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MAJOR ARTICLE

Respiratory Syncytial Virus and All-Cause Bronchiolitis Hospitalizations Among Preterm Infants Using the Pediatric Health Information System (PHIS)

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Background. In 2014, the American Academy of Pediatrics stopped recommending palivizumab to otherwise healthy 29–34 weeks' gestational age (wGA) infants aged <12 months at respiratory syncytial virus (RSV) season start. Here, we compare the burden of RSV hospitalizations (RSVH) and all-cause bronchiolitis hospitalizations (BH) before and after 2014 among otherwise healthy 29–34 wGA infants hospitalized at ≤6 months of age.

Methods. A historical, observational cohort study was conducted to evaluate RSVH and BH in 29–34 wGA infants during the 2010–2017 RSV seasons using encounter data from 51 United States children's hospitals that comprise the Pediatric Health Information System.

Results. The overall cohort included 67 570 RSVH out of 96 281 patients with BH. wGA was known for 22 937 RSVH and 33 289 BH. For 29–34 wGA infants, there were 8.7% and 14.2% RSVH before and after 2014, respectively ($P < .0001$). Intensive care unit admissions increased for RSVH (from 54.5% to 64.2%; $P = .0002$) and BH (from 46.7% to 54.5%; $P = .0005$) after controlling for sex, race, comorbidity, and cluster. The total cost of care increased for RSVH from $37 million to nearly $60 million.

Conclusions. RSVH, BH, and their severity increased among 29–34 wGA infants in the 3 RSV seasons following 2014.

Keywords. respiratory syncytial virus; bronchiolitis hospitalization; infants; epidemiology; palivizumab.

Respiratory syncytial virus (RSV) is a common RNA virus that causes severe respiratory disease and is a significant public health burden in elderly adults, infants, and children. Nearly all children are infected with RSV by 2 years of age [1, 2]. In the United States (US), RSV resulted in 2.1 million children aged <5 years seeking medical attention during the 2002–2004 RSV seasons [3]. RSV commonly causes mild, cold-like symptoms (upper respiratory infections) that resolve within 2 weeks. However, the infection can become severe, particularly in young children and older adults, resulting in acute lower respiratory infections such as acute bronchiolitis and pneumonia [1, 4]. RSV is the leading cause of bronchiolitis and pneumonia among children in the US aged <1 year [1, 4].

The primary treatment for RSV disease is supportive and includes hydration, use of supplemental oxygen if needed, and intubation and mechanical ventilation (MV) [2]. Palivizumab was licensed in 1998 by the US Food and Drug Administration to reduce serious lower respiratory tract infections caused by RSV among high-risk children [5]. Palivizumab is an RSV F-protein inhibitor monoclonal antibody approved for the prevention of severe RSV disease in high-risk populations, including ≤35 weeks' gestational age (wGA) infants, and children aged ≤24 months with chronic lung disease of prematurity (CLDP; formerly known as bronchopulmonary dysplasia [BPD]) or congenital heart disease (CHD) [6]. In 2014, the American Academy of Pediatrics (AAP) updated its recommendations, restricting the use of palivizumab to infants born at <29 wGA aged <12 months at RSV season start, children with CLDP born at <32 wGA requiring >21% oxygen during the first 28 days after birth (for the first 2 years of life if medical support was required in the past 6 months), and children with hemodynamically significant CHD (hs-CHD) aged <12 months at RSV season start [7]. With the updated guidance, the AAP did not recommend the use of palivizumab for otherwise healthy 29–34 wGA infants.

Studies based on insurance claims databases have examined the burden of RSV hospitalizations (RSVH) and bronchiolitis hospitalizations (BH) in 29–34 wGA infants in the US following the 2014 AAP RSV immunoprophylaxis guidance revisions

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[8–10]. It is important to understand how the guidance may influence the burden of RSV disease in different clinical settings. As such, a historical, observational cohort study was conducted to determine and compare the frequencies and characteristics of RSVH and all-cause BH in otherwise healthy US infants hospitalized aged <6 months during the RSV season (November–March) from 2010 to 2017 with particular focus on 29–34 wGA infants. The burden in 29–34 wGA infants was also compared with that of otherwise healthy full-term infants of the same chronological age. The data for this study were obtained from the Pediatric Health Information System (PHIS), a clinical and resource utilization database for patient encounters in pediatric hospitals that are part of the Children's Hospital Association. Hospitals in this network utilize palivizumab in the inpatient setting [11].

