as RV detection with $\geq$1 other virus. For virus-positive samples, a cycle threshold (Ct) was calculated.

Genomic Sequencing and Analysis

RV whole genome sequencing was attempted on RV-positive samples with Ct values <17 and a subset with Ct values ≥17. RNA was extracted using the Roche MagnaPure 96 DNA and viral NA small volume kit, Viral NA Universal SV 4.0 protocol (200µ input, 50µ elution). Shotgun metagenomic sequencing libraries were prepared as previously described [16, 17]. Raw reads were processed using a custom published pipeline [18]. Additional information is further detailed in Supplemental Methods.

Computational Analysis

We analyzed demographic and symptom data descriptively. We used SAS software version 9.4 (Cary, NC, USA) for general data analysis. NextStrain software was used to process consensus genomes and for the assembly and visualization of phylogenetic trees [19]. Bootstrap values were calculated using IQ-TREE (v1.6.12) [20]. In addition to the consensus genomes generated for this study (GenBank Accession Numbers: ON311150-ON311280; Supplemental Table 1), we downloaded and included in our analyses full length RV genomes available from GenBank.

Results

Between October 2019-May 2021, there were 14,464 encounters (Figure 1) linked to 3,281 unique participants (median age 37 years; range 0.3-85 years; 86% adults; 60% male; 40% White). Overall, 46% of participants reported smoking (of whom, 16% reported e-cigarette use), 31% reported ≥1 underlying medical condition and 17% were shelter staff. Among 14,421 encounters where the encounter date was known, 12,731 (88%) encounters occurred after April 1, 2020. There was a mean of 721 monthly encounters over the study period with a mean of 909

monthly encounters after April 1, 2020 (Supplemental Table 2). A total of 12% and 90% of encounters before and after April 1, 2020, respectively involved participants who were asymptomatic at enrollment. There were 12,895 (89%) encounters with samples where no respiratory virus was detected with 83% involving asymptomatic encounters. Among all symptomatic encounters before and after April 1, 2020, 27% and 13% of samples collected had ≥1 respiratory virus detected, respectively; of which 43% and 75% were RV-positive, respectively. Among all asymptomatic encounter before and after April 1, 2020, 16% and 9% had ≥1 respiratory virus detected; of which 56% and 78% were RV-positive, respectively.

A mean of 53 RV-positive samples were collected monthly over the entire study period with RV-positive samples present every month from October 2019-May 2021 (Figure 2). The percentage of RV-positive samples before April 2020 was 11% and 7% (a higher percentage than other viruses detected during this time) from April 1, 2020, onward. There was an increase in the proportion of RV-positive samples obtained from virus-positive asymptomatic participants (from 56% to 78% before and after April 2020, respectively) associated with enrollment symptom criteria expansion. RV was the most common respiratory virus throughout the study (Supplemental Table 3) with 66% involving adult participants and 10% shelter staff. RV was detected in 1,066 samples (7.4% of all samples) from 682 unique participants (median age 30 years; range 0.3-85 years; 58% male; 42% White; Table 1) representing 68% of all virus-positive samples. RV was the only virus detected in 986 samples from 647 participants (median age 29 years; range 0.3-85 years; 58% male; 41% White).

Participants in shelters housing families (adults and children) and young adults (18-25 years) had the highest prevalence of RV detection relative to other shelters constituting 12% and 8% of all encounters from these sites, respectively (Table 2). Participants aged <5 years had the greatest proportion of RV-positive samples (26%) while participants aged ≥65 years had the lowest among all encounters in those respective age groups (4%; Table 3). Viral co-detection with RV occurred among 80 (8%) RV-positive samples (49% were adult encounters) with adenovirus being the most common co-detected virus (36% of samples with rhinovirus co-detection; Supplemental Table 4).

Among the 647 unique participants with only RV detected, 69% had asymptomatic encounters compared to 56% of the 66 unique participants with RV co-detection (Table 4). Runny nose (79%), cough (61%) and sore throat (42%) were the most common symptoms reported by unique symptomatic adult participants with RV only while runny nose (65%), cough (58%), sore throat (26%) and nausea/vomiting (26%) were the most common symptoms in pediatric participants (Supplemental Table 5). Of note, 3 participants (2 adults and 1 child) with RV only reported new loss of sense of taste or smell, all of whom were tested for SARS-CoV-2 and did not have a positive or inconclusive SARS-CoV-2 test result. The proportion of unique symptomatic participants with RV infection reporting ILI and CLI symptoms was higher in those with RV co-detection than with RV only (ILI: 24% vs 17%; CLI: 21% vs 16%, respectively). Among all encounters where ILI was reported, 9% had RV infection only; and among all encounters where CLI was reported, 9% had RV infection only. Among all symptomatic encounters, 9% of adults had RV detected while 26% of children had RV detected.

