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Comparison of clinical presentations and burden of respiratory syncytial virus in infants across three distinct healthcare settings in Davidson County, Tennessee

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Abstract

Background: The burden of respiratory syncytial virus (RSV)-associated acute respiratory illnesses among healthy infants (<1 year) in the inpatient setting is well established. The focus on RSV-associated illnesses in the outpatient (OP) and emergency department (ED) settings are however understudied. We sought to determine the spectrum of RSV illnesses in infants at three distinct healthcare settings.

Methods: From 16 December 2019 through 30 April 2020, we performed an active, prospective RSV surveillance study among infants seeking medical attention from an inpatient (IP), ED, or OP clinic. Infants were eligible if they presented with fever and/or respiratory symptoms. Demographics, clinical characteristics, and illness histories were collected during parental/guardian interviews, followed by a medical chart review and illness follow-up surveys. Research nasal swabs were collected and tested for respiratory pathogens for all enrolled infants.

Results: Of the 627 infants screened, 475 were confirmed eligible; 360 were enrolled and research tested. Within this final cohort, 101 (28%) were RSV-positive (IP = 37, ED = 18, and OP = 46). Of the RSV-positive infants, the median age was 4.5 months and 57% had ⩾2 healthcare encounters. The majority of RSV-positive infants were not born premature (88%) nor had underlying medical conditions (92%). RSV-positive infants, however, were more likely to have a lower respiratory tract infection than RSV-negative infants (76% *vs* 39%, $p < 0.001$). Hospitalized infants with RSV were younger, 65% required supplemental oxygen, were more likely to have lower respiratory tract symptoms, and more often had shortness of breath and rales/rhonchi than RSV-positive infants in the ED and OP setting.

Conclusion: Infants with RSV illnesses seek healthcare for multiple encounters in various settings and have clinical difference across settings. Prevention measures, especially targeted toward healthy, young infants are needed to effectively reduce RSV-associated healthcare visits.

Keywords: RSV across healthcare settings, RSV in infants

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Introduction

Globally, respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections (LRTIs) and hospitalizations in infants (<1 year) and young children.[1–3] In the United States, more than 57,000 hospitalizations with direct medical costs of $400 million have been attributed to RSV infections each year in children younger than 5

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years.[1,2,4] More than three-quarters of annual hospitalizations in children younger than 5 years are among infants.[5,6] Known risk factors for hospitalization are primarily in preterm infants and those with congenital heart disease or chronic lung disease of prematurity; however, the majority of RSV-associated hospitalizations are among children without underlying medical conditions.[3,7,8] RSV burden is not exclusive to the inpatient (IP) setting, yet the relative impact of visits attributed to RSV in the emergency department (ED) and ambulatory care settings are unclear and understudied,[7,8] especially among infants.

At present, palivizumab prophylaxis (monthly intramuscular injections during RSV season) is the only product available to prevent LRTI hospitalization caused by RSV and is only indicated in high-risk infants.[9,10] Broader prevention, such as vaccines and long-acting monoclonal RSV-neutralizing antibodies targeting infants and children are under development, with multiple phase 1–3 trials being conducted.[11–13] Despite the development of pharmaceutical prevention, RSV epidemiology among infants primarily focus on palivizumab-eligible populations and the IP setting and is dependent on RSV detection through clinical testing. This focus has limited the evidence on the burden of RSV in the ED and outpatient (OP) clinic settings; and for full-term, otherwise healthy infants. Therefore, we aimed to (1) assess infant RSV infections across three distinct healthcare settings, (2) evaluate the differences in infant RSV sociodemographic characteristics and clinical presentations across healthcare settings, and 3) determine the number of healthcare encounters attributed to an infant's RSV illness.

Methods

Study design

We conducted an active, prospective RSV surveillance study among infants in Davidson County, Tennessee, from 16 December 2019 to 30 April 2020. Infants who presented to an IP setting, ED, or one of four OP clinics with fever (⩾100.4°F) and/or at least one respiratory symptom (i.e. wheezing, crackles, rales, diminished breath sounds, shortness of breath, cough, earache, nasal congestion, rhinorrhea, coryza, and/or sore throat) within 14 days of illness onset were eligible for enrollment.[14] Written informed consent was obtained from parents or legal guardians in English, Spanish, or Arabic prior to enrollment.

