



Original Article

Contrasting definitions and incidence of healthcare-associated respiratory viral infections in a pediatric hospital

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Abstract

Objective: To determine the difference in the incidence of healthcare-associated respiratory viral infection (HARVI) in a pediatric hospital depending on the definition used.

Design: Descriptive historical cohort study.

Setting and participants: Patients aged 0–21 years old who were admitted between July 2013 and June 2018 to a 490-bed primary to quaternary-care pediatric hospital serving northern Texas.

Methods: HARVI was defined using microbiologic confirmation, development of new symptoms while hospitalized, and exposure time greater than the minimum incubation period for each specific virus. Events that occurred following the maximum incubation period for that virus were classified as definite, otherwise they were classified as possible. This definition was compared to definitions using alternate timing of onset and symptomatology requirements. Data pertaining to demographics, diagnoses, and illness severity were collected.

Results: In total, 498 HARVIs (320 definite and 178 possible) were identified, with an incidence rate of 0.98 per 1,000 patient days (0.63 and 0.35, respectively). Rhinovirus or enterovirus and respiratory syncytial virus were the most identified viruses (58% and 10%, respectively). The median time from admission until HARVI was 10.5 days (interquartile range [IQR], 5–30 days). When alternate definitions were employed, the incidence of HARVI ranged from 0.96 to 2.00 per 1,000 admitted patient days.

Conclusions: HARVI remain a common nosocomial infection in pediatric hospitals and the measured incidence is dependent on the definition used. Because of the endemic and pandemic potential of respiratory viruses, standardized definitions are needed to facilitate intra- and interhospital comparisons.

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Healthcare-associated infections (HAIs) occur commonly in pediatric patients with the potential for long-term consequences.¹ Hospitalized pediatric patients may be at high risk of developing healthcare-associated respiratory viral infections (HARVIs). Viral infections lead to ~25% of pediatric hospital admissions,² and because these viruses are transmitted via respiratory droplets, contact with contaminated fomites, and inhalation of suspended particles following aerosol-generating procedures, the risk for acquiring such infections while hospitalized is potentially very high. With increasing numbers of patients with immunocompromising conditions and underlying pulmonary disorders, and limited effective antiviral therapies, the risk and potential morbidity to patients is increasing. HARVIs are not part of

mandatory public reporting in most states in the United States, and data on the incidence of HARVI are limited. Furthermore, standardized definitions that would facilitate interhospital comparisons and public reporting are not available.

HARVI outbreaks and their consequences have been reported in pediatric hospitals for decades,^{3,4} but only recently have many institutions begun to track and measure the incidence of HARVI continuously. The recognized incidence is likely changing over time as infection prevention strategies and their implementation have improved,^{5,6} new viruses have been identified,^{7,8} and rapid and more accurate viral diagnostic testing with nucleic acid amplification tests has become widely available.^{9,10} In addition, recent data have demonstrated large interhospital variability of HARVI incidence likely related to multiple factors including presence (or lack) of shared patient rooms, compliance with infection prevention guidance, and the size of the high-risk patient population.^{5,11–15} Most studies have used different definitions of HARVI with variable incubation periods, making interhospital comparisons difficult. With coronavirus disease 2019

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(COVID-19) pandemic and the emergence of severe acute respiratory coronavirus virus 2 (SARS-CoV-2), another respiratory virus, assessing the impact of HARVIs is critical.

Because of these variabilities and the lack of a standard case definition, the purpose of this study was to determine the incidence of HARVI at a large pediatric hospital over a 5-year period, to compare the incidence using different HARVI definitions, and to describe the epidemiology of HARVIs.

Methods

Design and setting

We conducted a retrospective cohort of all patients admitted to our 490-bed primary-to-quaternary care pediatric hospital in northern Texas for ≥ 2 days. We included patients aged 0–21 years admitted between July 1, 2013, and June 30, 2018. The hospital contains 64 intensive care unit (ICU) beds in addition to 47 neonatal ICU (NICU) beds and is a level I trauma center.