We generated full genome sequences for 131 of 176 RV-positive samples including 24 with Ct value ≥17 (one genome with ~23% missing data, all others with <10% missing data). Sequenced samples were collected from every month of the study period except for May-June 2020 and were from 10 different shelters. A total of 33 different RV types were represented among the sequenced samples: 14 RV-A types, four RV-B types, and 15 RV-C types. RV-A23 was most common (31 out of 131 sequenced samples) while 12 types were represented by only one sequence. Sequenced samples were collected across 18 months from October 2019-May 2021, but no individual type was observed for >4 months (Supplemental Table 6). Of the nine types observed before April 1, 2020, only one was also observed after this date when community-wide mitigation efforts were implemented.

Of the 33 total observed RV types, 14 originated from more than one shelter (Supplemental Table 7). RV-A23, RV-A34, and RV-B27 were all observed in five different shelters. Shelter D, a family shelter and the source of the most sequenced samples (n = 38), had the highest number of different RV types (n = 20) among its sequenced samples (Supplemental Table 6) and the highest number of types observed in a single shelter in one month (four in January 2021). In addition to having the highest overall number of RV cases and sequenced cases, family and young adult shelters had cases due to more RV types than other adult shelters (ranges 8-20 versus 1-4).

There were 27 instances where >1 sample of the same type was collected from the same shelter. Among these, there were ten pairs of identical sequences, four sets of three identical sequences, and one set each of four, five, and seven identical sequences, so that a total of 48 genomes were

identical to at least one other genome from the same shelter. We constructed RV-A, RV-B, and RV-C phylogenetic trees, which included sequenced study samples and 947 RV-A, 201 RV-B, and 348 RV-C genomes from GenBank. Within these trees, 17 of 27 sets of genomes of the same type and shelter of origin clustered together exclusive of all other shelters and all GenBank genomes with good bootstrap support (≥89%, Figure 3, Supplemental Figures 1, 2). Figure 3A shows several examples in which this was not the case as RV-A23 samples from Shelters C, D, and H formed more than one distinct phylogenetic grouping within this tree. While the two clusters for Shelters C and D represented samples collected at different times, there was chronologic overlap in sample collection dates for the two largest Shelter H clusters.

The relationship among sequenced genomes of the same type from different shelters varied across types. Fifteen types were observed in more than one shelter. For six of these 15 types, all shelter samples formed a monophyletic group exclusive of all GenBank genomes of that type while for five of these 15 types, the minimum genetic distance between sequenced samples from two different shelters was <5 single nucleotide changes. This includes two pairs of identical sequences for which each sequenced sample came from a different shelter.

Discussion

RV was the most common respiratory virus detected before and during the COVID-19 pandemic among individuals in homeless shelters in a major metropolitan region. There were RV-positive samples detected in every month during the study period. RV-positive samples were most common in younger age groups and among samples collected from shelters housing family and children. Although RV was prevalent throughout the study period, the number of viral co-

detections was relatively low. Sequenced RV samples included >30 different RV-A, RV-B, and RV-C types; the relative frequencies of which varied significantly over the study period. Our findings show that despite the implementation of community-wide mitigation efforts, including the Washington State Stay-At-Home Ordinance [21], RV persisted in homeless shelters throughout the study period, a trend similarly found in studies during the COVID-19 pandemic period.

RV was a substantial contributor to the respiratory viral infections in individuals of all ages in homeless shelters in this study, a finding reported by others in congregate settings. In a respiratory pathogen study in homeless shelters in France prior to the COVID-19 pandemic, RV was similarly found to be the most detected respiratory virus [22]. Nursing homes are another congregate setting where RV infections are common. In one study of symptomatic individuals, RV was the most common virus in nursing home staff, more common than RV in residents [23]. Another nursing home surveillance study from December 1989-March 1990 found RV to be the most common respiratory viral infection second to RSV in residents with ARI symptoms [24]. Direct comparison of RV frequency to these studies may be limited as study participants were mostly screened for the presence of symptoms and asymptomatic sample collection was limited. Our study adds to this congregate setting literature by showing that symptomatic disease is only a subset of RV infections and that RV asymptomatic encounters in homeless shelters was common. What role individuals play in RV transmission in homeless shelters when asymptomatic is not known. Furthermore, we found that ILI and CLI syndromic surveillance definitions are insufficient to capture the full breadth of symptomatic RV encounters and more sensitive definitions are needed for assessment of RV burden. In congregate settings,

transmission prevention between individuals may be more difficult placing those with co-morbid factors at increased risk of clinical complications [25, 26]. Longitudinal studies in homeless shelters with clinical outcomes are needed to better understand the scope of RV-associated burden in these settings.