Infants were excluded if they were hospitalized for more than 48 hours, were newborns never discharged from the hospital, presented with both fever and neutropenia (absolute neutrophil count $<500 \times 10^3/\mu L$), had a known non-infectious cause for their symptoms, and/or had been previously enrolled in the past 7 days.

Enrollment locations

IP/ED surveillance. Surveillance was conducted in a 307-bed academic children's hospital and ED. Enrollment was initiated on 16 December 2019 and occurred seven and three (i.e. Tuesday, Friday, and Saturday) days a week (2:00–10:00 p.m.) in the IP and ED settings, respectively. In the United States, EDs are typically reserved and used for emergencies or after hours when OP clinics are closed.

Pediatric OP clinic surveillance. Surveillance was conducted at four distinct pediatric OP clinics: one academic, one private/academic, and two private. Enrollment commenced on 16 and 19 of December 2019 at the academic clinic and the private/academic pediatric clinic, respectively; and subjects were approached for eligibility Monday through Thursday each week. At the private clinics, one began enrollment on 9 January 2020, and the other on 21 January 2020, with enrollment occurring 6 days per week (i.e. Monday to Saturday). On 16 March 2020, the study ceased enrollment at all OP clinics, except the academic clinic, because of coronavirus disease 2019 (COVID-19) pandemic-related restrictions. OP clinics in the United States generally include family practitioners and private care.

Clinical setting distribution was determined by the highest admission status of the infant (i.e. infants enrolled from the ED or OP clinics and later hospitalized within 7 days of enrollment were considered as IP).

Data and specimen collection

Trained staff interviewed parents or legal guardians of the enrolled infant for demographic, social,

illness, and epidemiologic histories using a standardized questionnaire in commonly spoken languages (i.e. English, Spanish, or Arabic). A research nasal swab and a medical chart review after discharge for clinical outcomes, antibiotic use, provider-ordered RSV testing, and clinical microbiological data were collected from all infants. Fourteen days following enrollment, parents or legal guardians were administered a follow-up interview to assess illness duration, and additional healthcare encounters (e.g. OP clinic, urgent care, ED visits, etc.). Parents who reported ongoing symptoms on the follow-up survey were administered a questionnaire every 7 days until the infant's symptoms resolved. All data and specimen information were maintained in a secure REDCap™ (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA) database.[15]

Definitions

An infant was defined to have LRTI if they had at least one of the following findings reported during their physical assessment: (1) wheezing; (2) crackles; (3) rales; (4) diminished breath sounds; or (5) shortness of breath/rapid or shallow breathing. Infants were considered to have an underlying medical condition if they had at least one of the following: asthma/reactive airway disease, atopic/allergic conditions, blood disorders, cancer, cerebral palsy, chronic lung conditions, cystic fibrosis, diabetes, Down's syndrome, eczema, endocrine diseases, food allergies, genetic/metabolic disorders, heart disease, immunocompromised conditions, kidney disease, liver disease, neurological disorders, sickle cell disease/trait, seizure disorder, and/or other (e.g. neonatal abstinence syndrome, congenital defects, etc.).[14]

Dates of enrollment were reported using the Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Reporting (MMWR) weeks of the epidemiological year.[16,17] Our study enrollment period took place from MMWR weeks 50 through 18 (i.e. 16 December 2019 to 30 April 2020).[16,17]

Laboratory testing and pathogen detection

Research nasal swabs were placed in viral transport medium and further aliquoted into a tissue lysis buffer (ATL Lysis Buffer, QIAGEN), snap-frozen, and stored at −80°C. All specimens were tested for RSV A and B, adenovirus, four human coronaviruses [(HCoVs): OC43, 229E, HKU1 and NL63)], human metapneumovirus, human rhinovirus/enterovirus, influenza (A and B), bocavirus, and parainfluenza virus (1, 2, 3, and 4), *Mycoplasma pneumonia* and *Chlamydophila pneumoniae* using Luminex® NxTAG Respiratory Pathogen Panel. Luminex NxTAG CoV extended panel was used to test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Statistical analysis

Differences in demographic and clinical characteristics between RSV-positive and RSV-negative infants and between RSV-positive infants by settings (IP, ED, and OP clinic) were evaluated using Pearson's χ^2 test for categorical variables and linear regression with robust standard errors for continuous variables. Statistical tests were based on a significance level (α) of 0.05 (two-sided, where applicable). All analyses were conducted using statistical software Stata/IC 16.0 (StataCorp LLC, College Station, TX).