METHODS

Study Design and Data Source

A historical, observational cohort study was performed based on the 2019 PHIS database. PHIS hospitals are 51 of the largest and most advanced children's hospitals in the United States, adhering to the most demanding standards of pediatric service [11]. The PHIS database provides clinical and financial details of millions of patient encounters and collects demographic information; *International Classification of Diseases, Ninth Revision* and *Tenth Revision, Clinical Modification* (*ICD-9-CM* and *ICD-10-CM*, respectively) diagnosis and procedure codes; and data on in-hospital mortality, utilized resources that are billed to the patient (eg, imaging, laboratory tests, medications), hospital charges, and total costs. PHIS data have been used in various studies evaluating patient characteristics and resource utilization in the pediatric population [12–15]. This well-established data set is suitable for the objective of this study.

Patient Selection

Patients aged ≤6 months admitted to 1 of the PHIS hospitals from 2010 to 2017 for their first RSVH or BH (RSV or unspecified bronchiolitis) between November and March were included in this study. RSVH was defined by at least 1 diagnosis code of RSV (*ICD-9-CM*: 079.6; *ICD-10-CM*: B97.4), pneumonia due to RSV (*ICD-9-CM*: 480.1; *ICD-10-CM*: J12.1), or acute bronchiolitis due to RSV (*ICD-9-CM*: 466.11; *ICD-10-CM*: J21.0). BH included both RSVH and unspecified BH (Supplementary Table 1). Only the first RSVH or BH for each patient during each RSV season was included in this study.

Additionally, prespecified eligibility criteria were used to exclude the following patients (Figure 1): (1) those aged >6 months at admission due to lower risks for RSVH compared with those aged ≤6 months [16]; (2) patients with noninpatient visits because the study focused on outcomes associated with RSVH and BH; (3) patients with 1 April to 31 October admissions, which fall outside the typical RSV season; (4) patients aged <5 days with admission to the neonatal intensive care unit (NICU) for RSV or all-cause bronchiolitis due to their susceptibility to nosocomial infections, which may be the true underlying condition for the hospitalizations; (5) patients readmitted within 14 days of RSVH and BH because readmission may be for the same illness; and (6) patients readmitted for a different RSV illness after their first RSVH or BH admission during each RSV season. All patient data were de-identified. No patient identifiers were revealed to the study investigators.