The combined effects of COVID-19 pandemic mitigation policies, including the local issuance of the Washington State Stay-At-Home ordinance on March 23, 2020 [21], on respiratory virus circulation continues to be an important area of study. With continuous study enrollment throughout the study period, we found that RV detection persisted in the homeless shelter setting as the COVID-19 pandemic progressed. Similar findings were found in a French shelter study early in the COVID-19 pandemic where only SARS-CoV-2 and RV were found over the study period [27]. In a California respiratory virus sentinel surveillance system study from May 2020-June 2021, rhinovirus/enterovirus activity returned to near normal levels in the fall of 2020 after initial decreases spanning the spring and summer of 2020 [28]. A national US surveillance study showed an overall decrease in number of specimens testing positive for non-SARS-CoV-2 respiratory viruses early in the pandemic [13]. Despite an initial decrease, rhinovirus/enterovirus increased back to levels seen before the pandemic from May 2020 onward. How RV case numbers rapidly returned back to pre-pandemic levels and persisted despite broad non-pharmaceutical interventions is likely multifactorial. Some explanations include prolonged RV shedding [29], ease of re-infection given type diversity [30], viral interference [28], transmission from contacts and fomites [31], decreased efficacy of face masks in respiratory spread [32] and environmental resistance as a non-enveloped virus [29]. In shelters, suboptimal ventilation may also contribute to RV persistence. Studies in closed environments have demonstrated effective

aerosol transmission of RV [33, 34]. These findings show the importance of additional virus-specific studies to identify the factors that affect their unique epidemiology.

Genetic sequencing in a subset of RV-positive samples illustrated the diversity of RV infections in these shelter sites including 20 types observed in one shelter site alone. RV types identified prior to the implementation of community-wide mitigation policies were largely not observed from April 1, 2020, onward. Across the study period, individual RV types were observed for limited periods of time (<4 months) before being replaced by other types. Despite the RV type diversity seen, there were also multiple examples where samples of the same type were collected from participants in the same shelter. These samples frequently formed phylogenetic clusters exclusive of other shelter sequences and over a third of all sequenced shelter samples were identical to at least one other sample from the same shelter; observations which may be indicative of intra-shelter spread. Two instances of identical sequence pairs collected from two different shelters also raises the possibility of RV spread between shelters. However, our ability to assess for this is limited, given the lack of RV samples collected in the surrounding community during the study period. Finally, our data suggest that multiple introductions of the same viral type into one shelter in a short time period is possible (RV-A23 in Shelter H). Overall, the genetic diversity of RV in our study sites highlights the importance of including RV sequencing analysis in studies of RV epidemiology in this population.

Limitations

Our study was subject to several limitations. First, there may have been an underestimation of RV-positive samples as non-pan-RV primers were used in the RT-PCR assay. Second, selection

bias may have occurred through participant self-recruitment. Third, participants were not followed longitudinally thus limiting our ability in differentiating asymptomatic infection from pre-symptomatic participants or from those with persistent shedding after symptomatic infection. Fourth, our study did not collect shelter site non-pharmaceutical interventions that were implemented over the course of the COVID-19 pandemic limiting inference on how they may have affected respiratory viral transmission. Fifth, we used ANS between July 2020-November 2020, which may have reduced sensitivity for respiratory viral detection over this time period. Sixth, despite utilizing an algorithm to differentiate RV and enterovirus-positive samples, there may have been misclassification in samples not sequenced. Seventh, human bocavirus and human parechovirus were not tested for towards the end of our study and samples over that period may have missed those viruses. Finally, we were able to perform genomic sequencing only on a subset of RV-positive samples and so it is likely that the diversity of RV types is not completely described.

Conclusion

RV is an important viral pathogen in homeless shelters affecting individuals of all ages. Similar to observations nationally, RV cases and diversity persisted in our study despite COVID-19 community-wide mitigation efforts. RV genomic analysis suggested that both intra-shelter spread and new introductions into shelters were common and impacted persons of all ages. Respiratory viral epidemiology, including RV, present unique public health challenges in congregate settings. Future congregate-setting-based studies of RV surveillance and transmission as pandemic interventions change can build upon the findings in our study.

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Figure 1 Study Flow Diagram

Figure 2 Frequency of Rhinovirus-Positive Samples by Participant Encounter Symptom Status Over the Study Period[a]

[a]n = 3 rhinovirus-positive samples with missing encounter dates were excluded from this figure; A symptomatic encounter was defined as a study encounter in which the participant reported any new or worsening symptom on the enrollment questionnaire and is not limited to symptoms required for enrollment; an asymptomatic encounter was defined as a study encounter in which the participant did not report any new or worsening symptoms on the enrollment questionnaire.

Figure 3 Maximum Likelihood Phylogenetic Tree of Select Rhinovirus Types[a]

A) Rhinovirus-A23 B) Rhinovirus-A34 C) Rhinovirus-B27

[a]Nodes are colored by the shelter of origin; GenBank samples are gray.

