Remote Household Observation for Non-influenza Respiratory Viral Illness

Anne Emanuels[1], Jessica Heimonen[1], Jessica O'Hanlon[1], Ashley E. Kim[1], Naomi Wilcox[1], Denise J. McCulloch[1], Elisabeth Brandstetter[1], Caitlin R. Wolf[1], Jennifer K. Logue[1], Peter D. Han[2], Brian Pfau[2], Kira L. Newman[1], James P. Hughes[3], Michael L. Jackson[4], Timothy M. Uyeki[5], Michael Boeckh[6], Lea M. Starita[2,7], Deborah A. Nickerson[2,7], Trevor Bedford[6], Janet A. Englund[1,8], Helen Y. Chu[1], *on behalf of Seattle Flu Study investigators*

[1] Department of Medicine, University of Washington

[2] Brotman Baty Institute

[3] Department of Biostatistics, University of Washington

[4] Kaiser Permanente Washington Health Research Institute

[5] Centers for Disease Control and Prevention

[6] Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center

[7] Department of Genome Sciences, University of Washington

[8] Seattle Children's Research Institute

Complete contact information for corresponding

Anne Emanuels, MPH

Corresponding Author

University of Washington

(206) 685-8702

aemanuel@uw.edu

Room E630
UW Medicine Box 358061
750 Republican St.
 Seattle WA, 98109

Key points: A household study using online recruitment and home-collection of respiratory specimens was conducted in 303 households during the emergence of SARS-CoV-2. Of 678 samples collected, 237 tested positive for one or more non-influenza viruses, and four tested positive for SARS-CoV-2.

1

Abstract

Background: Non-influenza respiratory viruses are responsible for a substantial burden of disease in the United States. Household transmission is thought to contribute significantly to subsequent transmission through the broader community. In the context of the COVID-19 pandemic, contactless surveillance methods are of particular importance.

Methods: From November 2019 to April 2020, 303 households in the Seattle area were remotely monitored in a prospective longitudinal study for symptoms of respiratory viral illness. Enrolled participants reported weekly symptoms and submitted respiratory samples by mail in the event of an acute respiratory illness (ARI). Specimens were tested for fourteen viruses, including SARS-CoV-2, using RT-PCR. Participants completed all study procedures at home without physical contact with research staff.

Results: In total, 1171 unique participants in 303 households were monitored for ARI. Of participating households, 128 (42%) included a child aged <5 years and 202 (67%) included a child aged 5-12 years. Of the 678 swabs collected during the surveillance period, 237 (35%) tested positive for one or more non-influenza respiratory viruses. Rhinovirus, common human coronaviruses, and respiratory syncytial virus were the most common. Four cases of SARS-CoV-2 were detected in three households.

Conclusions: This study highlights the circulation of respiratory viruses within households during the winter months during the emergence of the SARS-CoV-2 pandemic. Contactless methods of recruitment, enrollment and sample collection were utilized throughout this study, and demonstrate the feasibility of home-based, remote monitoring for respiratory infections.

Keywords: Households, Epidemiology, Transmission, Viruses, Respiratory

Background

Respiratory viruses cause notable rates of morbidity and mortality in the United States, especially among young children, the elderly, or the immunocompromised.[1] Respiratory syncytial virus (RSV), parainfluenza viruses (PIV), human metapneumovirus (hMPV), human rhinovirus (hRV), human coronavirus (hCoV), and adenovirus (AdV) often co-circulate with influenza viruses in the winter months and can cause acute respiratory illness (ARI) and lower respiratory tract infections (LRTI).[1–3] Globally, LRTIs are estimated to cause 2.3 million deaths annually.[3] In the United States, an estimated 500 million non-influenza viral respiratory infections occur annually.[1] However, most ARI surveillance is based on reports of outpatient visits, emergency department visits, or hospitalizations, which may underestimate disease incidence.[4–6]

Prospective household cohort studies are useful to study incidence of illness in the community across a range of age groups and identify chains of transmission between household contacts.[7,10] Households are an important setting for the spread of respiratory viruses between individuals and may play a role in community transmission.[7–11] Household study platforms can be expanded to study SARS-CoV-2 spread, based on preliminary data showing viral transmission among household contacts .[12,13] Contactless surveillance methods are of particular interest in context of the COVID-19 pandemic.

Using online contactless recruitment, enrollment, and surveillance, we conducted a longitudinal prospective cohort study of ARI in households of three or more individuals with at least one child from November 2019 to April 2020. The aims are to describe household-level risk factors for respiratory viral infections, estimate incidence of primary and secondary infections for non-influenza viral pathogens in households, and examine the association

3

between upper respiratory virus levels in primary cases and incidence of secondary infections in household contacts.