Definitions

A case of HARVI was defined using 3 criteria. First, the microbiologic criterion comprised an upper or lower respiratory specimen that tested positive on an antigen test, including the BD Directigen EZ Flu A+B or BD Directigen EZ RSV (Becton Dickinson, Franklin Lakes, NJ) for 2013–2017 and the Quidel Sofia Influenza A+B FIA or Quidel Sofia RSV FIA (Quidel, San Diego, CA) for 2017–2018; or a respiratory pathogen multiplex polymerase chain reaction (PCR) panel (BioFire FilmArray Respiratory Panel, bioMérieux, Marcy-l'Étoile, France) or Xpert Xpress influenza/RSV PCR (GeneXpert Dx system, Cepheid, Sunnyvale, CA) for one of the following viruses: adenovirus, endemic human coronavirus (HKU1, NL63, 229E, or OC43), human metapneumovirus, influenza A (H1N1pdm2009 or H3N2), influenza B, human parainfluenza virus (type 1, 2, 3, or 4), respiratory syncytial virus (RSV), or rhinovirus/enterovirus (the latter are not distinguished on the panel). Second, the symptomatic criterion comprised at least 1 new sign or symptom associated with a lower or upper respiratory infection following hospital admission including conjunctivitis, cough, hypoxia, increased endotracheal secretions, increased ventilator settings, increased work of breathing, nasal congestion, rhinorrhea, sneezing, or tachypnea. Fever was included if other sources of fever were ruled out. Third, the chronologic criterion was met if the day of first symptom onset occurred after the minimum incubation period from hospital admission for each specific virus (Table 1).^{16,17} The calendar day of symptom onset was compared to the calendar day of admission. Respiratory infections with symptoms that developed in fewer days from admission than the minimum incubation period for that virus were labeled community acquired. Infections with symptoms that occurred more days following admission than the maximum incubation period were labeled definite healthcare associated, and infections with symptoms that occurred between were labeled possible healthcare associated. Any repeated test that returned positive for the same virus as a test earlier during the same admission was excluded regardless of symptoms. In addition to measuring the incidence, patients who met the primary study definition had demographic characteristics classified.

We chose a subset of alternative definitions that have been used in other publications on HARVI. First, “>2 days” was defined as all patients who tested positive for a respiratory virus and had symptom onset on hospital day 3 or later, regardless of the virus.¹⁸ “Alt

Table 1. Comparison of Primary and Alternate Definitions of Healthcare-Associated Respiratory Viral Infections: Hospital Day Exposure Cutoffs^a

Infection	Study Definition			Alt A	Alt B
	Possible	Definite	>2 Days		
Adenovirus	5	15	3	N/A	7
Coronavirus	3	6	3	N/A	4
Metapneumovirus	4	6	3	4	6
Influenza A	3	5	3	2	2
Influenza B	3	5	3	2	1
Parainfluenza	3	7	3	3	4
RSV	4	7	3	3	5
Rhino/enterovirus	3	8	3	3	3

Note. N/A, not available; RSV, respiratory syncytial virus.

^aEach number represents the minimum length of stay, in days, prior to respiratory symptom onset for the chronologic criterion of the specific definition.

A”⁵ and “Alt B”¹³ were alternate incubation periods used to distinguish healthcare-associated infections from community-acquired infections (Table 1). Finally, “no symptom requirement” was the same as the primary study definition but did not require symptoms and used the date of viral testing as the event date rather than the date of symptom onset. The alternate definitions were only evaluated for incidence, and demographic characteristics were not classified according to study protocol.