Results

Study population

Of the 627 infants screened, 475 (76%) were confirmed eligible and of those 360 (76%) were enrolled and tested (IP = 73, ED = 58, OP clinics = 229; Figure 1). Primary reasons for not being able to determine eligibility were language barriers (47%) and missed patients due to multiple appointments scheduled at the same time (24%). Among the 360 infants in the final cohort, 101 (28%) were RSV-positive (RSV A = 80; RSV B = 22), with distribution of RSV cases by setting over time displayed in Figure 2.

Comparison of RSV-positive vs RSV-negative infants

RSV-positive infants had a lower mean age (RSV+, mean: 4.9 months, SD: 3.2 *vs* RSV–, mean: 6.6 months, SD: 3.2, $p < 0.001$) and fewer had an underlying medical conditions (8% *vs* 21%, $p = 0.004$) than RSV-negative infants. Compared to RSV-negative infants, RSV-positive infants were more likely to have LRTI (76% *vs* 39%, $p < 0.001$), be hospitalized (37% *vs* 14%,

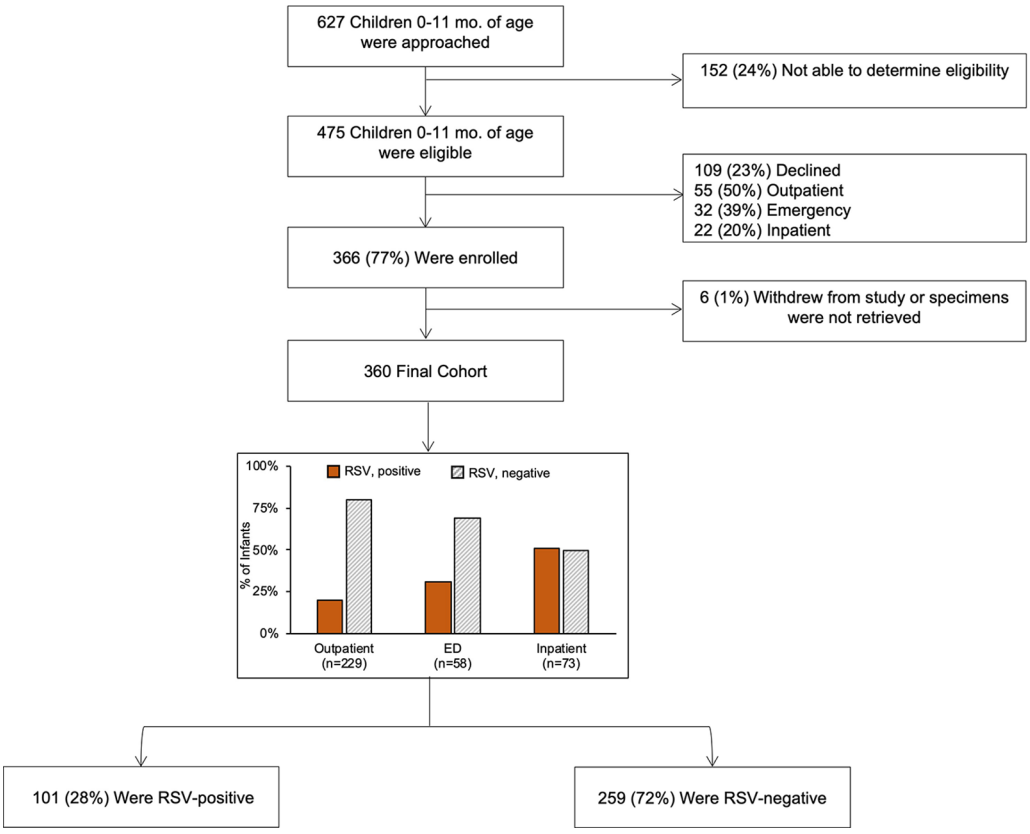

Figure 1. Consort diagram of RSV surveillance study in Davidson County infants, December 2019 through April 2020.