1 Table 1 Demographics and Medical History of Shelter Study Participants[a]

Characteristics	Rhinovirus Only	Rhinovirus Co-detection	Other Respiratory Viruses[b]	No Respiratory Virus Detected[c]
Number of Unique Participants, N	647	66	408	2,996
Age, years				
Overall, median (range)	29 (0.3-85)	22 (0.4-83)	36 (0.3-81)	37 (0.3-85)
< 5	72 (11.1)	21 (31.8)	43 (10.5)	154 (5.1)
5-11	71 (11.0)	7 (10.6)	36 (8.8)	189 (6.3)
12-17	33 (5.1)	1 (1.5)	16 (3.9)	101 (3.4)
18-49	321 (49.6)	21 (31.8)	193 (47.3)	1,635 (54.6)
50-64	131 (20.3)	11 (16.7)	99 (24.3)	752 (25.1)
≥65	19 (2.9)	5 (7.6)	21 (5.2)	164 (5.5)
Sex				
Male	372 (57.5)	43 (65.2)	245 (59.8)	1,815 (60.6)
Female	265 (41.0)	21 (31.8)	161 (39.3)	1,127 (37.6)
Other	2 (0.3)	1 (1.5)	0	16 (0.5)
Prefer not to say	8 (1.2)	1 (1.5)	4 (1.0)	38 (1.3)
Race				
White	268 (41.4)	28 (42.4)	167 (40.7)	1,208 (40.3)
Black	206 (31.8)	15 (22.7)	150 (36.6)	950 (31.7)

Asian	12 (1.9)	1 (1.5)	4 (1.0)	114 (3.8)
American Indian or Alaskan Native	15 (2.3)	3 (4.6)	16 (3.9)	121 (4.0)
Native Hawaiian or Pacific Islander	50 (7.7)	8 (12.1)	18 (4.4)	129 (4.3)
Other	32 (5.0)	3 (4.6)	35 (8.5)	263 (8.8)
Prefer not to say	64 (9.9)	8 (12.1)	20 (4.9)	211 (7.0)
Ethnicity				
Hispanic	105 (16.2)	15 (22.7)	58 (14.2)	440 (14.7)
Non-Hispanic	527 (815)	50 (75.8)	345 (84.2)	2502 (83.5)
Unknown	15 (2.3)	1 (1.5)	7 (1.6)	54 (1.8)
Pregnancy Status Among Women of Child-Bearing Age)	n = 179	n = 7	n = 100	n = 770
Pregnant	2 (1.1)	0	4 (4.0)	13 (1.7)
Not Pregnant	38 (21.2)	2 (28.6)	41 (41.0)	128 (16.6)
Prefer not to say	139 (77.7)	5 (71.4)	55 (55.0)	629 (81.7)
Smoking Status				
Current tobacco use	263 (40.7)	20 (30.3)	170 (41.5)	1,368 (45.7)
E-cigarette use/Vape	51 (19.4)	5 (25.0)	20 (11.8)	210 (15.4)
Underlying Medical Conditions				
None	475 (73.4)	51 (77.3)	291 (71.0)	2,081 (69.5)

At least 1 underlying medical condition	172 (26.6)	15 (22.7)	119 (29.0)	915 (30.5)
Neurological disease	12 (2.2)	0	13 (3.6)	63 (2.6)
Cardiovascular disease	13 (2.0)	2 (3.0)	12 (2.9)	95 (3.2)
Asthma	76 (11.8)	8 (12.1)	43 (10.5)	393 (13.1)
Bronchitis	16 (2.5)	0	13 (3.2)	93 (3.1)
COPD	30 (4.6)	1 (1.5)	11 (2.7)	116 (3.9)
Hepatic disease	12 (1.9)	1 (1.5)	9 (2.2)	85 (2.8)
Diabetes mellitus	35 (5.4)	5 (7.6)	37 (9.0)	199 (6.6)
Immunosuppression	7 (1.1)	1 (1.5)	8 (2.0)	36 (1.2)
Cancer	12 (1.9)	0	8 (2.0)	57 (1.9)
Other	7 (1.1)	0	4 (1.0)	31 (1.0)
Shelter Staff	78 (12.1)	6 (9.1)	34 (8.3)	50 (18.4)
Number of Encounters	986	80	503	12,895

[a]Categories are not mutually exclusive as participants may have had more than one encounter with different results

[b]There were n = 22 encounters where an inconclusive SARS-CoV-2 test was re-categorized as a negative result; of note, there were no other pathogens detected in these samples and n = 17 of these samples came from asymptomatic participants; n = 2 encounters where participant age is missing and were not included in the age analysis

[c]n = 1 encounter where participant age is missing and was not included in the age analysis