Case finding, case classification, and data abstraction

Microbiology records were queried to identify all patients who tested positive for a respiratory virus on hospital day 3 or later during the study period. For each patient, the electronic health record (EHR) was abstracted to determine the date of symptom onset, if any. In those who met the study definition for possible or definite HARVI, demographic and comorbidity data were collected. Severity of underlying illness was calculated using the Pediatric Complex Chronic Conditions Classification (CCC) version 2,^{19,20} and severity of acute illness was measured using the Pediatric Logistic Organ Dysfunction Score 2 (PELOD2).²¹ Two investigators (Z.M. and M.S.) reviewed a random sample of 40 cases, and interobserver agreement in HARVI classification was determined using the κ (kappa) coefficient.

Analysis

Patient demographics were recorded as proportions for categorical variables and median with interquartile range (IQR) for quantitative variables. Comparisons between baseline characteristics of definite and possible cases were made using the χ^2 test for categorical variables and the Mann-Whitney *U* test for quantitative variables.

The primary outcome was the incidence rate of definite HARVI and possible HARVI using the primary study definition. The total number of admitted patient days, including those with length of stay shorter than the minimum incubation period, was used for follow-up time. The incidence of HARVI for each month of the study period, and the incidence of infection with each viral pathogen were also assessed. The incidence of HARVI was calculated using the 4 alternate definitions of HARVI to evaluate how sensitive the diagnosis was to the diagnostic criteria. All statistical calculations were performed using Stata version 16.1 software (StataCorp, College Station, TX).

Infection prevention policies

During the study period, several infection prevention interventions were in place that remained standard. All patients with suspected respiratory viral infections were placed on contact, droplet, and standard precautions at the time of admission. If the patient tested negative on respiratory multiplex PCR, then all but standard precautions were removed unless a respiratory viral illness was still suspected. If the patient tested positive, the patient remained on contact and droplet precautions until discharge or until resolution of symptoms and a repeated respiratory multiplex PCR was negative. Nearly all patients in the hospital were in single rooms, except those in the neonatal ICU, which had a semiopen ward. A mandatory influenza vaccine policy was in place for all hospital staff, residents, and faculty. Those with medical or religious exemptions were required to wear a mask in patient care areas during influenza season. Hand hygiene was required for all employees, and compliance was monitored by human observers. All hospital visitors were screened for symptoms of respiratory infection, and nonprimary caretakers were not allowed entry into the hospital if they had respiratory symptoms or fever.

The study protocol was deemed exempt from approval by the University of Texas Southwestern Institutional Review Board.

Results

Over the 5-year study period, there were 509,294 patient days of observation. Among 1,838 events meeting the microbiologic criterion on hospital day 3 or later, 588 were excluded as repeat positive tests for the same virus, 609 were excluded due to the chronologic criterion, and 113 were excluded due to the symptomology criterion. After combining 30 events in which 1 individual tested positive for 2 viruses at the same time, 498 HARVIs were identified, with 320 definite HARVIs (64.3%) and 178 possible HARVIs by the primary study definition (Fig. 1). The interobserver agreement of classifying HARVI was good ($\kappa = 0.74$; 95% CI, 0.55–0.93).

The median times from admission to HARVI were 21.5 days (range, 5–831 days, with a very skewed right distribution) and 4 days (range, 3–14 days) for those with definite and possible HARVIs, respectively. The median age of patients with HARVIs was 1 year old, and the sex distribution was balanced (Table 2). A large proportion of patients had underlying comorbid illnesses, including 14.1% who had been born very preterm or extremely preterm, 25.1% with chronic lung disease, 11.7% with unrepaired or palliated hemodynamically significant congenital heart disease, and 24.9% with immunodeficiency. We detected several differences between the baseline characteristics of patients with definite and possible HARVIs. Those with definite HARVIs were younger (median age, 1 year vs 2 years; $P < .001$), were more likely to have been born preterm (19% vs 6%; $P < 0.001$), were more likely to have chronic lung disease (29% vs 18%; $P = .006$), were more likely to have congenital heart disease (14% vs 7%; $P = .02$), were more likely to develop HARVI in the NICU ($P < .001$ for unit), were more likely to have a greater CCC score [median, 1 (IQR, 1–2) vs 1 (IQR, 0–2); $P < .001$], and were more likely to have a higher PELOD2 score (median, 2 vs 0; $P = .002$) (Table 2). The demographics of patients with HARVI did not change substantially over time (Supplementary Table S1 online).