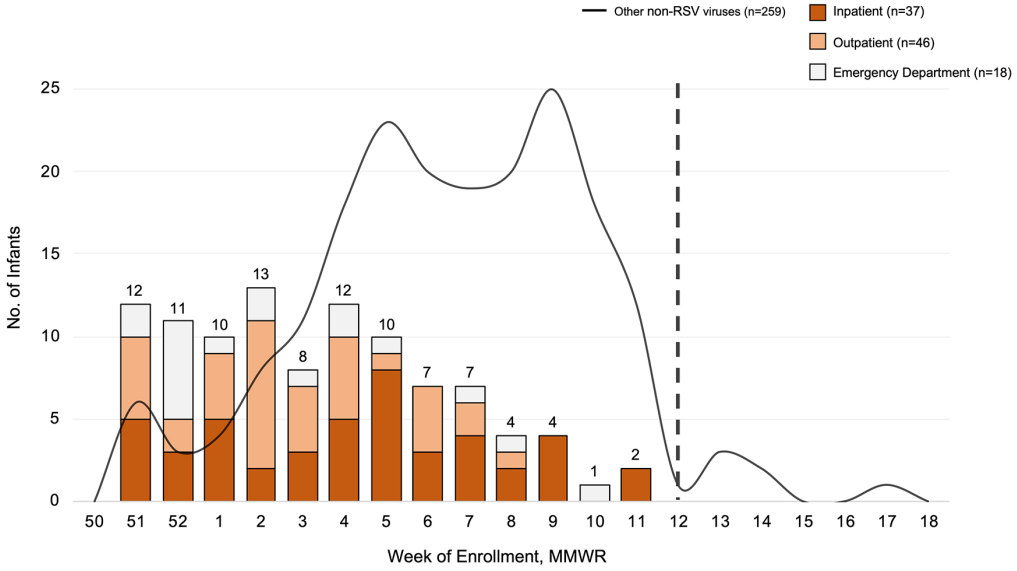

Figure 2. Davidson County infants with RSV compared to other respiratory viruses by MMWR week and setting, December 2019 to April 2020. Our study enrollment period took place from Morbidity and Mortality Weekly Report (MMWR) weeks 50–18 (i.e. 9 December 2019 to 30 April 2020). The dashed line denotes that the MMWR week enrollment was halted in the outpatient settings due to COVID-19.

$p < 0.001$), and require supplemental oxygen (65% *vs* 36%, $p < 0.001$). No infants with RSV were born younger than 29 weeks gestational age, and there were no statistically significant differences of prematurity (<37 weeks) between RSV-positive and RSV-negative infants ($p = 0.496$).

Among RSV-positive infants, those with LRTI were primarily seen in the IP and OP clinics than the ED (IP: 47% and OP: 37% *vs* ED: 17%, respectively, $p < 0.001$), and more often presented with irritability (91% *vs* 71%, $p = 0.013$) than infants without LRTI. No RSV-positive infants received palivizumab; only one 7-month old, born 26 weeks gestational age, who was RSV-negative received palivizumab. Moreover, 90% of infants in our cohort were born at normal birth weight (2500+ grams [RSV-positive: 95%; RSV-negative: 88%]), with 9% born weighing 1500 to <2500 g (RSV-positive: 4%; RSV-negative: 11%), and 1% weighing <1500 g (RSV-positive: 1%; RSV-negative: 1%).

