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SUPPLEMENT ARTICLE

# Respiratory Syncytial Virus During the COVID-19 Pandemic Compared to Historic Levels: A Retrospective Cohort Study of a Health System

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***Background.*** Surveillance in 2020–2021 showed that seasonal respiratory illnesses were below levels seen during prior seasons, with the exception of interseasonal respiratory syncytial virus (RSV).

***Methods.*** Electronic health record data of infants aged <1 year visiting the Duke University Health System from 4 October 2015 to 28 March 2020 (pre–COVID-19) and 29 March 2020 to 30 October 2021 (COVID-19) were assessed. International Classification of Diseases-Tenth Revision (ICD-10) codes for RSV (B97.4, J12.1, J20.5, J21.0) and bronchiolitis (RSV codes plus J21.8, J21.9) were used to detail encounters in the inpatient (IP), emergency department (ED), outpatient (OP), urgent care (UC), and telemedicine (TM) settings.

***Results.*** Pre–COVID-19, 88% of RSV and 92% of bronchiolitis encounters were seen in ambulatory settings. During COVID-19, 94% and 93%, respectively, occurred in ambulatory settings. Pre–COVID-19, the highest RSV proportion was observed in December–January (up to 38% in ED), while the peaks during COVID-19 were seen in July–September (up to 41% in ED) across all settings. RSV laboratory testing among RSV encounters was low during pre–COVID-19 (IP, 51%; ED, 51%; OP, 41%; UC, 84%) and COVID-19 outside of UC (IP, 33%; ED, 47%; OP, 47%; UC, 87%). Full-term, otherwise healthy infants comprised most RSV encounters (pre–COVID-19, up to 57% in OP; COVID-19, up to 82% in TM).

***Conclusions.*** With the interruption of historical RSV epidemiologic trends and the emergence of interseasonal disease during COVID-19, continued monitoring of RSV is warranted across all settings as the changing RSV epidemiology could affect the distribution of health care resources and public health policy.

**Keywords.** bronchiolitis; COVID-19; emergency department; infant; inpatient; laboratory testing; lower respiratory tract infection; outpatient; respiratory syncytial virus; United States.

Respiratory syncytial virus (RSV) is a common cause of illness for infants aged <1 year in the United States and is the leading cause of lower respiratory tract infections (LRTIs), including bronchiolitis and pneumonia [1]. RSV was the leading cause of infant hospitalizations between January 2009 and December 2019, accounting for greater than 9% of total infant hospitalizations [2]. However, RSV epidemiology in the emergency department (ED), outpatient (OP), and urgent care (UC) settings remains understudied. Additionally, a systematic literature review of RSV studies in the United States published between January 2000 and June 2021 found that all eligible infants were not laboratory tested for RSV, indicating the potential underestimation of the disease [3]. With the onset of the coronavirus disease 2019 (COVID-19) pandemic, health care seeking behaviors and delivery have changed dramatically, including increased use of telemedicine (TM), but the impact of the pandemic on RSV laboratory testing and epidemiology across all settings is unknown.

In response to the COVID-19 pandemic, public health interventions, including but not limited to mask mandates, school and business closures, and stay-at-home orders, were implemented and health care delivery and individuals' interactions with health care and society at large were disrupted [4–6]. Emerging reports suggest that since the start of the pandemic in March 2020 and the implementation of these public health measures, seasonal respiratory illnesses, including infant LRTI, remain below previously observed levels [7]. One retrospective study conducted using the Pediatric Health Information System (PHIS) database, which included comprehensive data from 44 US pediatric hospitals, showed fewer respiratory and nonrespiratory illness

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encounters were observed than expected with larger reductions for respiratory illnesses among children aged 2 months to 18 years from January to September 2020 [8]. The observed to expected encounter ratios for bronchiolitis was 0.93 (95% confidence interval [CI], .86–1.00) pre–COVID-19 in January–February 2020; 0.50 (95% CI, .46–.55) during early COVID-19 in March–April 2020; and 0.09 (95% CI, .08–.11) during COVID-19 in May–September 2020 [8]. In addition, COVID-19 impacted health seeking behaviors, leading to decreased health care utilization (HCU) in the US pediatric population. A retrospective chart review of pediatric ED health-seeking behaviors at 1 US children's hospital in New York found the proportion of asthma visits declined from 7% in March–July 2019 to 2% in the same interval for 2020 ($P < .0001$) among children aged <21 years evaluated in the ED [9]. These studies show the impacts of nonpharmaceutical intervention due to COVID-19 on both illness and associated HCU. However, literature specifically examining the impact of COVID-19 on RSV trends across all health care settings is limited and, thus, further investigations are warranted as the changing RSV epidemiology could impact distribution of health care resources and public health policy.

Duke University Health System (DUHS) is a single health system that serves populations in Durham and other nearby counties of North Carolina with comprehensive linkage of data across all health care settings. Within DUHS, there are over 90 facilities including hospitals, EDs, UC centers, and OP clinics [10]. Based on electronic health record-based surveillance from DUHS, a retrospective study was conducted to describe infant RSV and bronchiolitis epidemiology during the first year of life across all health care settings including inpatient (IP), ED, OP, UC, and TM before COVID-19 (4 October 2015 to 28 March 2020) and during COVID-19 (29 March 2020 to 30 October 2021).

## METHODS

### Study Design and Data Source

A retrospective cohort study was conducted using DUHS electronic health record (EHR) data. This study was approved by the DUHS Institutional Review Board (IRB) on 16 April 2020 (IRB No. Pro00104855).