Methods

Study Design:

A prospective longitudinal cohort study of children and their households was implemented in the Seattle metropolitan area from November 2019 to April 2020 as a part of the Seattle Flu Study.[14] Households were recruited at the beginning of the school year and remotely monitored weekly from November 14, 2019, until April 1, 2020, for symptoms of respiratory illness. Recruitment took place at elementary and middle schools beginning in September, and households continued to participate after the school district's closure on March 11, 2020. Participating schools advertised the study to families through social media, newsletters, posters on campus, and after-school events. Eligible households consisted of three or more individuals sleeping in the home for ≥4 days per week, with at least one adult English-speaker and one child aged three months through 17 years. Individuals in enrolled households were permitted to opt-out of participation if the remaining household members met eligibility criteria. Interested households completed an online screening questionnaire before informed consent took place over the phone between at least one adult household member and a research team member. Other adults and children in the household were then prompted to review and complete their documentation of consent through a web-based platform. Children aged 7-17 years provided electronic assent alongside a parent or guardian's consent.

This study was approved by the University of Washington Institutional Review Board. Upon completion of the informed consent process, households answered demographic questions in an online questionnaire before receiving mid-turbinate nasal swabs (Copan

4

Diagnostics, Murietta, CA), collection tubes with universal transport media (BD, Franklin Lakes, NJ), instructions, and returned shipping materials in the mail. One adult was designated as the household reporter and contacted weekly by text message and/or email to complete a symptom log each week on behalf of all household participants. Additions to households during the study were identified through monthly questionnaires and were invited to enroll and participate in the study. The study procedures did not require any physical contact between participants and researchers.

The study population included a subset of households enrolled in an interventional study focused on home-based diagnosis and treatment of influenza; detailed methods for the intervention study are registered with ClinicalTrials.gov (Trial no. NCT04141930). This analysis includes observational data on the non-influenza respiratory viruses detected in all households. Data on influenza viruses in households will be reported separately.

Data Collection:

After consent and enrollment, each participant was asked to collect a mid-turbinate nasal swab in the event of an acute respiratory illness (ARI) reported in the weekly symptom log as early as possible and within 72 hours of illness onset. Samples collected beyond 72 hours after illness onset were excluded from analysis. For children aged <13 years, a parent or guardian was advised to assist with swab collection and shipping. Home-collected nasal swabs were mailed at ambient-temperature to the Northwest Genomics Center at the University of Washington via USPS following standard IATA shipping procedures, with a median shipping time of two days. If a participant experienced ARI, defined as either a) acute cough, or b) two or more concurrent symptoms (see **Appendix A** for a complete list of qualifying symptoms) with symptom onset within 72 hours, or 48 hours in the interventional subset, the household reporter

was prompted to fill out a clinical illness questionnaire. One week following specimen collection, participants were sent a follow-up questionnaire to collect information about illness progression and its effects on healthcare seeking behavior, school/work attendance, and travel. If a participant experienced multiple illness episodes during the study period, these procedures were repeated. Reminders to complete questionnaires and collect swabs when prompted were delivered by automated messages and by personalized emails and phone calls from the study team. Study data were collected remotely via online questionnaires and entered and managed using Project REDCap (Research Electronic Data Capture).[15]

Laboratory Testing:

Samples were mailed in UTM at ambient temperature and aliquoted and stored at 4°C prior to testing. Upon receipt, samples were tested within approximately 7 days. Total nucleic acid was extracted using the Magnapure 96 platform (Roche) and tested for the presence of 24 respiratory pathogens (see **Appendix B** for a list of tested pathogens) by TaqMan RT-PCR on the OpenArray[16]. Assay methods and definitions of positive results are described in **Appendix D.**

Data Analysis:

To assess household-level risk factors for respiratory viral infection, demographic characteristics of participating households were compared using Chi-Squared tests or two-sided t-tests assuming independent variances between those with and without at least one positive test result for a respiratory viral infection. P-values of <0.05 were considered statistically significant. We restricted this analysis to households submitting at least one weekly symptom

6

log prior to April 1, 2020. Participants were required to experience at least seven days without symptoms before being eligible to record another illness episode and submit another specimen.

A primary case was defined as an ARI episode with a respiratory virus detected preceded by 14 days without the same virus identified in the household. Cases that occurred in one household with the same day of symptom onset were defined as co-primary. Pathogens analyzed included RSV subtypes A and B, PIV types 1-4, hMPV, hRV, coronavirus (hCoV - HKU1, NL63, 229E and OC43), AdV, human bocavirus (hBoV), and SARS-CoV-2. SARS-CoV-2 testing was added February 25, 2020, including testing of samples collected after January 1, 2020. The person-time at risk was defined as the total number of surveillance weeks multiplied by the number of people in the household. Surveillance was defined as the period between each household's first symptom log and either April 1st or date of their final symptom log. A secondary case was defined as identification of a virus preceded by an illness in a household member with the same virus within 14 days. Person-time at risk for each secondary case was defined as the fourteen days following illness onset for the primary case. Incidence rates were calculated with Poisson models, with an offset of log days at risk. Confidence intervals were based on a robust variance adjusted for clustering by household.