Negative respiratory PCR tests before the onset of HARVI were common; they occurred in 16.9% of those with possible HARVI and 35.3% of those with definite HARVI. The median time from admission to negative test was 39 days (IQR, 4–90) in those with

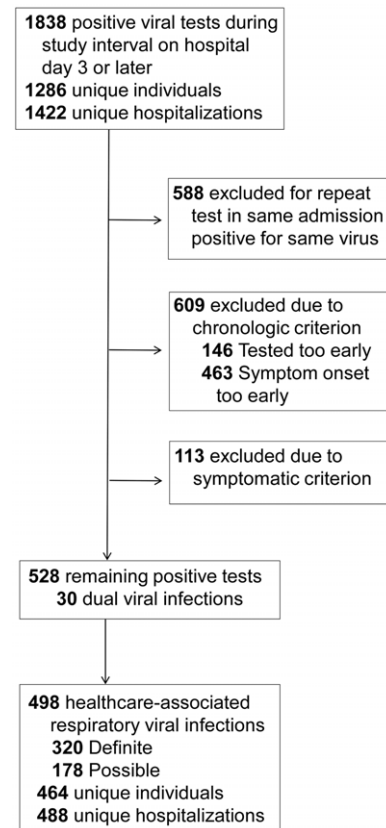


Fig. 1. Flow diagram for inclusion and exclusion of cases of healthcare-associated respiratory viral infections (HARVI). The chronologic criterion for HARVI definitions required that symptom onset occur after the minimum incubation period for the specific virus. The symptomatic criterion required that the individual have symptoms of a viral respiratory tract infection. Definite cases were defined as cases in which symptom onset occurred after the maximum incubation period for that virus had elapsed from the day of hospital admission. Possible cases were defined as those where symptom onset occurred between the minimum and maximum incubation period following hospital admission.

definite HARVI and 1 day (IQR, 1–2) in those with a possible HARVI (Supplementary Table S2 online).

The overall incidence rate of HARVI was 0.98 per 1,000 patient days (95% CI, 0.90–1.07), with definite and possible HARVIs causing 0.63 infections per 1,000 patient days (95% CI, 0.56–0.70) and 0.35 infections per 1,000 patient days (95% CI, 0.30–0.40), respectively. The incidence varied over time, with peaks most often occurring during the fall and winter months (Fig. 2A). The most common virus detected was rhinovirus or enterovirus, which accounted for 58.4% of all HARVIs, and 6.0% of HARVIs had >1 virus identified (Table 3). RSV and endemic coronaviruses were less common, accounting for 9.6% and 6.8%, respectively. Influenza was relatively rare, with only 3.6% of HARVIs attributed to influenza A and 2.2% attributed to influenza B. The incidence rates for each virus, except adenovirus, were seasonal, reflecting community respiratory virus transmission (Fig. 2B).

Using alternate HARVI case definitions, the incidence of HARVI varied from 0.96 to 2.00 per 1,000 patient days (Table 3). The “>2 days” definition resulted in a 28% greater incidence of HARVI compared to total and a 100% greater incidence of HARVI compared to definite cases by the primary study definition. The “Alt A” and “Alt B” definitions resulted in a similar incidence of HARVI compared to total, but “Alt B” had a 54% greater

Table 2. Comparison of Patient Demographics as Classified by Definite or Possible Healthcare-Associated Respiratory Viral Infections (HARVIs)