RSV by healthcare setting

Hospitalized infants with RSV were younger (i.e. 0–3 months) and more likely to have LRTI symptoms compared to RSV-positive infants seen in the ED and OP clinics (Table 1). Of note, provider-ordered RSV testing was primarily conducted in the IP setting, as compared to the ED and OP clinic (IP: 73% *vs* ED: 39% and OP: 28%, $p < 0.001$; Table 1). RSV-positive children in the ED had higher proportion of public insurance, secondhand smoke exposure, maternal education with high school, and shorter duration of illness compared to RSV-positive children in the IP and OP settings (Table 1). No differences of antibiotic or bronchodilator prescription/administration practices were observed among RSV-positive infants across healthcare settings. In addition, RSV-positive infants who presented to the OP setting were more likely to present with only upper respiratory symptoms (Figure 3). Infants who presented to the ED or were hospitalized had a higher proportion of shortness of breath than infants in the OP setting.

Spectrum of healthcare encounters

Of the RSV-positive infants, 57% (58/101) had more than one healthcare encounter, and among those, 66% (38/58) were hospitalized at some point during their illness [among those with only one visit: 19% (8/43 were hospitalized), Figure 4)]. In contrast, 13% (41/259) of RSV-negative infants reported more than one healthcare visit for their illness, and among those, 49% (20/41) were hospitalized [among those with only one visit: 11% (25/218) were hospitalized].

Discussion

In our active RSV surveillance study, among 360 infants who sought medical attention at an OP clinic, ED, or IP setting during the 2019–2020 respiratory season with fever and/or respiratory symptoms, nearly one-third were RSV-positive. RSV-positive infants were younger, presented with more severe illness as indicated by higher proportion being hospitalized with LRTI and receiving supplemental oxygen, yet were less likely to have an underlying medical condition compared to RSV-negative infants. In addition, we noted the majority of these children sought more than one healthcare encounter for their illness through our 14-day follow-up survey. Our findings highlight that RSV impacts young healthy children who seek medical attention across all clinical settings, including multiple visits for the same illness. Prevention strategies are essential to reduce illness and the attributed burden in our healthcare systems.

Our study included a follow-up survey to better understand the full spectrum of illness and to document if additional healthcare visits were sought for the same illness. Infants within our study had a median of two healthcare visits for a single RSV infection. Among these healthcare encounters, 45% of infants were hospitalized at least once throughout the course of their illness. Literature evaluating the burden of RSV typically groups healthcare encounters that are within 14 days of each other into the highest level of care.[1,18,19] This methodology is widely practiced, and we followed a similar approach in our initial analyses.[1,18,19] Given that the vast majority of prior surveillance studies are cross-sectional, they potentially underestimate the full illness spectrum of RSV-associated healthcare utilization across clinical settings in the United States.[1,6,18,20–22] For example, in a population-based surveillance study among children under 5 years, 61% of RSV-positive children were hospitalized and 39% were seen in ambulatory care (i.e. EDs, pediatric

Table 1. Sociodemographic and clinical characteristics of infants with respiratory syncytial virus (RSV) by setting, December 2019 through April 2020.

Characteristic	All RSV + (*n* = 101)	Inpatient (*n* = 37)	ED (*n* = 18)	Outpatient (*n* = 46)	*p* value[a]
Age, months – mean (SD)	4.9 (3.2)	3.8 (2.7)	4.5 (3.3)	5.9 (3.2)	**<0.001**
Age, group – *n* (%)					
0–3 months	48 (47)	23 (62)	10 (56)	15 (33)	**0.036**
4–6 months	26 (26)	9 (24)	2 (11)	15 (33)	
7–11 months	27 (27)	5 (14)	6 (33)	16 (35)	
Sex, male – no. (%)	57 (56)	22 (59)	8 (44)	27 (59)	0.526
Race – no. (%)					
White	45 (45)	18 (49)	10 (56)	17 (37)	0.620
Black	29 (29)	9 (24)	5 (28)	15 (33)	
Other	27 (27)	10 (27)	3 (17)	14 (30)	
Insurance – no. (%)					
Private	28 (28)	10 (27)	0	18 (39)	**0.025**
Public	67 (66)	26 (70)	16 (89)	25 (54)	
Self-pay/none	6 (6)	1 (3)	2 (11)	3 (7)	
Ethnicity, Hispanic – no. (%)	31 (31)	15 (41)	7 (40)	9 (20)	0.085
Premature, <37 weeks – no. (%)	12/100 (12)	4 (11)	3 (17)	5/45 (11)	0.797
Underlying medical condition – no. (%)	8 (8)	2 (5)	2 (11)	4 (9)	0.737
Breastfeeding history – no.(%)	84 (83)	32 (86)	14 (78)	38 (83)	0.714
Daycare attendance – no. (%)	29 (29)	9 (24)	3 (17)	17 (37)	0.207
Second-hand smoke exposure – no. (%)	19 (19)	5 (14)	9 (50)	5 (11)	**0.001**
Maternal education – no. (%)					
Less than high school	20 (20)	11 (30)	4 (22)	5 (11)	**0.010**
High school	38 (37)	12 (32)	12 (67)	14 (30)	
2- to 4-year college degree	28 (28)	10 (27)	2 (11)	16 (35)	
Graduate degree	15 (15)	4 (11)	0	11 (24)	
LRTI – no. (%)	77 (76)	36 (97)	13 (72)	28 (61)	**<0.001**
Supplemental oxygen – no. (%)	24 (24)	24 (65)	–	–	–
Illness duration, days – mean (SD)	19 (39)	14 (10)	12 (8)	28 (62)	0.205
Prescription/administration – no. (%)					
Antibiotic	28 (28)	9 (24)	3 (17)	16 (35)	0.293