Upper respiratory viral levels were evaluated using C_{rt} values from RT-PCR testing. Viral levels were compared between primary cases with and without an associated secondary case. Data analyses were performed using R version 4.0.0 (R Foundation for Statistical Computing) in RStudio Version 1.2.5042 (RStudio, Inc.).

Results

Between November 1, 2019, and April 1, 2020, 351 households were enrolled with a median household size of 4 individuals (range 3 - 7); and 303 completed at least one weekly symptom log in this time frame and were included in this analysis. The average weekly symptom log completion rate was 87%. Among participating households, 128 (42%) included a child aged <5 years, 202 (67%) included a child aged 5-12 years, and 64 (21%) included children in both age groups; 194 (64%) contained one or more children in elementary school, and 155 (51%) contained one or more children who attended childcare. Only 15 (5%) households included individuals aged ≥65 years (Table 1).

This cohort included 1,171 unique individuals, and over the study period, 213 households (70%) submitted at least one nasal swab during the surveillance period (Figure 1). In total, 678 samples were collected from 477 unique individuals. Laboratory-confirmed non-influenza virus infection was detected in 185/303 (61%) of included households, and in 185/213 (87%) of households collecting at least one sample. A higher proportion of households with non-influenza viral infection (52%) included at least one child aged <5 years compared to only 25% of households without laboratory-confirmed respiratory virus infection (p < 0.001). Households without confirmed respiratory virus infection more frequently included a child aged 13-17 years (p<0.001), or an individual aged 50 - 64 years (p < 0.001). A median of 2 swabs were collected per household.

Influenza virus was detected in 67/678 (10%) samples; these samples were excluded from this analysis, including those with detected coinfections. Of the 611 swabs received during the surveillance period from 434 unique individuals that did not test positive for influenza virus, 237 (39%) tested positive for one or more respiratory virus (Table 2). The most common viruses detected were hRV (86 cases), hCoV (65 cases), and RSV (19 cases). Coinfection with two

8

viruses was detected in 30 samples (**Appendix C**), most frequently in children aged <5 years. SARS-CoV-2 was detected in four cases in three households. Seeking medical care for symptoms was reported in either the illness questionnaire or at one-week follow-up in 72 (12%) of all illness episodes with complete survey data. Most samples were collected in the months of February and March, possibly due to the increased awareness of respiratory symptoms during the start of the COVID-19 pandemic. The monthly frequency of virus detection differed by organism (Figure 3).

The highest primary incidence rates in this cohort were found with hRV (21.7 primary cases per 100 person-years) and hCoV (19.6 primary cases per 100 person-years; Table 3). SARS-CoV-2 had a primary incidence rate of 1.4 cases per 100 person-years (CI: 0.8-2.4). Secondary cases were detected among hMPV infections (2 of 6), and SARS-CoV-2 infections (1 of 3) where 33% index cases were associated with a secondary case, and in RSV infections, where 28% of index cases were associated with a secondary case (Table 3). Of 197 primary cases, 53 (27%) were among children aged <5 years, 63 (32%) among those 5-17 years, 77 (39%) were among those aged 18-64, and 2 (1%) among those aged ≥65.

Symptom data were reported for 209 samples of non-influenza laboratory-confirmed respiratory viral infections. Heat maps of the symptoms reported on the day of sample collection are shown stratified by age group (Figure 2). Cough and runny nose were reported frequently across viruses and age groups, while fever was reported less frequently among those aged ≥18 years.

C_{rt} values between index cases with and without an associated secondary household case did not differ significantly ($p > 0.05$, **Appendix E**). C_{rt} values between index and secondary cases are reported in **Appendix F**. RSV secondary cases reported the shortest period of time between primary and secondary cases (2.6 days), and AdV cases experienced the longest time

9

(12.1 days). One secondary case of SARS-CoV-2 was recorded. Further information about the ages of individuals with primary infections and the age groups of transmission events can be found in **Appendices G and H**.

Discussion

This study describes results from a contactless research approach that did not involve in-person interactions between study staff and household members to detect circulating non-influenza respiratory viruses within households during the winter of the emergence of the SARS-CoV-2. The presence of young children was a household-level risk factor for viral infection, as expected. Of the 303 households included, 185 (61%) had at least one case of respiratory viral infection between November 14, 2019, and April 1, 2020, most of which were from hRV, hCoV, and RSV.[12,17] Four cases of SARS-CoV-2 were detected among three participating households, all in adults, with one case of possible transmission between household members. This study design may be useful to capture additional cases of SARS-CoV-2 in future efforts.

This design permitted detection of symptomatic respiratory viral infection without direct contact between participants and researchers. Online enrollment, symptom monitoring via email or text messaging, home-collected swabs, and electronic illness questionnaires allowed this study to be conducted with minimal inconvenience and risk of exposure to participating households. Households could receive weekly symptom log reminders via email or text messages, which previous research has shown to be an effective mechanism for rapid, home-based detection of ARI.[9] Social distancing has become a necessary component of further research on SARS-CoV-2 transmission, and this remote study design provides a safe mechanism for investigation.