### Study Population

Infants aged <1 year with an encounter for RSV or bronchiolitis in the DUHS system between October 2015 and October 2021 were eligible. RSV was identified through any one of the following International Classification of Diseases [ICD]-10 codes listed in the EHR: RSV (B97.4); pneumonia due to RSV (J12.1); acute bronchiolitis due to RSV (J21.0); or acute bronchitis due to RSV (J20.5). As RSV is a one of several causes of bronchiolitis, bronchiolitis was defined by one of the RSV codes or one of the following codes: acute bronchiolitis due to other specified organisms (J21.8); or acute bronchiolitis, unspecified (J21.9). As laboratory testing for RSV is currently not recommended in US hospitals and other settings [11], bronchiolitis was included as an upper estimate of RSV. Encounters were excluded from the analyses if they were of those aged ≥1 year at presentation or if the infant hospitalization or visit did not include any of the specified diagnosis codes for RSV or bronchiolitis.

### Variables and Statistical Analysis

Variables ascertained from the EHR included weeks' gestational age (wGA), chronological age in months, sex (male and female), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, American Indian/Alaskan Native, Asian Pacific Islander, and other), month of birth, intensive care unit admission (ICU), and antibiotic administration (proportion of infant encounters administered antibiotics). Comorbidities including congenital heart disease (CHD), chronic lung disease, Down syndrome, and other genetic, metabolic, and immunodeficiencies, which have been evaluated in the RSV and bronchiolitis literature [12], were also identified. For RSV, hemodynamically significant CHD (hsCHD) is the relevant comorbidity as palivizumab, the only approved immunoprophylaxis for RSV, is recommended for infants with hsCHD up to 24 months [13]. However, standard clinical definitions for hsCHD are not available. As hsCHD cannot be easily identified from the EHR, ICD codes for higher-risk CHD as previously defined in the literature were used as a proxy [12, 14]. The ICD codes used to define the variables are provided in Supplementary Table 1.

Analyses were conducted for 2 time periods: 4 October 2015 to 28 March 2020 and 29 March 2020 to 30 October 2021 to reflect pre–COVID-19 and COVID-19, respectively, as Durham's stay-at-home order went into effect on 26 March 2020 [15]. The historical pattern of RSV and bronchiolitis were also described by epidemiological week, which is commonly referred to as an epi week or Centers for Disease Control and Prevention (CDC) week, and begins on a Sunday and ends on a Saturday [16]. The pre–COVID-19 era started in October 2015 with epi week 40 and ended in March 2020 with epi week 13 to reflect the end of the 2019–2020 RSV season (Figure 1). For the COVID-19 era, this study included epi week 14 of March 2020 through epi week 43 of October 2021. Categorical variables were presented as the count and percentage of RSV/bronchiolitis hospitalizations or visits in each category. All descriptive analyses were conducted using Python and data visualizations were done using Microsoft Excel for Mac version 16.56 and GraphPad Prism version 9.3.0.

## Results

### Infant RSV and Bronchiolitis Encounters

Cohort identification is presented in Figure 1. Infant RSV and bronchiolitis encounters comprised up to 2% and 7%, respectively,

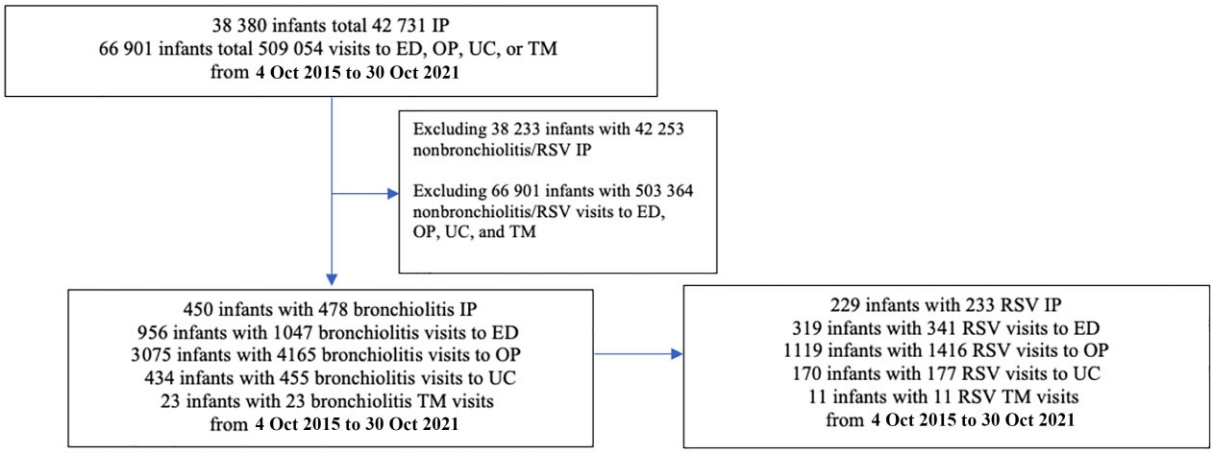


**Figure 1.** Cohort diagram of RSV and bronchiolitis in infants aged <1 year seen in DUHS, 4 October 2015 through 30 October 2021. RSV and bronchiolitis were defined by ICD-10 diagnosis codes: RSV (B97.4, J12.1, J20.5, J21.0) and bronchiolitis (RSV codes plus unspecified bronchiolitis: B97.4, J12.1, J20.5, J21.0 J21.8, J21.9). Infant counts by setting may not sum to the overall number of infants because an infant can have more than one encounter across multiple settings. TM in DUHS was not used in earnest until 18 March 2020. Abbreviations: DUHS, Duke University Health System; ED, emergency department; ICD-10, International Classification of Diseases-Tenth Revision; IP, inpatient; OP, outpatient; RSV, respiratory syncytial virus; TM, telemedicine; UC, urgent care.

of the total infant encounters seen in each setting during pre–COVID-19 (4 October 2015 to 28 March 2020) (data not shown). Among infant RSV and bronchiolitis encounters, 88% and 92% of the total RSV and bronchiolitis encounters, respectively, were seen in the ambulatory care settings (Table 1 and Table 2).