1 Table 2 Rhinovirus-positive Encounters by Shelter Type[a]

Shelter	**Type of Shelter**	**All Encounters**			**Virus-Positive Encounters**		
		Total	**Rhinovirus only**	**Rhinovirus Co-detection**	**Total**	**Rhinovirus Only**	**Rhinovirus Co-detection**
	N	**14,464**	**986**	**80**	**1,569**	**966**	**80**
Surveillance		**N**	n(%)	n(%)	N	n(%)	n(%)
D, E, H, N, O	**Shelters: Family (Adults and Children)**	4,761	513 (10.8)	48 (1.0)	756	513 (67.9)	48 (6.4)
A, B, F, G, L, J, K	**Shelters: Adults ≥18 years old**	6,241	274 (4.4)	20 (0.3)	467	274 (58.7)	20 (4.3)
C	**Shelters: Adults 18-25 years old**	1179	93 (7.9)	3 (0.3)	120	93 (77.5)	3 (2.5)
I, M	**Shelters: Adults ≥**	849	46 (5.4)	5 (0.6)	103	46 (44.7)	5 (4.9)

	50 years old						
Surge Testing		**N**	n(%)	n(%)	N	n(%)	n(%)
D, E, H, OF, OG	**Shelters: Family (Adults and Children)**	318	19 (6.0)	0	30	19 (63.3)	0
A, F, G, J, K, OB, OD	**Shelters: Adults ≥18 years old**	704	18 (2.6)	2 (0.3)	39	18 (46.2)	2 (5.1)
C, OH	**Shelters: Adults 18-25 years old**	143	8 (5.6)	0	11	8 (72.7)	0
I, M, OA, OC, OE	**Shelters: Adults ≥ 50 years old**	269	15 (5.6)	2 (0.7)	43	15 (34.9)	2 (4.7)

[a]These are row percentages

1 Table 3 Rhinovirus-positive Encounters by Age Group and Symptom Status[a]

All Encounters			
Age group, years	Symptom Status[b]	Total	Rhinovirus-positive Encounters
		N	n (%)
< 5	All	651	170 (26.1)
	Asymptomatic	546	138 (25.3)
	Symptomatic	105	32 (30.5)
5-11	All	885	143 (16.2)
	Asymptomatic	824	127 (15.4)
	Symptomatic	61	16 (26.2)
12-17	All	506	47 (9.3)
	Asymptomatic	475	43 (9.1)
	Symptomatic	31	4 (12.9)
18-49	All	7716	475 (6.2)
	Asymptomatic	6303	339 (5.4)
	Symptomatic	1413	136 (9.6)
50-64	All	3795	196 (5.2)
	Asymptomatic	2795	102 (3.7)
	Symptomatic	1000	94 (9.4)
≥65	All	908	35 (3.9)
	Asymptomatic	766	27 (3.5)
	Symptomatic	142	8 (5.6)

All age groups	All	14,464	1066 (7.4)
	Asymptomatic	11,709	776 (6.6)
	Symptomatic	2755	290 (10.5)
Virus-positive Encounters			
Age group, years	Symptom Status	Total	Rhinovirus-positive Encounters
		N	n (%)
< 5	All	221	170 (76.9)
	Asymptomatic	158	138 (87.3)
	Symptomatic	63	32 (50.8)
5-11	All	188	143 (76.1)
	Asymptomatic	157	127 (80.9)
	Symptomatic	31	16 (51.6)
12-17	All	64	47 (73.4)
	Asymptomatic	57	43 (75.4)
	Symptomatic	7	4 (57.1)
18-49	All	708	475 (67.1)
	Asymptomatic	441	339 (76.9)
	Symptomatic	267	136 (50.9)
50-64	All	322	196 (60.9)
	Asymptomatic	156	102 (65.4)
	Symptomatic	166	94 (56.6)
≥65	All	64	35 (54.7)

	Asymptomatic	40	27 (67.5)
	Symptomatic	24	8 (33.3)
All age groups	All	1569	1066 (67.9)
	Asymptomatic	1009	776 (76.9)
	Symptomatic	560	290 (51.8)

[a]Excludes n = 3 samples where age of participant is unknown; none of these samples were positive for rhinovirus; these are row percentages

[b]A symptomatic encounter was defined as a study encounter in which the participant reported any new or worsening symptom on the enrollment questionnaire and is not limited to symptoms required for enrollment; an asymptomatic encounter was defined as a study encounter in which the participant did not report any new or worsening symptoms on the enrollment questionnaire

1

2 Table 4 Symptoms Among Unique Participants with and without Rhinovirus Infection[a]

	Rhinovirus Only	**Rhinovirus Co-detection**	**Other Respiratory Viruses**
Total Number of Encounters	986	80	503
Number of Unique Participants	647	66	410
	n (%)	**n (%)**	**n (%)**
Asymptomatic	445 (68.8)	37 (56.1)	190(46.3)
Symptomatic	202 (31.2)	29 (43.9)	220 (53.7)
Runny nose or congestion	155 (76.7)	22 (75.9)	177 (80.5)
Cough	122 (60.4)	23 (79.3)	156 (70.9)
Sore throat	80 (39.6)	9 (31.0)	99 (45.0)
Headaches	75 (37.1)	6 (20.7)	76 (34.6)
Myalgias	67 (33.2)	7 (24.1)	90 (40.9)
Fatigue	62 (30.7)	12 (41.4)	90 (40.9)
Nausea or vomiting	54 (26.7)	9 (31.0)	65 (29.6)
Chills	45 (22.3)	4 (13.8)	57 (25.9)
Sweats	38 (18.8)	5 (17.2)	53 (24.1)
Subjective fevers	37 (18.3)	9 (31.0)	75 (34.1)
Shortness of breath	37 (18.3)	4 (13.8)	53 (24.1)