10

The presence of children under 5 years old was a predictor of non-influenza virus detection in a household.[18,19] Over half of households with at least one confirmed infection had a child aged <5 years, compared to only 26% of those without a non-influenza viral infection (p < 0.001). However, the presence of a child aged 13-17 years old was negatively correlated with infection, with 33% of households without viral infection containing a child in this age range compared to 14% of households with at least one infection. Families with adolescent children may be less likely to also include a younger child. A higher proportion of households with an infection than those without infection included adults aged 18-49 years, while more households with adults aged 50-64 years had no cases of viral infection. This may be due to younger adults being more likely to have children under 5 years of age.

A majority of recorded illness episodes were not medically attended, confirming another cohort study where only 17% of influenza cases were medically attended.[20] Non-influenza viruses were responsible for 34% of illness samples, and only 12% of these cases were medically attended. hRV and hCoV cases alone accounted for a majority of positive swabs. These findings align with other prospective cohort studies in children and adults, where hRV and hCoV were detected at greater frequency in the community than in hospital-based ARI studies.[21–23] Additionally, these results show a majority of coinfection cases and AdV cases occurring in children younger than five years, a majority of PIV cases in children 5-17 years, and the remaining organisms predominating in adults 18-64 years old, although sample sizes are small after stratifying by virus type and age group. Overall, children under 5 years had the highest percent positivity rate (70%). These findings are comparable to previous household studies conducted in the United States.[10,24]

The relative thresholds (C_{rt} values) of primary cases did not differ significantly between the primary cases that were and were not associated with a secondary infection. Possible explanations for this finding include that C_{rt} values may not be a direct quantitative measure of

11

viral load. Additionally, due to the 72-hour window of eligibility to collect swabs and variation in home-swab collection among individuals, specimen collections likely varied among samples included in this analysis. Finally, given the broad time frame under which a case may be considered a secondary case, it is possible that some secondary cases became infected from sources outside of the household.

There are several limitations to this study. First, participants were instructed to self-collect a nasal swab in the event of an acute respiratory illness. While this approach allows for more complete capture of respiratory pathogens with limited inconvenience to participants, it allows for some uncertainty in validity of the reported symptoms, as well as uncertainty due to potential inconsistency of at-home specimen collection. Additionally, this approach did not capture asymptomatic cases during the surveillance period and may have resulted in an underestimation of the incidence of the viruses analyzed. The rarity of smokers and high rates of influenza immunization, the exclusion of non-English speakers, the low enrollment of individuals older than 65 years, and the number of households with an annual income greater than $150,000 indicate that this study population may not be representative of the Seattle area.[25,26] Another limitation is absence of clinical data for some cases of illness. Households occasionally mailed a swab to the laboratory without filling out the corresponding illness questionnaire (n=74). While these events were infrequent, they unfortunately included all four of the SARS-CoV-2 cases detected in this population, so our ability to describe these cases is limited. In our statistical analysis, we included weeks between first and last symptom log for each household within the study period to be time at risk. This includes time in which no symptom logs were submitted, potentially lowering the primary incidence rates. Finally, the study includes time before and after the COVID-19 pandemic, and illness reporting and care-seeking behavior likely changed over the study period.

12

This study demonstrates the feasibility of home-based, longitudinal monitoring of respiratory viral illness in households with children. Conducting remote, prospective surveillance for detection of respiratory viral infections may be especially important during the COVID-19 pandemic when in-person monitoring may compromise the safety of researchers and participants. Remote, longitudinal surveillance of households may also provide further insight into signs and symptoms of non-medically attended SARS-CoV-2 infection. This prospective observational study of households over a single season demonstrates the incidence of a variety of respiratory illnesses commonly not receiving medical attention, emphasizing the household as an important setting for viral surveillance.

13

NOTES

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

14

References

1.   Fendrick AM, Monto AS, Nightengale B, Sarnes M. The economic burden of non-influenza-related viral respiratory tract infection in the United States. *Arch Intern Med*. 2003;163(4):487-494. doi:10.1001/archinte.163.4.487

2.   Walter JM, Wunderink RG. Severe Respiratory Viral Infections: New Evidence and Changing Paradigms. *Infect Dis Clin North Am*. 2017;31(3):455-474. doi:10.1016/j.idc.2017.05.004

3.   Troeger C, Blacker B, Khalil IA, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Infect Dis*. 2018;18(11):1191-1210. doi:10.1016/S1473-3099(18)30310-4

4.   Marsden-Haug N, Foster VB, Gould PL, Elbert E, Wang H, Pavlin JA. Code-based syndromic surveillance for influenzalike illness by International Classification of Diseases, Ninth Revision. *Emerg Infect Dis*. 2007;13(2):207-216. doi:10.3201/eid1302.060557

5.   Lewis MD, Pavlin JA, Mansfield JL, et al. Disease outbreak detection system using syndromic data in the greater Washington DC area. *Am J Prev Med*. 2002;23(3):180-186. doi:10.1016/S0749-3797(02)00490-7

6.   Molinari N-AM, Ortega-Sanchez IR, Messonnier ML, et al. The annual impact of seasonal influenza in the US: Measuring disease burden and costs. *Vaccine*. 2007;25(27):5086-5096.