Characteristic	HARVI Classification, No. (%)			P Value ^a
	Total (n=498)	Definite (n=320)	Possible (n=178)	
Age, median y (IQR)	1.34 (0.37–4.73)	0.99 (0.18–3.89)	2.30 (0.75–7.33)	<.001
Age group				<.001
0–11 mo	215 (43.2)	162 (50.6)	53 (29.8)	
1–5 y	177 (35.5)	102 (31.9)	75 (42.1)	
6–10 y	53 (10.6)	28 (8.8)	25 (14.0)	
11–15 y	36 (7.2)	19 (5.9)	17 (9.6)	
16+ y	17 (3.4)	9 (2.8)	8 (4.5)	
Sex, female	236 (47.4)	142 (44.4)	94 (52.8)	.07
Race				.12
White	303 (60.8)	201 (62.8)	102 (57.3)	
Black	104 (20.9)	67 (20.9)	37 (20.8)	
Asian	20 (4.0)	12 (3.8)	8 (4.5)	
Other	71 (14.3)	40 (12.5)	31 (17.4)	
Hispanic ethnicity	211 (42.4)	139 (43.4)	72 (40.5)	.73
Obesity ^b	61 (12.3)	39 (12.2)	22 (12.4)	.96
Preterm ^c	71 (14.3)	60 (18.8)	11 (6.2)	<.001
Chronic lung disease	125 (25.1)	93 (29.1)	32 (18.0)	.006
Asthma	9 (1.8)	6 (1.9)	3 (1.7)	.88
CHD	58 (11.7)	45 (14.1)	13 (7.3)	.02
Immunodeficiency	124 (24.9)	83 (25.9)	41 (23.0)	.47
Malignancy	73 (14.7)	42 (13.1)	31 (17.4)	.19
Solid-organ transplant	22 (4.4)	17 (5.3)	5 (2.8)	.19
HSCT	20 (4.0)	19 (5.9)	1 (0.6)	.003
Primary immunodeficiency	7 (1.4)	4 (1.3)	3 (1.7)	.69
Medication	2 (0.4)	1 (0.3)	1 (0.6)	.67
Unit				<.001
Non-ICU	338 (67.9)	201 (62.8)	137 (77.0)	
Neonatal UCI	51 (10.2)	48 (15.0)	3 (1.7)	
Cardiovascular ICU	33 (6.6)	26 (8.1)	7 (3.9)	
Pediatric ICU	76 (15.2)	45 (14.1)	31 (17.4)	
LOS prior, median d (IQR)	10.5 (5–30)	21.5 (11– 50.5)	4 (3–6)	N/A
CCC score, median (IQR)	1 (0–2)	1 (1–2)	1 (0–2)	<.001
PELOD2 score, median (IQR)	0 (0–3)	2 (0–3)	0 (0–2)	.002

Note. HARVI, healthcare-associated respiratory viral infection; IQR, interquartile range; CHD, unrepaired or palliated hemodynamically significant congenital heart disease; HSCT, hematopoietic stem cell transplant; Medication, on immunosuppressive medication; ICU, intensive care unit; LOS, length of stay; CCC, Pediatric Complex Chronic Conditions Classification version 2; PELOD2, Pediatric Logistic Organ Dysfunction Score 2; N/A, not available.

^aP values based on null hypothesis that variable is equal between definite and possible cases in the population. Calculated using the Mann-Whitney U test for quantitative variables and the χ^2 test for categorical variables.

^bObesity defined as body mass index >95th percentile for age and sex.

^cPreterm includes only very preterm and extremely preterm infants (born at 32 weeks estimated gestational age or earlier).

incidence of HARVI compared to definite cases by the primary study definition. The largest differences were due to reductions in the influenza, RSV, and rhinovirus/enterovirus incidence. Removing the symptomatic criterion doubled the number of HARVIs identified, most of which would have been classified as possible healthcare associated.