Diarrhea	22 (10.9)	6 (20.7)	39 (17.7)
Ear pain or discharge	20 (9.9)	1 (3.5)	12 (5.5)
Rash	8 (4.0)	1 (3.5)	12 (5.5)
Loss of taste or smell[b]	n = 160	n = 26	n = 160
	3 (1.9)	0	2 (1.3)
Influenza-like illness[c]	35 (17.3)	7 (24.1)	68 (30.9)
COVID-19-like illness[d]	32 (15.8)	6 (20.7)	66 (30.0)
Fulfill both influenza-like illness and COVID-19-like illness criteria	32 (15.8)	6 (20.7)	64 (29.1)

[a]A symptomatic encounter was defined as a study encounter in which the participant reported any new or worsening symptom on the enrollment questionnaire and is not limited to symptoms required for enrollment; an asymptomatic encounter was defined as a study encounter in which the participant did not report any new or worsening symptoms on the enrollment questionnaire

[b]Loss of taste or smell was added from April 1, 2020, onward. N's represent the number of people who were asked this question and proportion is out of total N.

[c]Influenza-like illness is defined as the presence of fever and (cough or sore throat)

[d]COVID-19-like illness is defined as the presence of fever and (cough or shortness of breath)

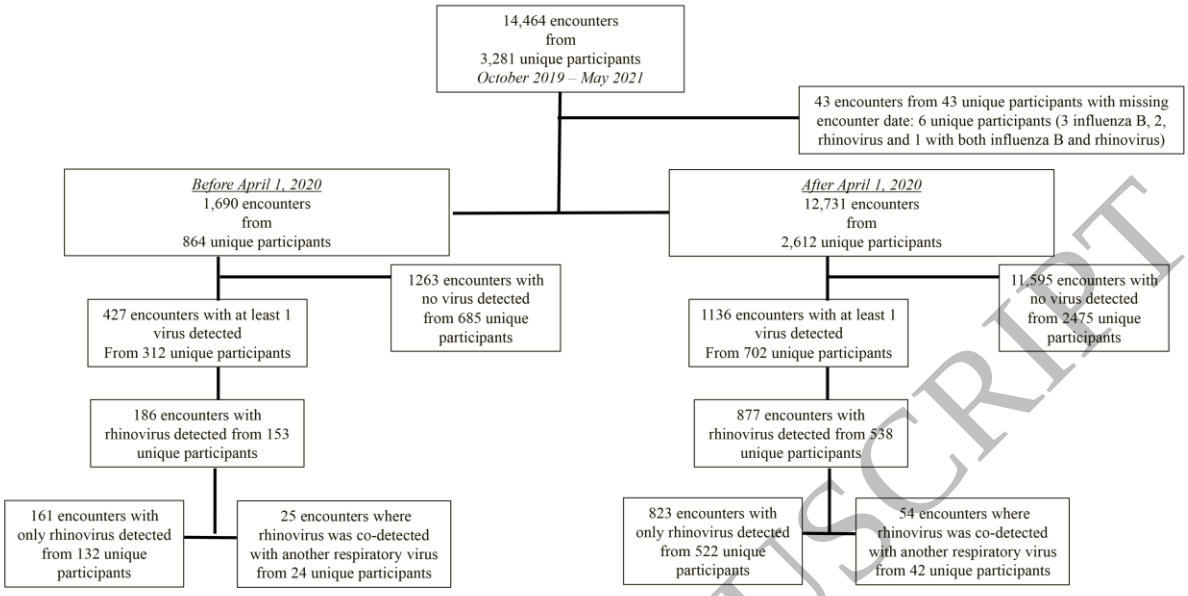

Figure 1
165x79 mm (.45 x DPI)

Month	Asymptomati	Symptomatic
Oct-19	0	35
Nov-19	0	26
Dec-19	5	40
Jan-20	2	27
Feb-20	3	28
Mar-20	8	12
Apr-20	25	16
May-20	1	0
Jun-20	2	1
Jul-20	8	4
Aug-20	42	15
Sep-20	62	12
Oct-20	54	10
Nov-20	77	14
Dec-20	80	11
Jan-21	106	11
Feb-21	69	4
Mar-21	178	17
Apr-21	36	3
May-21	18	1