(Continued)

Table 1. (Continued)

Characteristic	All RSV+ (*n* = 101)	Inpatient (*n* = 37)	ED (*n* = 18)	Outpatient (*n* = 46)	*p* value[a]
Bronchodilator	9 (9)	6 (16)	1 (6)	2 (4)	0.145
Co-detection – no. (%)					
Virus	12 (12)	4 (11)	0	8 (17)	0.149
Bacteria	3 (3)	3 (8)	0	0	0.069
Provider-ordered RSV testing – no. (%)	47 (47)	27 (73)	7 (39)	13 (28)	**<0.001**
Positive	46 (98)	26 (96)	7 (100)	13 (100)	0.685

ED, emergency department; RSV, respiratory syncytial virus; SD, standard deviation.
Definitions: Underlying medical conditions had at least one of the following conditions: asthma/reactive airway disease, atopic/allergic conditions, blood disorders, cancer, cerebral palsy, chronic lung conditions, cystic fibrosis, diabetes, Down's syndrome, eczema, endocrine diseases, food allergies, genetic/metabolic disorders, heart disease, immunocompromised conditions, kidney disease, liver disease, neurological disorders, sickle cell disease/trait, seizure disorder, and/or other.
P values were calculated using linear regression with robust standard errors for continuous variables and Pearson χ^2 test for categorical variables, alpha set at <0.05.
[a]*P* values are across healthcare settings (i.e. inpatient, ED, outpatient). P values <0.05 are bolded.