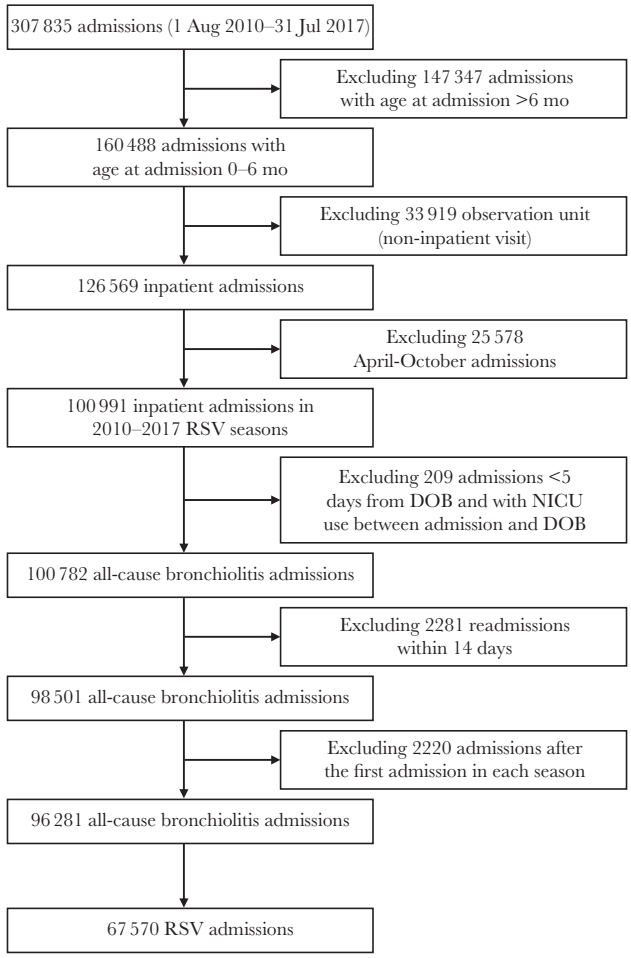

Figure 1. Data flow diagram in the Pediatric Health Information System database (November 2010 through March 2017). Abbreviations: DOB, date of birth; NICU, neonatal intensive care unit; RSV, respiratory syncytial virus.

Baseline Measures

Demographic information was assessed for each eligible patient and included chronological age at admission (0–3 months, 4–6 months) and gestational age (22–28 wGA, 29–34 wGA, 35–36 wGA, and ≥37 wGA) based on *ICD-9-CM* codes 765.21–765.29 and *ICD-10-CM* codes P07.21–P07.26 and P07.31–P07.39 (Supplementary Table 2). Information was also collected on sex, race, and insurance plan type for each patient. In addition, comorbidities were identified from the patient data using

ICD-9-CM and *ICD-10-CM* codes; specifically, chronic respiratory disease arising in the perinatal period and CHD (specified as higher and lower risk by *ICD-9-CM* and *ICD-10-CM*) were evaluated (Supplementary Table 3).

Baseline Measures for Infants Born Between 29 and 34 wGA

For both RSVH and BH in 29–34 wGA infants, data on sex, race, ethnicity, and comorbidities were extracted and stratified according to the RSV seasons before and after 2014 (1 November 2010–31 March 2014, and 1 November 2014–31 March 2017).

Outcome Measures

Outcome measures for this study included duration of hospitalization (length of stay), total days in intensive care, readmission within 14 days, receipt of MV, and adjusted estimated cost. Intensive care unit (ICU) admission was defined by admission to the NICU or pediatric intensive care unit (PICU). If most of the patient's hospital stay was spent in the NICU or PICU, then the total days in the NICU or PICU was used as the length of stay. MV was identified by *ICD-9-CM* procedure codes 96.70, 96.71, or 96.72 and *ICD-10-CM* procedure codes 5A1935Z, 5A1945Z, or 5A1955Z. Additionally, MV use was indicated if a charge was mapped to a Clinical Transaction Classification (CTC) 521166 or 521169. As a unique characteristic of PHIS, CTC was created to map each hospital's charge codes to a common classification system, thereby increasing comparability of charge-level data [17, 18]. Estimated costs were adjusted to the Centers for Medicare and Medicaid Services' wage/price index based on the hospital's location as well as 2017 US dollars.

Outcome Measures for Infants Born Between 29 and 34 wGA

For 29–34 wGA infants, disease severity outcomes were obtained for the RSV seasons before and after the guidance implementation (1 November 2010–31 March 2014, and 1 November 2014–31 March 2017). Data were obtained for readmission, MV use, admission to ICU, length of stay, days in ICU, and adjusted estimated cost and were stratified according to the RSV season.

Statistical Analyses

All statistical analyses were performed in SAS version 9.4 software (SAS Institute). RSVH and BH were described by the patient characteristics (eg, sex, race, age, and insurance type). Descriptive statistics were defined by gestational age and were used to compare the frequency and demographic/clinical characteristics of RSVH and BH and birth characteristics during the typical RSV season before and after 2014.

Categorical variables were presented as the count and percentage of infants in each category; continuous variables were summarized with the median and interquartile range (IQR). Associations between categorical or continuous variables were analyzed using the χ^2 test or Wilcoxon rank-sum test, as appropriate. Logistic regression and quantile regression model adjusted for sex, race, comorbidity, and cluster (hospital) were used to compare the outcomes before and after 2014. Statistical significance was assigned for a P value < .05.