7.   Tsang TK, Lau LLH, Cauchemez S, Cowling BJ. Household Transmission of Influenza

15

Virus. *Trends Microbiol*. 2016;24(2):121-133.

8. Glezen WP, Couch RB, MacLean RA, et al. Interpandemic Influenza in the Houston Area, 1974–76. *N Engl J Med*. 1978;298(11):587-592. doi:10.1056/nejm197803162981103

9. Stockwell MS, Reed C, Vargas CY, et al. MoSAIC: Mobile surveillance for acute respiratory infections and influenza-like illness in the community. *Am J Epidemiol*. 2014;180(12):1196-1201. doi:10.1093/aje/kwu303

10. Monto AS, Malosh RE, Petrie JG, Thompson MG, Ohmit SE. Frequency of Acute Respiratory Illnesses and Circulation of Respiratory Viruses in Households With Children Over 3 Surveillance Seasons. *J Infect Dis*. 2014;210. doi:10.1093/infdis/jiu327

11. MacIntyre CR, Ridda I, Seale H, et al. Respiratory viruses transmission from children to adults within a household. *Vaccine*. 2012;30(19):3009-3014. doi:10.1016/j.vaccine.2011.11.047

12. Li W, Zhang B, Lu J, et al. The characteristics of household transmission of COVID-19. *Clin Infect Dis*. 2020;[published.

13. Ramanathan K, Antognini D, Combes A, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis*. 2020;(April):19-21.

14. Chu HY, Boeckh M, Englund JA, et al. The Seattle Flu Study: A Community-Based Study of Influenza. *Open Forum Infect Dis*. 2019;6:S1002. https://doi.org/10.1093/ofid/ofz415.2504.

15. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. NIH Public Access Author Manuscript J Biomed Inform. Author manuscript; available in PMC 2010 April 1.

Published in final edited form as: J Biomed Inform. 2009 April ; 42(2): 377–381.
doi:10.1016/j.jbi.2008.08.010. Research Electronic Data Capture (REDCap. *J Biomed Inf*.
2009;42(2):377-381. doi:10.1016/j.jbi.2008.08.010.Research

16.   Chu HY, Englund JA, Starita LM, et al. Early Detection of Covid-19 through a Citywide
Pandemic Surveillance Platform. *N Engl J Med*. 2020;Correspond.
doi:10.1056/NEJMc2008646

17.   Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in
China, 2019. *N Engl J Med*. 2020;382(8):727-733. doi:10.1056/NEJMoa2001017

18.   Drosten C, Meyer B, Müller MA, et al. Transmission of MERS-coronavirus in household
contacts. *N Engl J Med*. 2014;371(9):828-835. doi:10.1056/NEJMoa1405858

19.   Scott EM, Magaret A, Kuypers J, et al. Risk factors and patterns of household clusters of
respiratory viruses in rural Nepal. *Epidemiol Infect*. 2019;147:e288.
doi:10.1017/S0950268819001754

20.   Hayward AC, Fragaszy EB, Bermingham A, et al. Comparative community burden and
severity of seasonal and pandemic influenza: Results of the Flu Watch cohort study.
Lancet Respir Med. 2014;2(6):445-454. doi:10.1016/S2213-2600(14)70034-7

21.   Fowlkes A, Giorgi A, Erdman D, et al. Viruses associated with acute respiratory infections
and influenza-like illness among outpatients from the influenza incidence surveillance
project, 2010-2011. *J Infect Dis*. 2014;209(11):1715-1725. doi:10.1093/infdis/jit806

22.   Shi T, Arnott A, Semogas I, et al. The Etiological Role of Common Respiratory Viruses in
Acute Respiratory Infections in Older Adults: A Systematic Review and Meta-analysis. *J
Infect Dis*. 2019;(Xx Xxxx):1-6. doi:10.1093/infdis/jiy662

17

23.   Sarna M, Lambert SB, Sloots TP, et al. Viruses causing lower respiratory symptoms in young children: Findings from the ORChID birth cohort. *Thorax*. 2018;73(10):969-979. doi:10.1136/thoraxjnl-2017-210233

24.   Monto AS, Sullivan KM. Acute respiratory illness in the community. Frequency of illness and the agents involved. *Epidemiol Infect*. 1993;110(1):145-160. doi:10.1017/S0950268800050779

25.   Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System, State Tobacco Activities Tracking and Evaluation System.

26.   U.S. Census Bureau. American Community Survey 1-year Estimates. Census Reporter Profile for Seattle, WA. https://censusreporter.org/profiles/16000US5363000-seattle-wa/. Published 2018.

Table 1. Demographic characteristics of households enrolled in the Seattle area between November 2019 and April 2020 with and without laboratory confirmed cases of non-influenza respiratory viral infection.