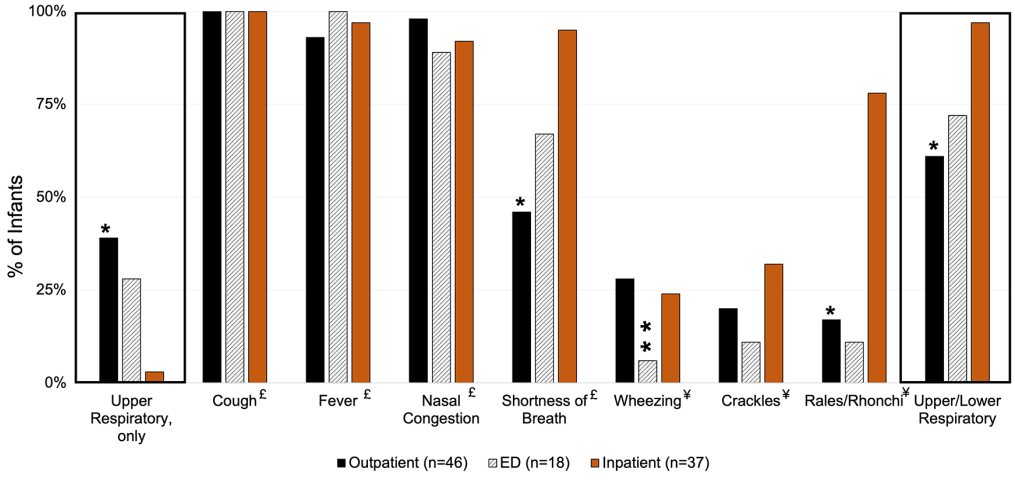

Figure 3. Proportion of Davidson County infants by respiratory syncytial virus by healthcare setting, December 2019 to April 2020. No infant presented with only lower respiratory symptoms.
Definitions: Lower respiratory symptoms: wheezing, crackles, rales/rhonchi, diminished breath sounds, shortness of breath; upper respiratory symptoms: fever, cough, earache, nasal congestion, rhinorrhea, and sore throat.
ED, emergency department.
**p* value < 0.05 for the pairwise comparison between outpatient and inpatient setting.
***p* value < 0.05 for the pairwise comparison between outpatient and emergency department.
£Symptoms collected during parent/guardian interview.
¥Symptoms collected during physical exam.

offices).[1] Owing to the cross-sectional nature of the study design however, the authors were unable to establish whether those hospitalizations required additional OP follow-up visits. Therefore, our approach of following infants until their illness subsided provided an opportunity to define the subsequent visits required. While we show that the majority of RSV visits were in the OP and ED settings, infants hospitalized also required further medical attention in the

	Encounter						
	-3	-2	-1	0	1	2	3
One Encounter							
Outpatient, only (n=25)				OP			
Emergency Department, only (n=10)				ED			
Inpatient, only (n=8)				IP			
Two Encounters							
Inpatient, Outpatient (n=3)			IP	OP			
Outpatient, Inpatient (n=2)			OP	IP			
ED, Outpatient (n=3)				ED	OP		
ED, Inpatient (n=1)			ED	IP			
Inpatient, ED (n=1)			IP	ED			
Inpatient, ED (n=1)				IP	ED		
Inpatient, Inpatient (n=1)			IP	IP			
Outpatient, Outpatient (n=9)				OP	OP		
Outpatient, ED (n=1)			OP	ED			
Outpatient, ED (n=4)				OP	ED		
Outpatient, Urgent Care (n=1)				OP	UC		
Inpatient, Outpatient (n=14)				IP	OP		
Three Encounters							
Outpatient (n=1)				OP	OP	OP	
Inpatient, Outpatient, ED (n=1)				IP	OP	ED	
Inpatient, Outpatient, Urgent Care (n=1)				IP	OP	UC	
Inpatient, Outpatient, Inpatient (n=1)				IP	OP	IP	
Inpatient, Inpatient, Outpatient (n=2)			IP	IP	OP		
Inpatient, Outpatient Outpatient(n=1)				IP	OP	OP	
Outpatient, Inpatient, Outpatient (n=1)			OP	IP	OP		
Outpatient, ED, Inpatient (n=1)		OP	ED	IP			
Outpatient, ED, Inpatient (n=1)				OP	ED	IP	
Outpatient, ED, Outpatient (n=2)			OP	ED	OP		
Four Encounters							
ED, Outpatient, Outpatient, ED (n=1)				ED	OP	OP	ED
Inpatient, Inpatient, Outpatient, Urgent Care (n=1)			IP	IP	OP	UC	
Inpatient, Outpatient, ED, Inpatient (n=1)				IP	OP	ED	IP
Outpatient, Urgent Care, ED, Outpatient (n=1)				OP	UC	ED	OP
Five Encounters							
Inpatient, Outpatient, ED, Inpatient, Outpatient (n=1)			IP	OP	ED	IP	OP

Figure 4. Healthcare encounters associated with the initial respiratory syncytial virus illness. Infants who were enrolled as an inpatient, but first sought medical care through the emergency department on 'encounter 0' were classified as an inpatient. 0 = enrollment visit; 1 to 3 = healthcare encounters after enrollment reported in the follow-up survey; –3 to –1 = healthcare encounters before enrollment reported during the initial interview.
ED, emergency department; IP, inpatient; OP, outpatient; UC, urgent care.