RESULTS

Characteristics of RSVH and BH for the Overall Cohort

Over the 7 RSV seasons studied (2010–2011 through 2016–2017), 307 835 hospitalizations were identified in the PHIS database. Of these, the overall cohort was composed of 96 281 BH; ultimately, 67 570 RSVH were identified (Figure 1). Among 67 570 RSVH, 76.9% of patients were 0–3 months old at the time of admission and 23.1% were 4–6 months old (Table 1). Similarly, for BH, most patients were 0–3 months old at the time of admission. Among the patients hospitalized for RSV, 56.5% were males and 43.5% were females; 59.4% were white

Table 1. Characteristics of Patients With Respiratory Syncytial Virus Hospitalizations and All-Cause Bronchiolitis Hospitalizations in the Pediatric Health Information System Database (November 2010–March 2017)

Characteristic	RSVH	BH
No. of infants	67 570	96 281
Admission age, %		
0–3 mo	76.9	72.5
4–6 mo	23.1	27.5
Sex, %		
Male	56.5	57.8
Female	43.5	42.2
Race, %		
White	59.4	58.0
Black	15.6	16.9
Asian	2.5	2.4
American Indian	0.7	0.7
Pacific Islander	0.5	0.5
Other	15.2	15.6
Unknown	6.2	5.9
Ethnicity, %		
Hispanic	24.4	24.7
Non-Hispanic	65.5	65.5
Unknown	10.1	9.8
Median length of stay (IQR), d	3 (2–6)	3 (2–5)
Readmission in 14 d, %	1.8	2.1
RSV season, %		
Nov 2010–Mar 2011	15.8	14.7
Nov 2011–Mar 2012	11.8	12.2
Nov 2012–Mar 2013	17.3	16.1
Nov 2013–Mar 2014	12.2	12.2
Nov 2014–Mar 2015	15.2	15.3
Nov 2015–Mar 2016	13.2	14.1
Nov 2016–Mar 2017	14.6	15.4
MV use, %	13.8	11.8
Median adjusted estimated cost (IQR), USD	$6,480 ($3,606–$13,556)	$5,943 ($3,371–$12,072)
Median total No. of days in intensive care (IQR)	4 (2–7)	4 (2–7)

Abbreviations: BH, bronchiolitis hospitalizations; IQR, interquartile range; MV, mechanical ventilation; RSVH, respiratory syncytial virus hospitalizations; USD, US dollars.

and 24.4% were Hispanic. Similar trends in sex, race, and ethnicity were observed for BH (greater proportions of males than females and whites than other races and decreased proportion of Hispanics compared with non-Hispanics).

The median length of stay for RSVH was 3 days (IQR, 2–6 days), and readmission within 14 days occurred in 1.8% of cases. Of all RSVH observed across the 7 RSV seasons, the proportion of RSVH was lowest (11.8%) in the 2011–2012 season. MV use occurred in 13.8% of RSVH. The median adjusted billed charges for RSVH were $6480 (IQR, $3606–$13556). The median total number of days in ICU was 4 (IQR, 2–7 days) (Table 1).

Characteristics of RSVH and BH by wGA

Over 7 RSV seasons, there were 22 937 RSVH and 33 289 BH with known wGA (Table 2). Infants born at 29–34 wGA represented 2585 RSVH. The proportion of RSVH increased after 2014 across all wGA groups, except for term infants (≥37 wGA) (Table 2). For 29–34 wGA infants, proportions of hospitalizations increased dramatically (almost 2-fold), transitioning from the 2013–2014 RSV season to the 2014–2015 RSV season and onward (Figure 2). Notably, the proportion of RSVH significantly increased ($P < .001$) for 29–34 wGA infants after 2014 (from 8.7% to 14.2%). A similar pattern was seen for BH (Table 2).

Demographic Characteristics of 29–34 wGA Infants Before and After 2014

The demographic characteristics of 29–34 wGA infants who were hospitalized for RSV and all-cause bronchiolitis were assessed before and after the guidance implementation (Supplementary Table 4).