Characteristic	Total N = 303	Households with no eligible respiratory viral infection N = 118	At least 1 (≥1) confirmed respiratory viral infection*** N = 185	p value**
Households With:				
Children <5 Years	128 (42%)	31 (26%)	97 (52%)	**<0.001**
Children 5-12 Years	202 (67%)	76 (64%)	126 (68%)	0.716
Children 13-17 Years	64 (21%)	39 (33%)	25 (14%)	**<0.001**
Individuals 18-49 Years	280 (92%)	101 (86%)	179 (97%)	**0.002**
Individuals 50-64 Years	62 (20%)	39 (33%)	23 (12%)	**<0.001**
Individuals ≥65 Years	15 (5%)	4 (3%)	11 (6%)	0.466
Household size (median, IQR)	4 (3-4)	4 (3-4)	4 (3-4)	0.461
All eligible members vaccinated for seasonal influenza*	192 (63%)	74 (63%)	118 (64%)	0.947
Household income				0.85
<$50,000	6 (2%)	3 (3%)	3 (2%)	
$50,000 - $100,000	44 (15%)	15 (13%)	29 (16%)	
$100,001 - $150,000	51 (17%)	20 (17%)	31 (17%)	
>$150,000	174 (57%)	70 (59%)	104 (56%)	
≥1 tobacco smoker or e-cigarette user in the home	8 (3%)	3 (3%)	5 (3%)	1.00
≥1 individual with history of comorbid condition(s)				
Asthma	89 (29%)	36 (31%)	53 (29%)	0.828
Chronic bronchitis or COPD	6 (2%)	2 (2%)	4 (2%)	0.903
Cancer	20 (7%)	9 (8%)	11 (6%)	0.736
Diabetes	7 (2%)	4 (3%)	3 (2%)	1.00
Heart disease	6 (2%)	2 (2%)	4 (2%)	1.00

*Includes those aged 6 months and older

**p-values generated by Chi-Squared tests, or independent two-sided t-tests

***Confirmed viral infection includes the viruses examined in this analysis: RSV, PIV I-IV, hMPV, hRV, hCoV, AdV, hBoV, SARS-CoV-2. Influenza cases are included in the "no eligible infection" column.

19

Table 2. Cases of acute respiratory illnesses in Seattle households by age, positive PCR test result, and illness

characteristics between November 2019 and April 2020

	All Samples ** (N = 611)	No Virus Detected (N = 374)	Cases (%) by positive PCR Test Result								
			RSV (N=19)	PIV 1-4 (N=12)	hMPV (N=7)	hRV (N=86)	hCoV (N=65)	AdV (N=10)	hBoV (N=4)	SARS-CoV-2 (N=4)	Coinf-ection (N=30)
Age Group	N (%)										
0-5 years	85 (14)	23 (6)	4 (21)	3 (25)	2 (29)	20 (23)	9 (14)	4 (40)	1 (25)	0 (0)	19 (63)
5-17 years	175 (29)	104 (28)	6 (32)	2 (17)	2 (29)	32 (37)	19 (29)	2 (20)	1 (25)	0 (0)	7 (22)
18-64 years	346 (57)	244 (65)	9 (47)	7 (58)	3 (43)	33 (38)	36 (55)	4 (40)	2 (50)	4 (100)	4 (16)
>=65 years	5 (1)	3 (1)	0 (0)	0 (0)	0 (0)	1 (1)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)
Sought Medical Care*	72 (12)	44 (12)	6 (32)	0 (0)	3 (43)	7 (8)	7 (11)	2 (20)	0 (0)	NA	3 (10)
Absent from Work or School* (N=421)	155 (25)	92 (25)	8 (42)	3 (25)	4 (57)	20 (23)	15 (23)	1 (10)	1 (25)	NA	11 (37)

Instances where the same virus with the same symptom onset date were detected in a household are listed as two, co-

primary infections.

Abbreviations: RSV = respiratory syncytial virus (types A and B), PIV 1-4 = parainfluenza virus types I-IV, hMPV = human

metapneumovirus, hRV = rhinovirus, hCoV = coronavirus (HKU1, NL63, 229E and OC43), AdV = adenovirus, hBoV =

human bocavirus.

*Missingness: Seeking medical care and absenteeism were missing for 106 (17%) illness episodes. Both of these

Table 3. Estimated incidence rates of primary and secondary cases of eight different viruses detected among Seattle households between November 2019 and April 2020

	RSV	PIV 1-4	hMPV	hRV	hCoV	AdV	hBoV	SARS-CoV-2
Primary Cases	18	10	6	73	64	13	10	3
Primary incidence rate per 100 person-years (95% CI)	5.4 (3.4-8.6)	3.0 (1.6-5.6)	1.8 (0.8-4.0)	21.7 (17.3-27.4)	19.3 (15.1-24.7)	4.2 (2.5-7.1)	3.0 (1.6-5.6)	1.4 (0.8-2.4)
Secondary Cases* **(% of Primary)**	5 (28)	0 (0)	2 (33)	19 (26)	8 (12)	2 (15)	0 (0)	1 (33)
Epidemiologic secondary incidence per 100 person-years (95% CI)	79.5 62.2–102	0	45.8 (35.8-58.4)	302 (237-386)	127 (99.6-163)	31.8 (24.9-40.6)	0	18.7 (15.1-22.9)

Instances where the same pathogen with the same symptom onset date were detected in a household are listed in two, co-primary infections. Coinfections are listed in two columns: one per virus type.