Discussion

HARVIs often occur in high-risk patients and the incidence of HARVI in hospitalized pediatric patients was 0.98 infections per 1,000 patient days by our primary study definition. However, the incidence rate is highly dependent on the case definition used,

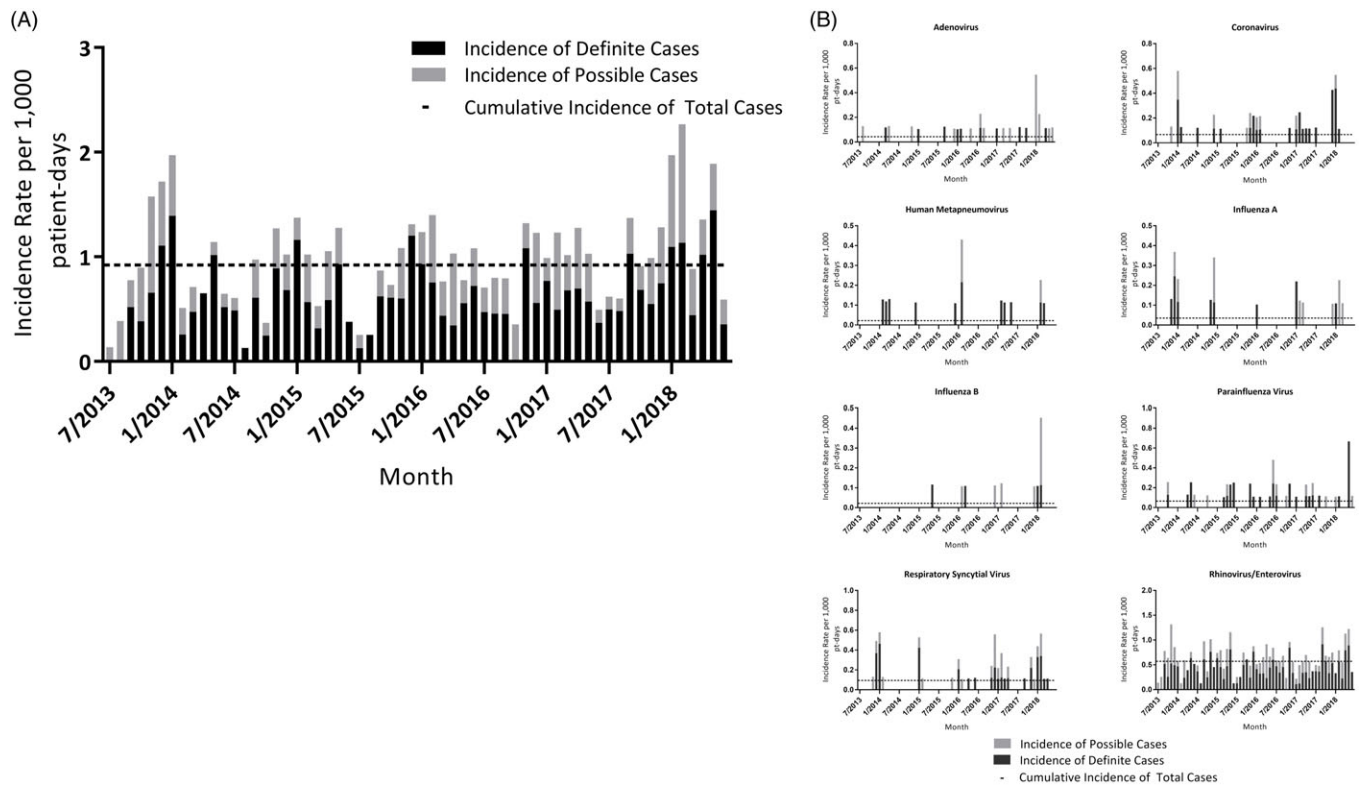


Fig. 2. Incidence rate (total, 498 events during 509,294 patient days) of healthcare-associated respiratory viral infections (HARVIs) between 2013 and 2018. The stacked total sums to the combined incidence rate of definite and possible HARVI cases per number of patient days at risk each month. Left: The combined HARVI incidence of all viruses. (Right) The incidence for each specific responsible virus. Note that the y-axis is scaled differently based on the frequency for each virus.

specifically regarding the viral incubation periods and symptoms. This incidence of HARVI was similar to reports at other pediatric hospitals ranging from 0.51 to 1.91 per 1,000 patient days.^{5,6,11,12,22,23} The frequency at which HARVIs occur likely depends on several factors including the number of high-risk patients at the institution and the infection prevention interventions in place. The comparison of these data was difficult because they used different definitions of HARVI. Importantly, using a stringent case definition (definite HARVI) that accounted for the upper bound of viral incubation periods, the rate decreased by nearly one-third to 0.63 infections per 1,000 patient days. Our definition of a HARVI includes 2 important aspects that are absent from many of the other reports on HARVI.