More white infants (>50%) were hospitalized with RSV than any other racial group regardless of the period analyzed. The proportion of RSVH among white and black infants increased after 2014, whereas the proportion of RSVH among infants of other races and unknown race decreased ($P = .006$). The proportion of RSVH among Hispanic infants decreased slightly after 2014 (25.2% before and 23.9% after), whereas the proportion of RSVH among non-Hispanic infants increased (64.1% before and 70.1% after). Comorbidities were observed for 13% and 16% of RSVH before and after the guidance implementation, respectively. However, this change was not statistically significant. Similar findings were observed for BH.

Clinical Characteristics of 29–34 wGA Infants Before and After 2014

Readmission for RSVH did not significantly change after 2014 (2.6% of infants readmitted before and 2.4% readmitted after; $P = .708$, adjusted model) (Table 3). Likewise, readmission did not significantly change for BH (3.6% before and 3.4% after; $P = .795$, adjusted model). Use of MV among 29–34 wGA infants remained high before and after the guidance implementation, and no statistically significant differences in the proportions were detected (30.2% vs 31.8% for RSVH; $P = .572$, adjusted model). MV use associated with BH also remained high (24.4% and 26.4%), but proportions before and after 2014 did not differ significantly ($P = .247$, adjusted model).

The proportion of patients with an ICU admission increased significantly for patients with RSVH (from 54.5% to 64.2%; $P = .0002$, adjusted model) and for patients with BH (from 46.7% to 54.5%; $P = .0005$, adjusted model) after 2014. However, the median number of days in ICU did not increase

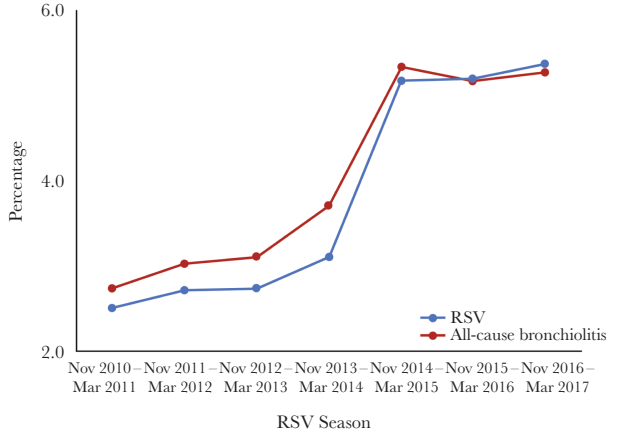

Figure 2. Proportions of hospitalizations among 29–34 weeks' gestational age infants by respiratory syncytial virus season in the Pediatric Health Information System database (November 2010 through March 2017). Abbreviation: RSV, respiratory syncytial virus.

Table 2. Proportion of Respiratory Syncytial Virus Hospitalizations and All-Cause Bronchiolitis Hospitalizations in the Pediatric Health Information System Database (November 2010–March 2017)

	RSVH					BH				
	1 Nov 2010–31 Mar 2014		1 Nov 2014–31 Mar 2017			1 Nov 2010–31 Mar 2014		1 Nov 2014–31 Mar 2017		
wGA Category	No.	(%)	No.	(%)	*P* Value	No.	(%)	No.	(%)	*P* Value
22–28 wGA	233	(1.9)	243	(2.3)	.052	505	(3.0)	591	(3.6)	.001
29–34 wGA	1061	(8.7)	1524	(14.2)	<.0001	1661	(9.8)	2270	(13.9)	<.0001
35–36 wGA	1692	(13.8)	1503	(14.0)	.624	2283	(13.4)	2201	(13.5)	.785
≥37 wGA	9253	(75.6)	7428	(69.4)	<.0001	12 563	(73.8)	11 215	(68.9)	<.0001
All	12 239	(100.0)	10 698	(100.0)		17 012	(100.0)	16 277	(100.0)	

Abbreviations: BH, bronchiolitis hospitalizations; RSVH, respiratory syncytial virus hospitalizations; wGA, weeks' gestational age.