During COVID-19 (29 March 2020 to 30 October 2021), infant RSV and bronchiolitis encounters comprised up to 3% and 5%, respectively, of the total infant encounters seen in each setting (data not shown). Slightly more RSV was seen outside the IP setting in the COVID-19 period; 94% of RSV encounters and 93% of bronchiolitis encounters of the total RSV and bronchiolitis encounters, respectively, occurred in ambulatory care settings (Tables 1 and Table 2).

#### Pattern of Infant RSV and Bronchiolitis Encounters by Epidemiological Week

During pre–COVID-19, historical levels of RSV and bronchiolitis were highest during the in-season months (November–March) compared to the out-of-season months (April–October): the majority of infant RSV encounters occurred from November to March across all settings (IP, 95%; ED, 98%; OP, 94%; UC, 97%; Table 1). The 2019–2020 RSV season yielded the highest number of RSV and bronchiolitis encounters compared to earlier seasons (605 RSV and 1050 bronchiolitis from November 2019 epi week 45 to March 2020 epi week 12). For all years, immediate peaks were observed following late autumn and winter holidays (Figure 2). By the admission or visit month, RSV proportions were highest in December (IP, 34%; ED, 38%; OP, 30%; UC, 38%) and January (IP, 26%; ED, 33%; OP, 31%; UC, 26%) during pre–COVID-19 (Table 1).

With the onset of COVID-19, infant RSV and bronchiolitis encounters were reduced during the in-season months of November 2020 (epi week 44) to March 2021 (epi week 12) (up to 4 RSV and 6 bronchiolitis in March 2021 epi week 11; Table 1). Infant RSV encounters did not occur from November to March across all settings as historically expected (IP, 0%; ED, 1%; OP, 2%; UC, 3%; TM, 0%; Table 1). Instead, an interseasonal rebound was observed with higher volume of infant RSV and bronchiolitis encounters seen from May 2021 (epi week 20) through October 2021 (epi week 43) (up to 65 RSV and 76 bronchiolitis in August 2021 epi week 32). By the admission or visit month, the highest RSV proportion among infant RSV encounters was seen in July (IP, 31%; ED, 23%; OP, 26%; UC, 23%; TM, 10%), August (IP, 28%; ED, 41%; OP, 35%; UC, 33%; TM, 24%), and September (IP, 22%; ED, 26%; OP, 19%; UC, 25%; TM, 19%) across all settings during COVID-19 (Table 1). Patterns were similar among bronchiolitis encounters (Table 2).

#### Laboratory Testing Among Infant RSV Encounters Identified Through ICD Codes

Among all RSV encounters identified through ICD diagnosis codes, RSV laboratory testing varied across settings with about 50% or fewer being tested outside of the UC setting (IP, 51%; ED, 51%; OP, 41%; UC, 84%) during pre–COVID-19 (Figure 3). During COVID-19, the proportion of infant encounters being tested for RSV was the lowest for the IP setting compared to other settings (IP, 33%; ED, 47%; OP, 47%; UC, 87%).

Among the infant RSV encounters laboratory tested for RSV, those testing positive for RSV was lowest in the IP (pre–COVID-19, 88%; COVID-19, 83%) setting compared to the

**Table 1. Infant RSV Encounters Seen in the Duke University Health System, by Pre–COVID-19 (4 October 2015 to 28 March 2020) and COVID-19 (29 March 2020 to 30 October 2021) and Setting (Inpatient, Emergency Department, Outpatient, Urgent Care, and Telemedicine)[a,b]**