Abbreviations: RSV = respiratory syncytial virus (types A and B), PIV 1-4 = parainfluenza virus types I-IV, hMPV = human metapneumovirus, hRV = rhinovirus, hCoV = coronavirus (HKU1, NL63, 229E and OC43), AdV = adenovirus, hBoV = human bocavirus.
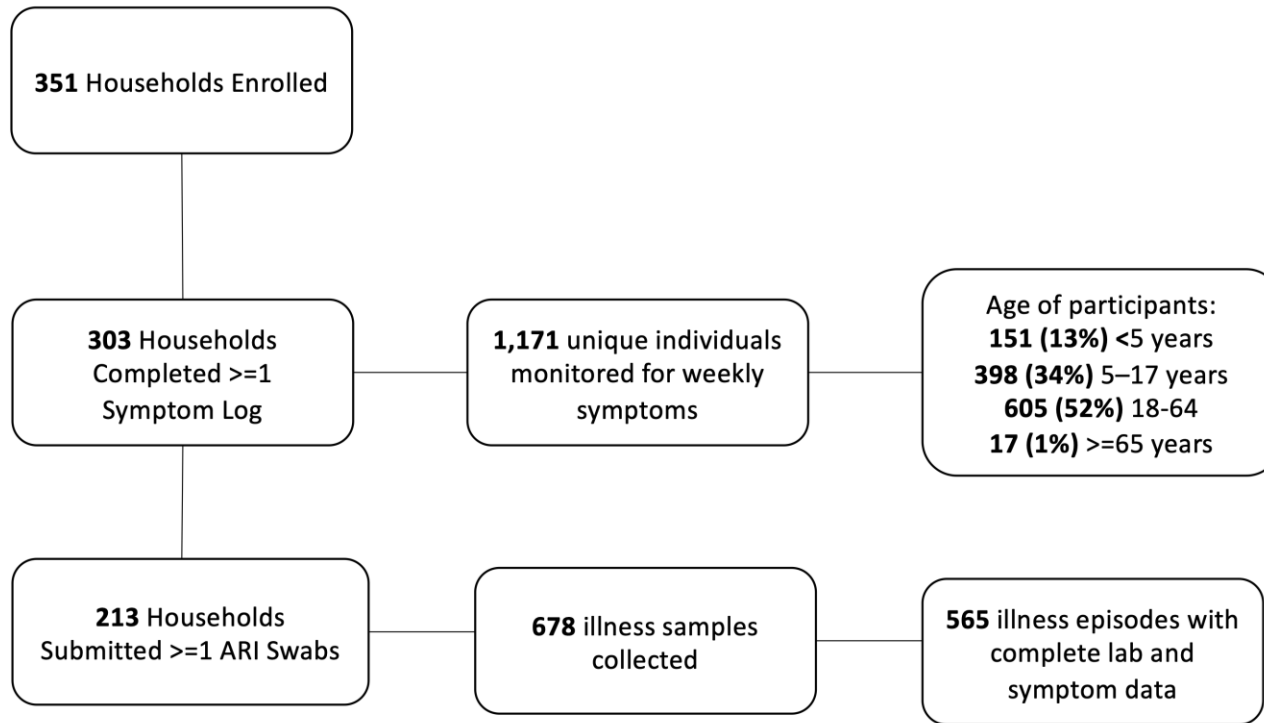
Figures

Figure 1. Number of households and individuals completing various steps of study procedures.

Figure 2. Symptom profiles of respiratory viral illnesses stratified by age group. Includes 209 samples of non-influenza respiratory viral infection where symptoms were recorded. Darker colors indicate a higher percentage of infected individuals of the specific virus type reporting the symptom. 30 cases of coinfection are excluded from this figure.

Figure 3. Panel A: Number of illness samples collected from participants between November 2019 and March 2020. Panel B: the percentage of positive samples detected of different viruses out of the number of samples collected each month. Lines color coded by virus type. Cases of coinfection are included twice, once per virus detected.