First, we included a requirement that patients show symptoms of a respiratory viral infection, and we counted the date of event as the day of symptom onset rather than the day of testing. This approach had several advantages. It aligned with the date-of-event definition for other healthcare-associated infections; thus, the earliest day of symptom onset could be used to distinguish healthcare-associated from community-acquired infections.²⁴ The symptom requirement helped control for nontesting bias (ie, only patients from a higher-risk subpopulation would be tested for asymptomatic infection). An asymptomatic patient who tests positive is more likely to have continued shedding from a prior community-acquired infection given the prolonged shedding time of respiratory viruses.^{25,26} Also, we observed that most of the patients who were excluded based on the chronologic criterion had been admitted for a viral infection, such as bronchiolitis, and had no viral testing on admission, which is in accordance with the protocol for managing low-risk patients with bronchiolitis at our

institution. However, they were tested for a virus upon subsequent transfer to the ICU several days later. These patients clearly had community onset and not healthcare-associated infections, as determined by the date of symptom onset. A disadvantage of including symptomatology in the definition is that performing retrospective case identification may have the potential for misclassification due to incomplete documentation or gaps in retrieval of symptom data from the EHR. We attempted to mitigate this problem by having 2 observers identify the date of symptom onset (if any), and we found good interobserver reliability. However, the possibility that we misclassified some HARVIs as asymptomatic infections due to incomplete EHR documentation remains a limitation of this study. In addition, this definition explicitly excluded asymptomatic HARVI from our analysis. Had we removed the symptomatic criterion and used the date of testing (rather than the date of symptom onset) as the date of event, the measured incidence of HARVI would have been twice as great. This difference demonstrates how responsive this measurement is to the exact definition used.

Second, our definition differentiated between definite and possible HARVIs using the upper and lower bounds of the viral incubation periods. Using intermediate values may misclassify some community-acquired infections as healthcare associated. By using the maximum reported incubation period for each virus, we likely avoided misclassifying community-acquired infections as definitely healthcare associated. This definition is more specific and might be better for public reporting. We considered the possible HARVIs to have a lower likelihood of being healthcare associated. However, including possible HARVIs within surveillance may enhance internal quality improvement efforts in institutions.

Table 3. HARVI Incidence Rate per 1,000 Admitted Patient Days Comparing Different Case Definitions^a

Virus	Primary Study Definition			>2 Days ^e	Alt A ^f	Alt B ^g	No Symptom Requirement ^h		
	Possible ^b	Definite ^c	Total ^d				Possible	Definite	Total
Adenovirus	0.027	0.016	0.043	0.100	n/a	0.031	0.043	0.027	0.071
Coronavirus	0.020	0.047	0.067	0.067	n/a	0.059	0.067	0.071	0.137
Metapneumovirus	0.004	0.018	0.022	0.067	0.022	0.018	0.024	0.024	0.047
Influenza A	0.020	0.016	0.035	0.035	0.053	0.053	0.043	0.026	0.069
Influenza B	0.014	0.008	0.022	0.022	0.027	0.027	0.031	0.022	0.053
Parainfluenza	0.022	0.043	0.065	0.065	0.065	0.059	0.098	0.059	0.157
RSV	0.035	0.059	0.094	0.251	0.096	0.086	0.094	0.082	0.177
Rhinovirus/enterovirus	0.196	0.375	0.571	0.571	0.571	0.571	0.628	0.511	1.139
Two Viruses	0.012	0.047	0.059	0.077	n/a	0.059	0.094	0.053	0.147
Total	0.350	0.628	0.978	1.255	n/a	0.964	1.123	0.874	1.997

Note. HARVI, healthcare-associated respiratory viral infection; RSV, respiratory syncytial virus.