| | Pre–COVID-19 RSV, 4 October 2015 to 28 March 2020 | | | | | COVID-19 RSV, 29 March 2020 to 30 October 2021 | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Characteristic | IP (n = 197) | ED (n = 263) | OP (n = 1062) | UC (n = 73) | Total (n = 1595) | IP (n = 36) | ED (n = 78) | OP (n = 354) | UC (n = 104) | TM (n = 11) | Total (n = 583) |
| Chronological age, mo | | | | | | | | | | | |
| 0–5 | 74 (146) | 61 (160) | 57 (599) | 33 (24) | 58 (929) | 67 (24) | 68 (53) | 52 (183) | 43 (45) | 82 (9) | 54 (314) |
| 6–11 | 26 (51) | 39 (103) | 44 (463) | 67 (49) | 42 (666) | 33 (12) | 32 (25) | 48 (171) | 57 (59) | 18 (2) | 46 (269) |
| Month of admission | | | | | | | | | | | |
| January | 26 (52) | 33 (86) | 31 (331) | 26 (19) | 31 (488) | 0 (0) | 0 (0) | 0.3 (1) | 0 (0) | 0 (0) | 0.2 (1) |
| February | 16 (31) | 12 (32) | 16 (172) | 19 (14) | 16 (249) | 0 (0) | 1 (1) | 1 (3) | 1 (1) | 0 (0) | 1 (5) |
| March | 7 (14) | 6 (15) | 7 (72) | 4 (3) | 7 (104) | 0 (0) | 0 (0) | 1 (4) | 2 (2) | 0 (0) | 1 (6) |
| April | 2 (3) | 1 (3) | 2 (25) | 0 (0) | 2 (31) | 3 (1) | 0 (0) | 3 (9) | 2 (2) | 0 (0) | 2 (12) |
| May | 0 (0) | 0.4 (1) | 1 (8) | 0 (0) | 1 (9) | 6 (2) | 1 (1) | 1 (5) | 1 (1) | 0 (0) | 2 (9) |
| June | 0 (0) | 0 (0) | 0.1 (1) | 1 (1) | 0.1 (2) | 3 (1) | 6 (5) | 6 (20) | 3 (3) | 0 (0) | 5 (29) |
| July | 0 (0) | 0 (0) | 0.1 (1) | 0 (0) | 0.1 (1) | 31 (11) | 23 (18) | 25 (90) | 23 (24) | 9 (1) | 25 (144) |
| August | 1 (1) | 0.4 (1) | 1 (5) | 0 (0) | 0.4 (7) | 28 (10) | 41 (32) | 35 (123) | 33 (34) | 36 (4) | 35 (203) |
| September | 1 (1) | 0 (0) | 1 (6) | 0 (0) | 0.4 (7) | 22 (8) | 26 (20) | 19 (66) | 25 (26) | 27 (3) | 21 (123) |
| October | 2 (4) | 0.4 (1) | 2 (16) | 1 (1) | 1 (22) | 8 (3) | 1 (1) | 9 (33) | 11 (11) | 27 (3) | 9 (51) |
| November | 13 (25) | 10 (25) | 11 (111) | 10 (7) | 11 (168) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| December | 34 (66) | 38 (99) | 30 (314) | 38 (28) | 32 (507) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Received palivizumab | 3 (5) | 1 (2) | 1 (8) | 0 (0) | 1 (15) | 3 (1) | 3 (2) | 0.3 (1) | 0 (0) | 0 (0) | 1 (4) |
| Received antibiotics | 53 (105) | 8 (21) | 0.2 (2) | 0 (0) | 8 (128) | 44 (16) | 3 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (18) |

Data are % (No.).

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; IP, inpatient; OP, outpatient; RSV, respiratory syncytial virus; TM, telemedicine; UC, urgent care.

[a]RSV was defined by International Classification of Diseases-Tenth Revision (ICD-10) diagnosis codes: B97.4, J12.1, J20.5, J21.0.

[b]Percentages may not add up to 100% due to rounding.

ED (pre–COVID-19, 98%; COVID-19, 100%), OP (pre–COVID-19, 100%; COVID-19, 99%), and UC (pre–COVID-19, 100%; COVID-19, 100%) settings (Figure 2).

Polymerase chain reaction (PCR) tests were 14 times more likely to be used in the IP setting during pre–COVID-19 and 6 times more likely during COVID-19 compared to antigen tests (data not shown). In the ED, PCR tests were 2 and 3 times more likely to be used compared to antigen tests during pre–COVID-19 and COVID-19, respectively. In contrast, the use of PCR tests for OP and UC settings was nonexistent or close to zero during pre–COVID-19 and COVID-19.

### Laboratory Testing Among Infant Bronchiolitis Encounters Identified Through ICD Codes

Among all bronchiolitis encounters identified through ICD diagnosis codes, RSV laboratory testing varied across settings with less than 25% being tested in the ED and OP settings (IP, 54%; ED, 23%; OP, 19%; UC, 26%) during pre–COVID-19 (Supplementary Figure 1). During COVID-19, the proportion of bronchiolitis encounters being tested for RSV was 50% or less in the IP, ED, and OP settings (IP, 50%; ED, 41%; OP, 40%; UC, 72%).

Among the infant bronchiolitis encounters laboratory tested for RSV, those testing positive for RSV were the lowest in the IP (pre–COVID-19, 65%; COVID-19, 55%) setting compared to the ED (pre–COVID-19, 77%; COVID-19, 79%), OP (pre–COVID-19, 71%; COVID-19, 83%), and UC (pre–COVID-19, 100%; COVID-19, 82%) settings (Supplementary Figure 1).

PCR tests were 18 times more likely to be used in the IP setting during pre–COVID-19 and 5 times more likely during COVID-19 compared to antigen tests (data not shown). In the ED, PCR tests were 2 and 3 times more likely to be used compared to antigen tests during pre–COVID-19 and COVID-19, respectively. The use of PCR tests was nonexistent or close to zero during pre–COVID-19 and COVID-19 in the OP and UC settings.

### Infant RSV and Bronchiolitis Encounters, by Clinical and Sociodemographic Variables

When infant RSV encounters were stratified by clinical and sociodemographic variables, infants younger than 6 months in the IP (pre–COVID-19, 74%; COVID-19, 67%), ED (pre–COVID-19, 61%; COVID-19, 68%), and OP (pre–COVID-19, 56%; COVID-19, 52%) had the highest proportion; the lowest was observed among infants younger than 6 months in the UC (pre–COVID-19, 33%; COVID-19, 43%) setting (Table 1).