Figure 1

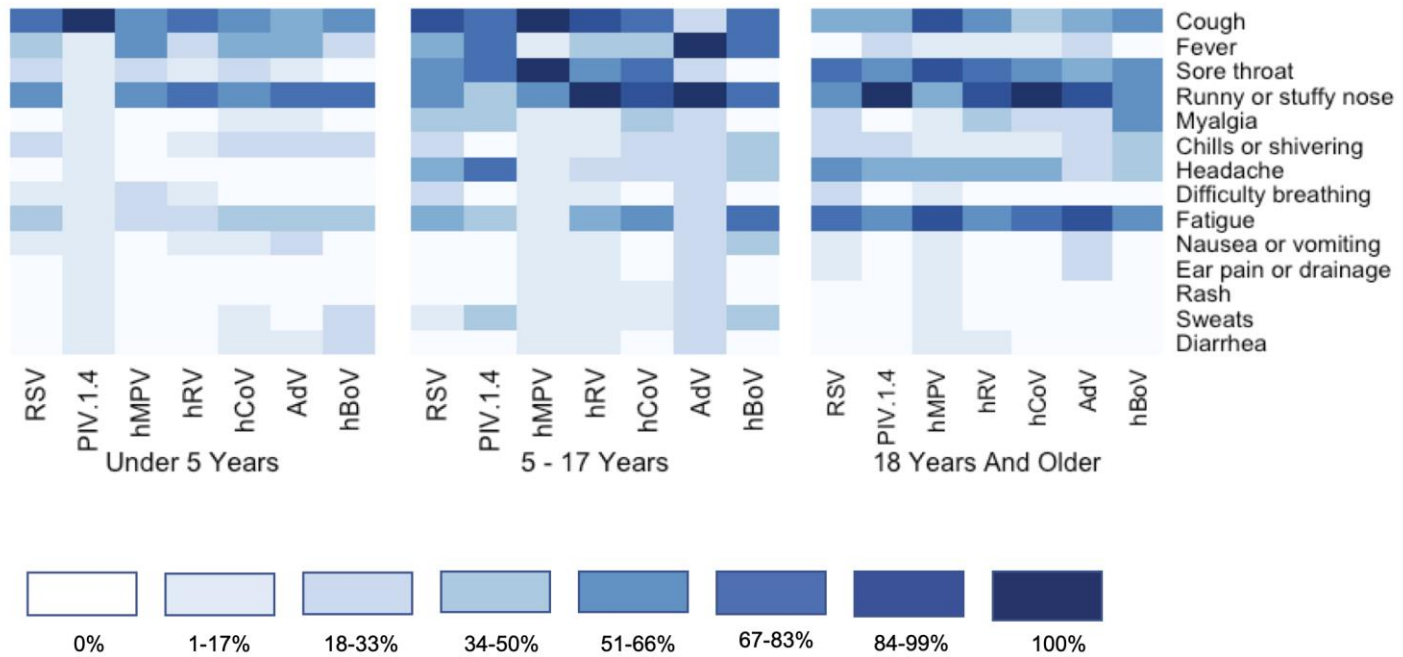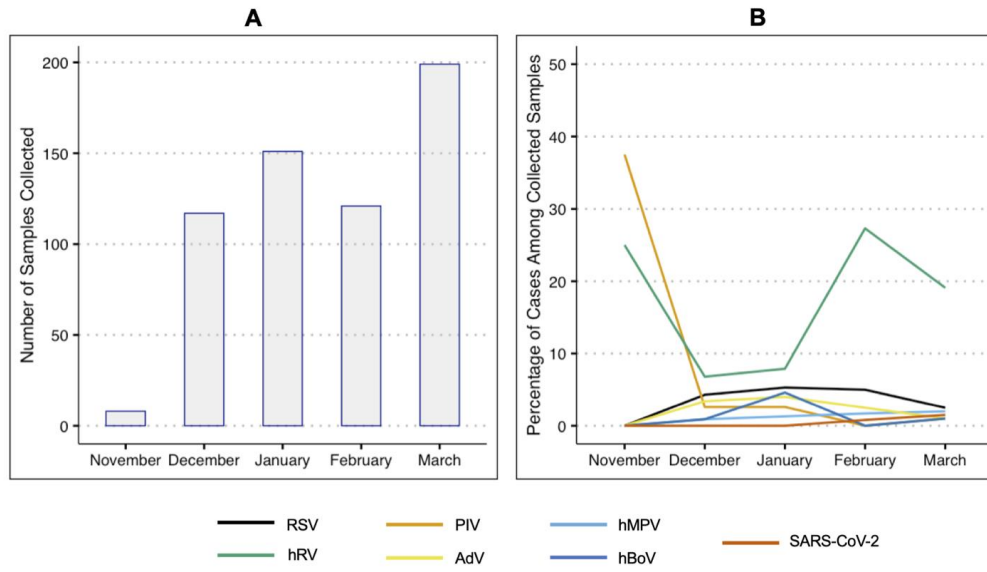351 Households Enrolled

303 Households Completed >=1 Symptom Log

1,171 unique individuals monitored for weekly symptoms

Age of participants:
151 (13%) <5 years
398 (34%) 5–17 years
605 (52%) 18-64
17 (1%) >=65 years

213 Households Submitted >=1 ARI Swabs

678 illness samples collected

565 illness episodes with complete lab and symptom data

1

Figure 2

Figure 3