^aCase definitions all required a positive test for a respiratory virus and either (b) or (c) below.

^bCompatible respiratory symptoms and a difference between day of symptom onset and day of hospitalization that occurred between the minimum and maximum incubation period.

^cCompatible respiratory symptoms and a difference between the day of symptom onset and the day of hospitalization greater than the maximum incubation period.

^dSum of definite and possible cases.

^eCompatible respiratory symptoms and difference between day of symptom onset and day of hospitalization >2 days.

^fThe minimum length of hospital stay prior to respiratory symptom onset for the following viruses: metapneumovirus, 4 days; influenza A, 2 days; influenza B, 2 days; parainfluenza, 3 days; RSV, 3 days; rhinovirus/enterovirus, 3 days.⁵

^gThe minimum length of hospital stay prior to symptom onset: adenovirus, 7 days; coronavirus (endemic), 4 days; metapneumovirus, 6 days; influenza A, 2 days; influenza B, 1 day; parainfluenza, 4 days; RSV, 5 days; rhinovirus/enterovirus, 3 days.¹³

^hUses the same HARVI definition for possible and definite cases but removes symptom requirement and uses day of testing rather than day of symptom onset.

Prior negative PCR tests before the onset of HARVI were common among individuals with definite and possible HARVIs. Prior negative testing was not included in our study definition of HARVI. However, community-acquired infections may still be incubating at the time of admission, so earlier negative tests do not confirm healthcare association.

We used a pre-COVID-19 pandemic study period, and rhinovirus or enterovirus was the most common cause of HARVI, which is consistent with other reports.^{5,11,23} Endemic coronaviruses accounted for 7% of HARVIs, highlighting the growing recognition of the clinical importance of coronaviruses. Notably, influenza infections were rare, which may reflect the institution's requirement of influenza vaccination for employees and providers. Many institutions have focused on testing for RSV and influenza, but such strategies may miss many causes of HARVI.

Not unexpectedly, this cohort of patients had a high prevalence of underlying medical comorbidities, especially prematurity and chronic lung disease. To some extent this reflects a selection bias because low-risk patients are probably less likely to be tested for a viral infection than high-risk patients. These associations are also a reflection of the type of patients that have a long length of stay in a pediatric institution. Regardless, the patients that appear to be at higher risk for HARVIs are likewise at higher risk for severe outcomes of respiratory infections.

Apart from the case definition, another strength is that we included data from a 5-year period and identified 498 cases of HARVI despite our stringent definitions. Thus, our study is one of the largest cohorts of HARVIs reported from a pediatric hospital.

The generalizability of this study needs to be taken into consideration. These findings represent the experience of a single, albeit large, institution providing primary and specialty care to children. Smaller pediatric hospitals that serve fewer high-risk patients may have very different HARVI incidence and demographics. The

prevalence of respiratory viruses varies with time and geography, which has been made apparent by the emergence of SARS-CoV-2 in 2020.²⁷ Finally, differences in infection prevention policies, adherence to those policies, and surveillance strategies, likely play a role in HARVI incidence, yet which specific interventions have the greatest effect is not clear.

In conclusion, HARVIs remain common and occur in our more vulnerable children. The measured incidence depends on the definition used. Distinguishing between possible and definite HARVIs may have benefits, depending on the purpose. Given the frequency and potential outcomes of these events, HARVI surveillance should be routine in pediatric hospitals and may be needed in other high-risk settings. However, a standardized definition of HARVI is needed for interhospital comparisons and for examining public health trends. Further studies are needed to identify pragmatic methods to apply HARVI definitions, to determine outcomes, and to implement infection prevention methods that can effectively reduce HARVIs.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/ice.2022.33>

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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