Most infant RSV encounters did not have higher-risk CHD across all settings during pre–COVID-19 (IP, 4%; ED, 2%; OP, 1%; UC, 1%) and COVID-19 (IP, 3%; ED, 0%; OP, 1%;

**Table 2. Infant Bronchiolitis Encounters Seen in Duke University Health System, by Pre–COVID-19 (4 October 2015 to 28 March 2020) and COVID-19 (29 March 2020 to 30 October 2021) and Setting (Inpatient, Emergency Department, Outpatient, Urgent Care, and Telemedicine)[a,b]**

| | Pre–COVID-19 Bronchiolitis (4 October 2015 to 28 March 2020) | | | | | COVID-19 Bronchiolitis (29 March 2020 to 30 October 2021) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Characteristic | IP (n = 412) | ED (n = 918) | OP (n = 3602) | UC (n = 297) | Total (n = 5229)[c] | IP (n = 66) | ED (n = 129) | OP (n = 563) | UC (n = 158) | TM (n = 21) | Total (n = 937) |
| Chronological age | | | | | | | | | | | |
| 0–5 months | 65 (267) | 53 (484) | 50 (1805) | 41 (121) | 51 (2677) | 56 (37) | 61 (78) | 52 (291) | 44 (69) | 81 (17) | 53 (492) |
| 6–11 months | 35 (145) | 47 (434) | 50 (1797) | 59 (176) | 49 (2552) | 44 (29) | 40 (51) | 49 (272) | 56 (89) | 19 (4) | 48 (445) |
| Month of admission | | | | | | | | | | | |
| January | 22 (90) | 25 (225) | 23 (814) | 16 (47) | 23 (1176) | 2 (1) | 0 (0) | 1 (4) | 0 (0) | 0 (0) | 1 (5) |
| February | 11 (47) | 11 (99) | 12 (441) | 12 (36) | 12 (623) | 0 (0) | 2 (2) | 2 (10) | 2 (3) | 5 (1) | 2 (16) |
| March | 8 (33) | 8 (69) | 9 (306) | 7 (22) | 8 (430) | 0 (0) | 0 (0) | 3 (14) | 3 (4) | 19 (4) | 2 (22) |
| April | 3 (12) | 4 (36) | 4 (150) | 6 (18) | 4 (216) | 6 (4) | 0 (0) | 4 (21) | 3 (4) | 10 (2) | 3 (31) |
| May | 4 (15) | 3 (25) | 3 (100) | 6 (17) | 3 (157) | 6 (4) | 5 (6) | 4 (23) | 2 (3) | 0 (0) | 4 (36) |
| June | 1 (5) | 1 (9) | 2 (71) | 2 (7) | 2 (92) | 3 (2) | 9 (11) | 8 (45) | 5 (8) | 0 (0) | 7 (66) |
| July | 1 (3) | 1 (8) | 1 (42) | 1 (2) | 1 (55) | 24 (16) | 26 (33) | 21 (117) | 27 (43) | 10 (2) | 23 (211) |
| August | 1 (4) | 1 (7) | 2 (68) | 2 (5) | 2 (84) | 23 (15) | 33 (42) | 30 (167) | 25 (40) | 24 (5) | 29 (269) |
| September | 2 (7) | 2 (18) | 2 (88) | 2 (6) | 2 (119) | 23 (15) | 21 (27) | 18 (100) | 22 (34) | 19 (4) | 19 (180) |
| October | 4 (18) | 4 (34) | 5 (174) | 4 (11) | 5 (237) | 11 (7) | 4 (5) | 10 (57) | 10 (15) | 14 (3) | 9 (87) |
| November | 15 (61) | 12 (111) | 12 (442) | 11 (33) | 12 (647) | 0 (0) | 1 (1) | 1 (3) | 1 (1) | 0 (0) | 1 (5) |
| December | 28 (117) | 30 (277) | 25 (906) | 31 (93) | 27 (1393) | 3 (2) | 2 (2) | 0.4 (2) | 2 (3) | 0 (0) | 1 (9) |
| Received palivizumab | 6 (24) | 2 (14) | 1 (35) | 1 (2) | 1 (75) | 3 (2) | 2 (3) | 0.4 (2) | 1 (1) | 0 (0) | 1 (8) |
| Received antibiotics | 49 (203) | 6 (59) | 0.2 (7) | 0 (0) | 5 (269) | 33 (22) | 2 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (24) |

Data are % (No.).

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; IP, inpatient; OP, outpatient; RSV, respiratory syncytial virus; TM, telemedicine; UC, urgent care.

[a]Bronchiolitis was defined by International Classification of Diseases-Tenth Revision (ICD-10) diagnosis codes: RSV codes (B97.4, J12.1, J20.5, J21.0) plus unspecified bronchiolitis (B97.4, J12.1, J20.5, J21.0 J21.8, J21.9).

[b]Percentages may not add up to 100% due to rounding.

[c]Two TM bronchiolitis encounters occurred during the pre–COVID-19 era. Data not shown. TM was not used in earnest until 18 March 2020.

UC, 1%; TM, 0%) (data not shown). Chronic lung disease was not noted for any of the infant RSV encounters. Among the infant RSV encounters, palivizumab was not widely received during pre–COVID-19 (IP, 3%; ED, 1%; OP, 1%; UC, 0%) and COVID-19 (IP, 3%; ED, 3%; OP, 0%; UC, 0%; TM, 0%) (Table 1). Although 40% of the encounters were missing wGA status, full term, otherwise healthy infant encounters comprised most RSV encounters during pre–COVID-19 (IP, 32%; ED, 45%; OP, 57%; UC, 48%; Figure 4) and COVID-19 (IP, 33%; ED, 45%; OP, 57%; UC, 55%; TM, 82%; data not shown) when evaluated by comorbidity conditions and wGA status. Higher RSV proportions were seen among male and non-Hispanic white and non-Hispanic black infants in all settings except TM (Supplementary Table 2). Similar patterns for chronological age, comorbidity status, palivizumab use, wGA status, gender, and race/ethnicity were observed among bronchiolitis encounters (Table 2, Supplementary Figure 2, and Supplementary Table 3).