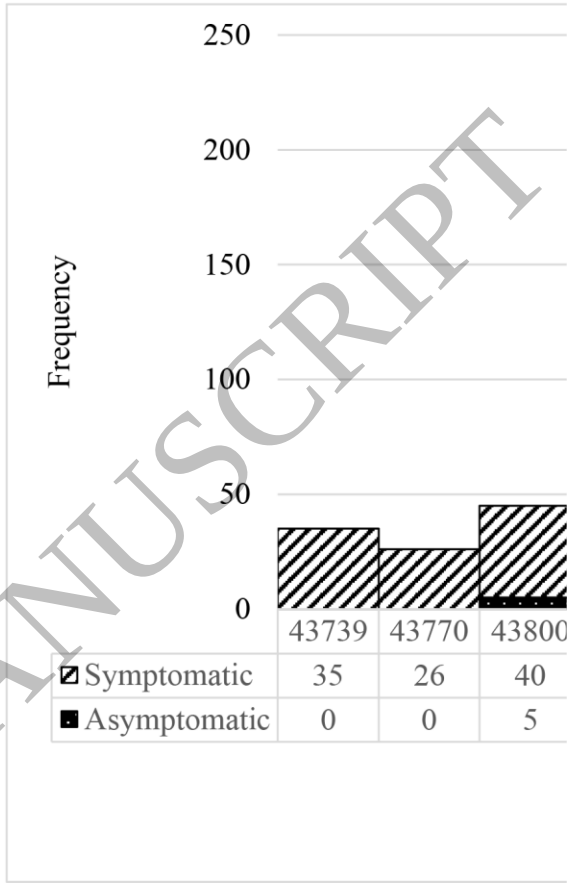

Figure 2
165x127 mm (.45 x DPI)

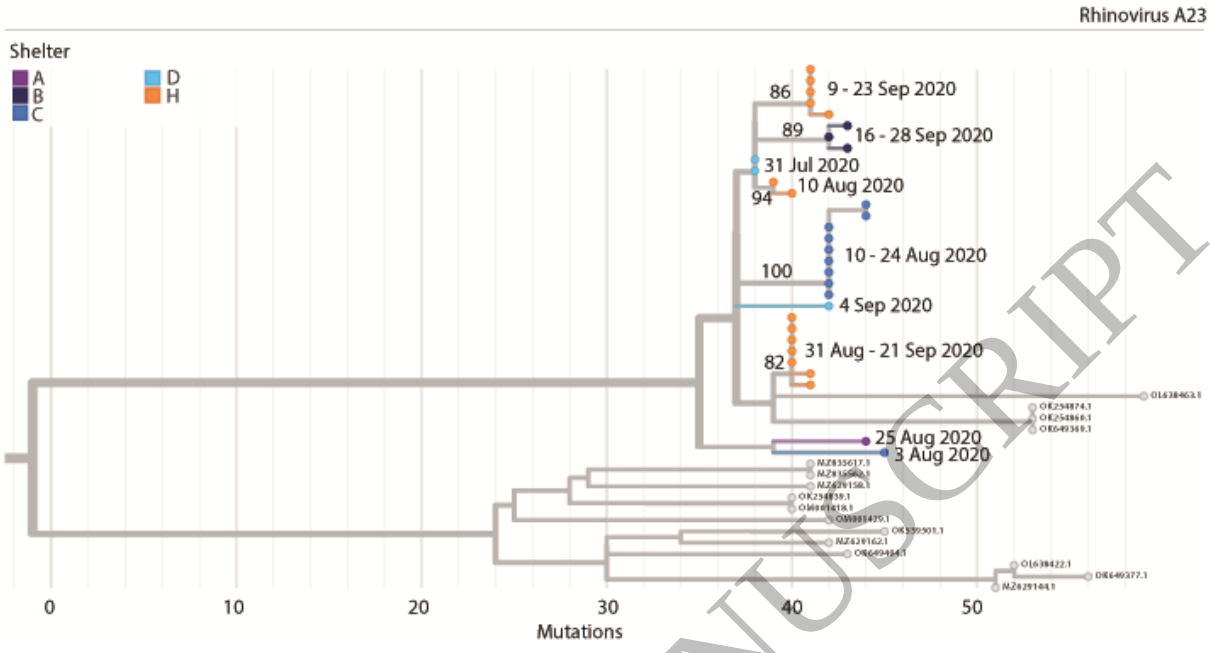

Figure 3A
165x125 mm (.45 x DPI)