OP settings, thus highlighting the importance of surveillance studies with extended follow-up across multiple settings to understand the burden of a single RSV infection in infants and the healthcare infrastructure. In addition, each subsequent healthcare visit also contributes to additional family and healthcare burden and costs[23,24] and further studies are needed to document the true healthcare resource use and costs attributable to RSV illness.

We also noted RSV patients were younger, more likely to have severe illness, including LRTI symptoms and higher frequency of oxygen use, yet less likely to have underlying medical conditions compared to infants without RSV. These findings are consistent with other studies noting that children with RSV had more severe illness than RSV-negative children.[1,5,6,18,20,21] We also found that provider-ordered RSV testing was minimally performed in the ED and OP clinics, which is consistent with previous studies finding only 3% of RSV illnesses in the OP setting being clinically diagnosed.[1] Thus, if the estimated burden of RSV is dependent on provider-ordered viral testing, the prevalence of RSV in the ED and OP settings will be substantially underrecognized.[1,21,25] Therefore, our study highlights the importance of active, prospective, surveillance in all settings to accurately document the burden of RSV illness and the need for new prevention interventions.

Currently, the only licensed preventive strategy is palivizumab, which is recommended only for high-risk children under 2 years and premature infants <29 weeks gestational age and is not widely available worldwide due to multiple injections and the associated financial burden.[9,10] Prematurity has consistently been identified as a risk factor associated with severe RSV infection;[21,22,26–28] however, in our cohort only 12% of the RSV-positive infants were born earlier than 37 weeks' gestational age. Among the premature RSV-positive infants, we did not identify a difference between healthcare settings but rather found higher proportions of infants younger than 3 months in the IP setting. Notably, none of the RSV-positive infants enrolled in our study were born younger than 29 weeks' gestation and only one infant in our entire cohort received palivizumab. Our findings do not elucidate the impact palivizumab has on preventing RSV infections in high-risk infants but does highlight that the development of additional prophylactic interventions is essential to prevent RSV infections among otherwise healthy, full-term infants.

The strengths of our study include the active, prospective study design, the assessment of RSV across three distinct healthcare settings, and the inclusion of a follow-up period after enrollment to capture the full spectrum of illness. Although our study had several strengths, we also acknowledge its limitations. First, our findings may not be generalizable to other counties or regions outside of Nashville, Tennessee, as our study population was restricted to infants in Davidson County and only evaluated a single IP and ED setting. Second, the number of healthcare encounters for a single illness was captured by a 2-week follow-up survey. Thus, our healthcare encounters potentially are impacted by differential recall bias. We do not, however, believe this largely impacted our study as we had a 91% (329/360) response rate. Third, due to language barriers, we were unable to approach all infants' parents for study enrollment, thus potentially introducing selection bias. Finally, we report 45% of infants had at least one hospitalization during our study period. This high proportion may be explained by a higher RSV circulation compared to prior RSV seasons. Additional population-based studies are needed to establish RSV-attributed healthcare visit rates among infants.

In summary, RSV contributes to substantial burden of healthcare visits, including in the ambulatory care settings. Infants with RSV are more likely to be previously healthy, yet are more likely to present with LRTI symptoms and have more severe illnesses compared to RSV-negative children. Robust surveillance and accessibility to point-of-care testing would potentially assist in defining the true prevalence of RSV across all clinical settings during the respiratory seasons further underscoring the importance of preventive measures for young healthy infants.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board at Vanderbilt University (Ref no. 151683). Written informed consent was obtained from parents or legal guardians prior to enrollment.

Consent for publication
Not Applicable.

Author contributions
Danielle A. Rankin: Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Zaid Haddadin: Conceptualization; Data curation; Methodology; Writing – review & editing.

Loren Lipworth: Conceptualization; Investigation; Project administration; Supervision; Writing – review & editing.

Anna L. Stahl: Data curation; Formal analysis; Validation; Writing – review & editing.

Jon Fryzek: Conceptualization; Methodology; Supervision; Writing – review & editing.

Mina Suh: Conceptualization; Methodology; Supervision; Writing – review & editing.

Donald S. Shepard: Conceptualization; Methodology; Supervision; Writing – review & editing.

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Availability of data and materials
The data that support the findings of this study are available on request from the corresponding author upon reasonable request.

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