#### Intensive Care Unit Admission, Length of Stay During Hospitalization, and Deaths

During pre–COVID-19, 60% of IP RSV encounters and 56% of bronchiolitis encounters were admitted to the ICU (data not shown). ICU admissions among IP RSV and bronchiolitis encounters were 69% and 71%, respectively, during COVID-19. Among the 193 IP RSV encounters with hospitalization length of stay (LOS) information, the median days were 4.7 (minimum, 0.2; maximum, 143.9) during pre–COVID-19 and among the 35 IP RSV encounters during COVID-19, the LOS days were 3.5 (minimum, 0.4; maximum, 38.4). The hospitalization LOS days were 4.0 (minimum, 0.2; maximum, 143.9) for the 400 pre–COVID-19 IP bronchiolitis encounters and 3.0 (minimum, 0.4; maximum, 74.2) for the 64 COVID-19 IP bronchiolitis encounters. Pre–COVID-19, there were 2 deaths (1%) among the IP RSV encounters and 3 deaths (0.7%) among the IP bronchiolitis encounters. No deaths were recorded during COVID-19 among IP RSV and bronchiolitis encounters.

#### Antibiotic Administration, by Pre–COVID-19 and COVID-19

Antibiotic administration was highest for infant RSV encounters in the IP setting compared to the other settings during pre–COVID-19 (IP, 53.3%; ED, 8.0%; OP, 0.2%; UC, 0%; TM, 0%) and COVID-19 (IP, 44.4%; ED, 2.6%; OP, 0%; UC, 0%; TM, 0%) (Table 1). Bronchiolitis encounters exhibited similar patterns for antibiotic administration (Table 2).

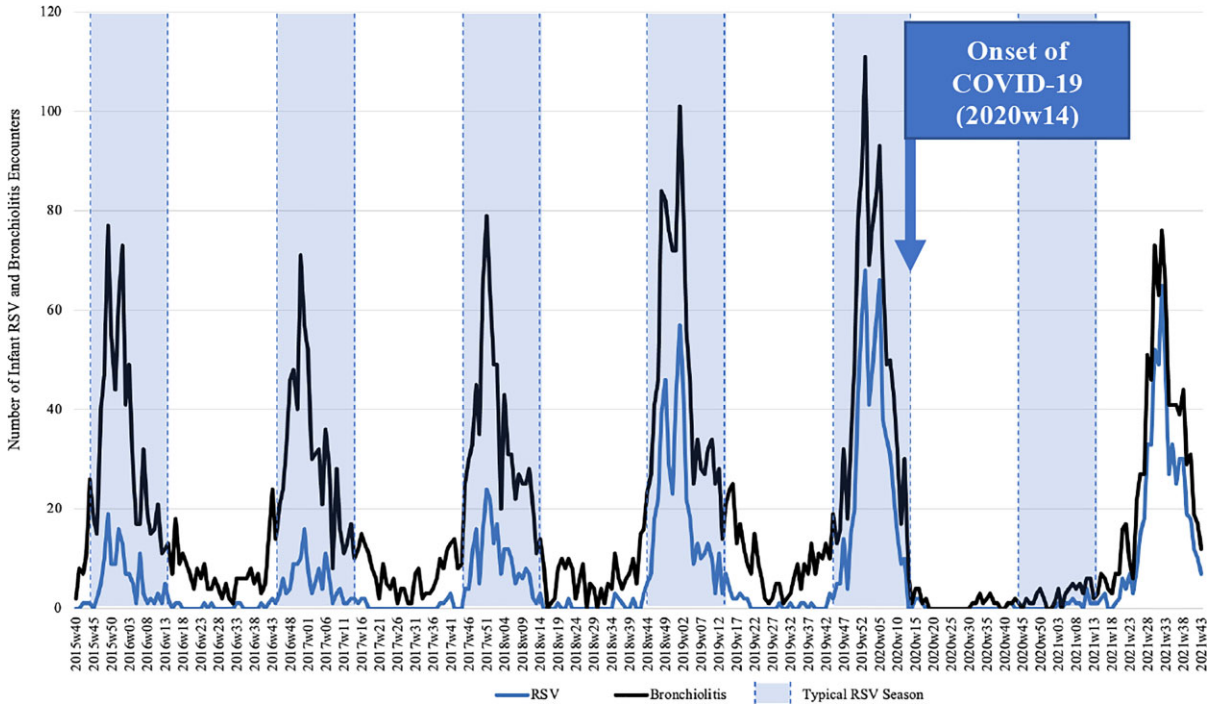


**Figure 2.** Historical pattern of infant RSV and bronchiolitis seen in the Duke University Health System, Durham County, NC (4 October 2015 to 30 October 2021). Number of encounters for RSV and bronchiolitis among infants aged <1 year, by epidemiological week. RSV and bronchiolitis were defined by ICD-10 diagnosis codes: RSV (B97.4, J12.1, J20.5, J21.0) and bronchiolitis (RSV codes plus unspecified bronchiolitis: B97.4, J12.1, J20.5, J21.0 J21.8, J21.9). Epidemiological week, commonly referred to as an epi week or MMWR week, begins in the United States on a Sunday and ends on a Saturday [17]. The first MMWR week of the year is the first week that has at least 4 days in the calendar year [18]. Abbreviations: ICD-10, International Classification of Diseases-Tenth Revision; MMWR, Morbidity and Mortality Weekly Report; RSV, respiratory syncytial virus.