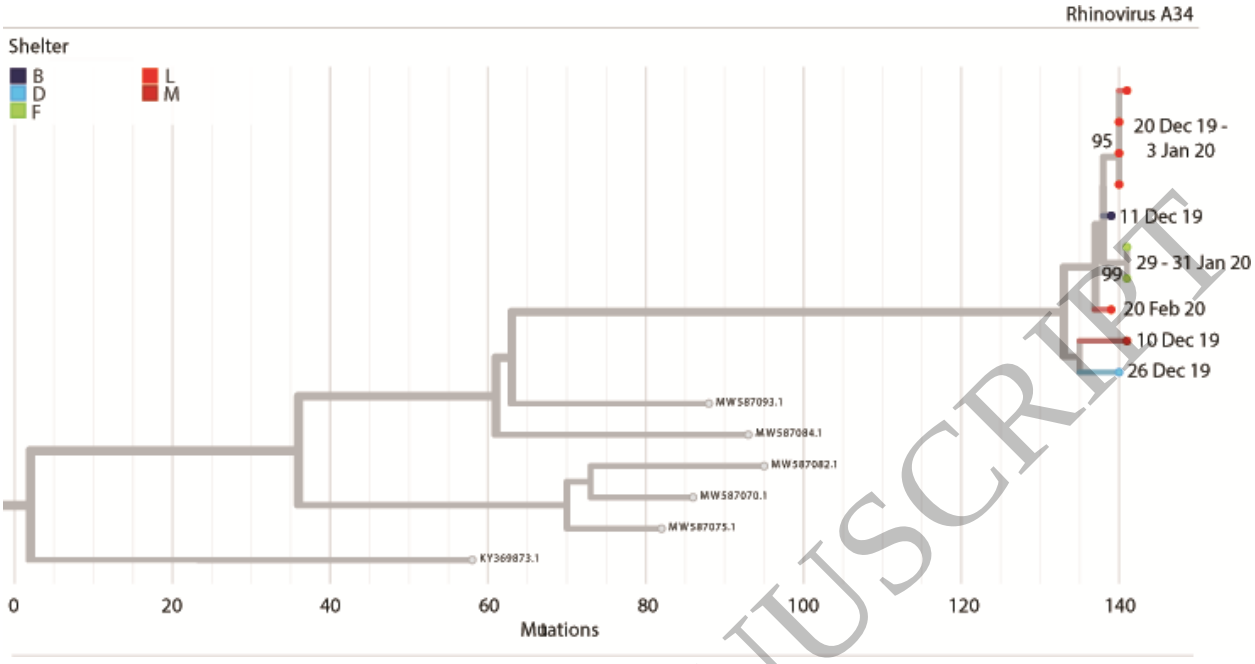

Figure 3B
165x86 mm (.45 x DPI)

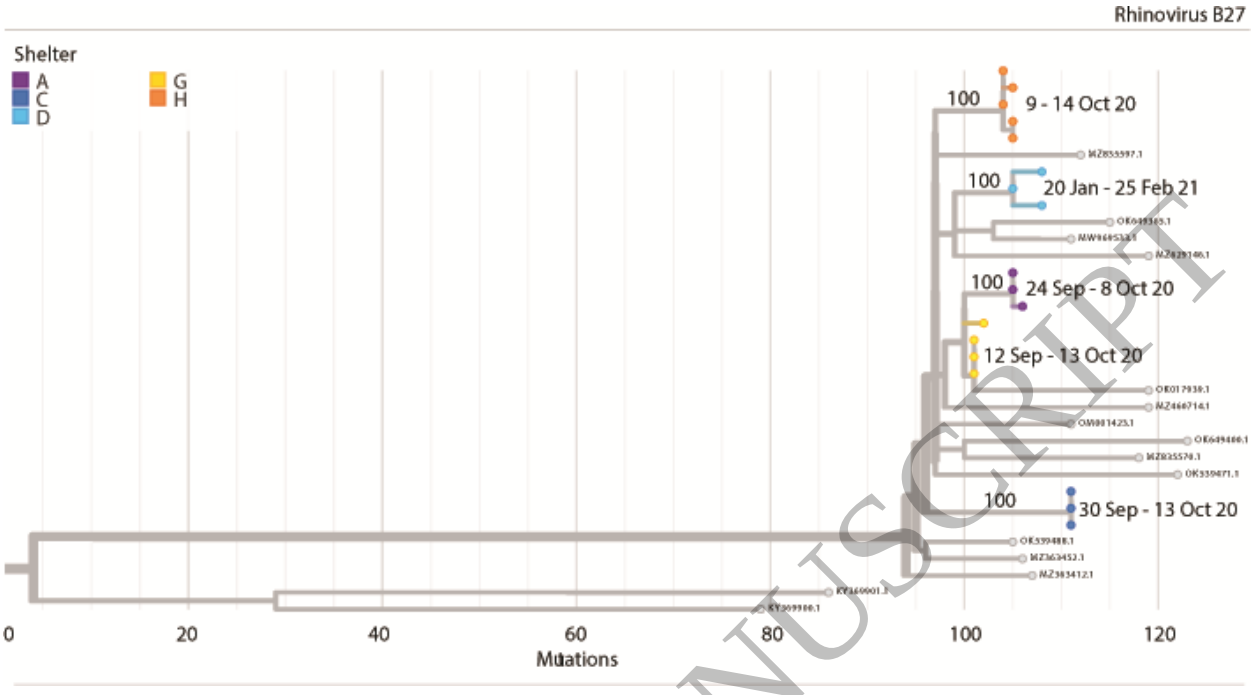

Figure 3C
165x90 mm (.45 x DPI)