## DISCUSSION

This retrospective cohort study was conducted in a single health system with comprehensive linkage across all settings (IP, ED, OP, UC, and TM) and multiple sites to describe infant RSV and bronchiolitis epidemiology and associated HCU. RSV seasonality patterns have changed with the onset of COVID-19 as RSV did not increase from November to March as expected compared with historical norms. The proportion laboratory tested for RSV among RSV encounters was low in the IP, ED, and OP settings and was even lower among bronchiolitis encounters; this indicates the potential underestimation of RSV in the health system. Among the RSV encounters laboratory tested for RSV, the testing positivity was the lowest in the IP setting. High volumes of RSV and bronchiolitis encounters were observed outside of the IP setting during pre–COVID-19 and COVID-19. The proportions of RSV and bronchiolitis encounters were the highest among full-term, otherwise healthy infants during pre–COVID-19 and COVID-19. These study findings emphasize the need to capture all infants across all health care settings to comprehensively understand RSV epidemiology.

Inconsistent with historical norms, there was an interseasonal rebound of RSV during COVID-19 with a higher volume of encounters seen from May to October 2021. This may be due to the COVID-19 prevention measures put in place by the state of North Carolina [19]. A state of emergency was declared on 10 March 2020 and within the week, schools, restaurants, and bars were closed. Between May 2020 and September 2020, the state had moved to various phases of reopening. In December 2020, state-wide modified stay-at-home orders were established including a specific closure time for certain businesses. By February 2021, North Carolina had returned to phase 3 opening, which included increased capacity at restaurants, bars, and other gatherings. These data support changes in HCU due to COVID-19 and related public health measures. Additionally, in this study, ICU admission for RSV and bronchiolitis encounters was increased during COVID-19. A study of the PHIS database, as mentioned previously in the introduction, showed there were fewer than expected encounters for respiratory and nonrespiratory illnesses during COVID-19 for children aged 2 months to 18 years, [8] which suggests changing HCU. Perhaps, infants with mild illnesses were not seeking medical care. At DUHS, sick patients were often being triaged away from outpatient provider appointments (Malcolm WF, unpublished) [20]. As the pandemic continues and policies evolve, RSV needs to be monitored to understand the changing patterns in epidemiology and HCU.

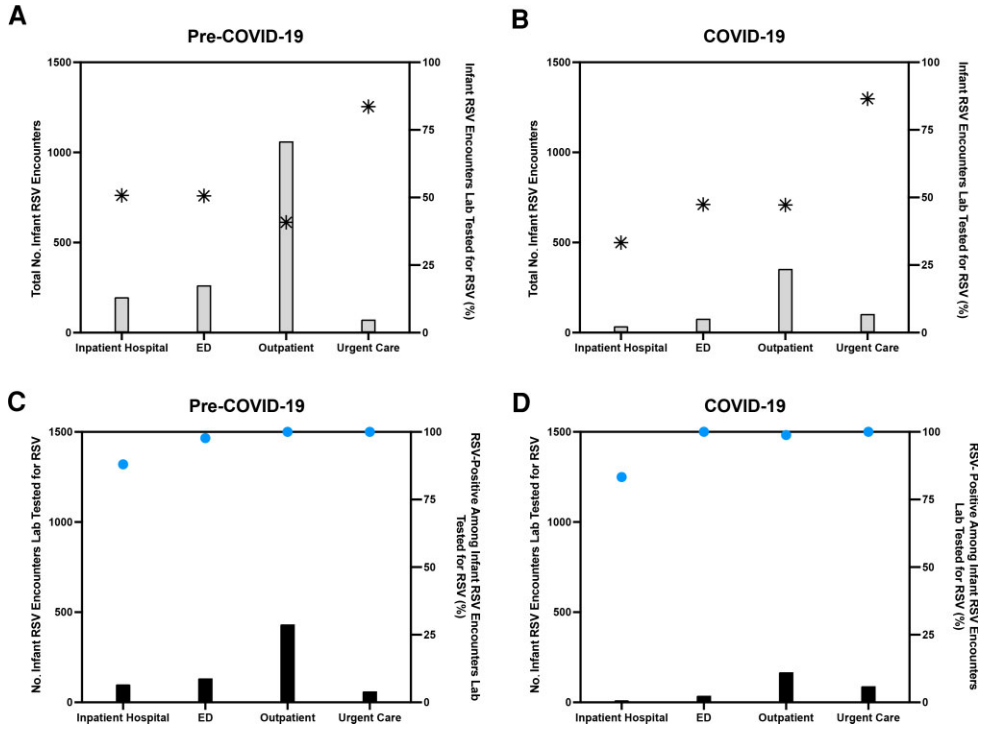


**Figure 3.** *A–D*, RSV laboratory testing among infant RSV encounters seen in the Duke University Health System, by pre–COVID-19 (4 October 2015 to 28 March 2020) and COVID-19 (29 March 2020 to 30 October 2021) and setting. RSV was defined by ICD-10 diagnosis codes: B97.4, J12.1, J20.5, J21.0. Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; ICD-10, International Classification of Diseases-Tenth Revision; RSV, respiratory syncytial virus.

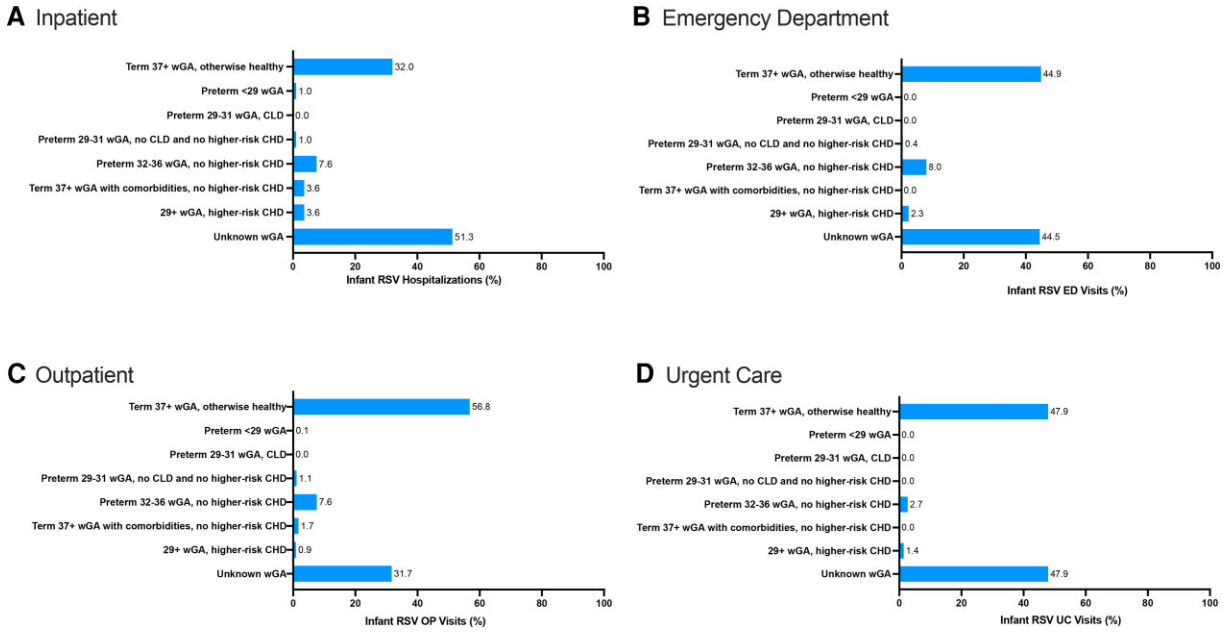


**Figure 4.** Infant RSV encounters seen in the Duke University Health System, Durham County, NC, during pre–COVID-19 (4 October 2015 to 28 March 2021), by risk groups in (*A*) inpatient setting; (*B*) emergency department; (*C*) outpatient setting; and (*D*) urgent care setting. RSV was defined by ICD-10 diagnosis codes: B97.4, J12.1, J20.5, J21.0. Similar patterns in risk groups were observed during COVID-19. Abbreviations: CHD, congenital heart disease; CLD, chronic lung disease; COVID-19, coronavirus disease 2019; ICD-10, International Classification of Diseases-Tenth Revision; RSV, respiratory syncytial virus; wGA, weeks' gestational age.

The proportion of those laboratory tested for RSV among all RSV and bronchiolitis encounters with ICD diagnoses for RSV and bronchiolitis was not 100% across all settings, which indicates not everyone is being laboratory tested and there is an underestimation of RSV burden. Testing across settings at DUHS is variable and this finding is consistent with a recent systematic review describing RSV laboratory testing in the United States based on literature published from 2000 to 2021 [3]. Further research using comprehensive infant health data is needed during COVID-19 to understand the current trends of who is being tested, where the tests are occurring, why the tests are being performed, and what is the consistency between ICD code diagnosis and laboratory test positivity.

One strength of this study was the use of comprehensive EHR data, which provides longitudinal records on the infants and links encounters across multiple settings to each infant. Furthermore, this study documents the burden of RSV and bronchiolitis across all settings and by sociodemographic and clinical data, such as chronological age, wGA, comorbidity conditions, and month of admission. Limitations of this study include the small sample size during COVID-19 because the pandemic is still on-going. Although, a considerable proportion of encounters were missing wGA data, this study captures the profile of all infants rather than just palivizumab eligible or formerly eligible infant populations (eg, those born <28 wGA or 29–34 wGA). Additionally, the unit of analysis was the number of health care encounters rather than infants so an infant could have contributed multiple RSV and bronchiolitis health care encounters in the study. Furthermore, ICD-10 diagnosis codes were used to define RSV and bronchiolitis in the study, which could potentially result in misclassification of outcome because the sensitivity and specificity of the codes for different diseases and cohorts may vary. Infants may have had additional health encounters outside of DUHS that were not captured in this study leading to potential underestimation of RSV. Lastly, these findings may not be generalizable to other geographic areas or health systems.

In conclusion, the impact of RSV and bronchiolitis is highest among otherwise healthy full-term infants. There is also a high volume of infant RSV and bronchiolitis encounters in the ambulatory settings. Future studies should consider utilizing other health systems and databases, such as claims data, to support these study findings in other geographical locations in the United States across all health care settings. Continued monitoring is needed to understand how RSV detection and the co-detection of RSV and COVID-19 will impact the infant, caregiver, and the health system.

## Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

## Notes

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