Table 3. Comparison of Disease Severity for 29–34 Weeks' Gestational Age Infants With Respiratory Syncytial Virus Hospitalizations and All-Cause Bronchiolitis Hospitalizations in the Pediatric Health Information System Database Before and After the 2014 American Academy of Pediatrics Guidance Change for Palivizumab

Characteristic	RSVH				BH			
	1 Nov 2010–31 Mar 2014	1 Nov 2014–31 Mar 2017	*P* Value[a]	*P* Value[b]	1 Nov 2010–31 Mar 2014	1 Nov 2014–31 Mar 2017	*P* Value[a]	*P* Value[b]
Readmission, No. (%)	28 (2.6)	37 (2.4)	.736	.708	59 (3.6)	77 (3.4)	.786	.795
MV use[c], No. (%)	320 (30.2)	484 (31.8)	.388	.572	405 (24.4)	600 (26.4)	.146	.247
Intensive care, No. (%)	578 (54.5)	979 (64.2)	<.0001	.0002	775 (46.7)	1237 (54.5)	<.0001	.0005
Length of stay, d, median (IQR)	6 (3–11)	7 (3–12)	.047	1	5 (2–10)	5 (3–10)	.008	1
Days in intensive care, median (IQR)	6 (3–11)	6 (3–12)	.462	1	6 (3–10)	6 (3–11)	.383	1
Adjusted estimated cost[d], USD, median (IQR)	$14077 ($6047–$33312)	$16057 ($6601–$35272)	.038	.255	$10688 ($4963–$28048)	$12486 ($5234–$29731)	.058	.241
Adjusted total cost[d], USD	$37 090 388	$59 891 980			$52 077 003	$76 827 621		

Abbreviations: BH, bronchiolitis hospitalizations; IQR, interquartile range; MV, mechanical ventilation; RSVH, respiratory syncytial virus hospitalizations; USD, United States dollars.

[a]Unadjusted was recorded during their visit.

[b]Adjusted by sex, race, comorbidity, and cluster (hospital).

[c]A patient received mechanical ventilation if *International Classification of Diseases (ICD), Ninth Revision* procedure code of 96.70, 96.71, or 96.72; *ICD, Tenth Revision* procedure code of 5A1935Z, 5A19945Z, or 5A1955Z; or a charge mapped to Clinical Transaction Classification code 521166 or 521169.

[d]The charges were adjusted to the Centers for Medicare and Medicaid Services wage/price index based on the hospital's location as well as 2017 USD.

significantly after the guidance change for either RSVH or BH (median, 6 days before and after; adjusted $P = 1.000$). Similarly, the overall length of hospitalization stay did not change for either RSV or all-cause bronchiolitis after 2014. Although the median adjusted estimated cost for RSVH ($14 077 before and $16 058 after; $P = .255$, adjusted model) and BH ($10 688 before and $12 486 after; $P = .241$, adjusted model) did not change significantly after 2014, the total adjusted estimated cost of care in PHIS hospitals dramatically increased for RSVH (from $37 million to nearly $60 million) and BH ($52 million to $77 million).

DISCUSSION

This study evaluated the impact of the updated 2014 AAP RSV immunoprophylaxis policy recommendations on RSVH and BH and their severity among 29–34 wGA otherwise healthy infants using the comprehensive PHIS database. We observed that infants hospitalized for RSV in the PHIS database across 7 RSV seasons (2010–2011 through 2016–2017) were mostly aged 0–3 months at the time of admission, that is, 77% of RSVH. This is consistent with the findings of other RSVH studies [16, 19–22]. One study of the OUTSMART-RSV surveillance program during the 2016–2017 winter viral season in the US reported that 46.7% of the inpatient sample consisted of children aged <1 year [23]. The recent modeling tool developed by the Centers for Disease Control and Prevention showed the potential impact of multiple immunization products on medically attended RSV infections in infants [24]. These results affirm that infants are susceptible to RSV disease in their first few months of life, and interventions for RSV should be a strategic priority for children aged <1 year.

Recent evidence based on other large databases (Truven Health MarketScan and Optum Research claims data) have reported a significant increase in RSVH risk among 29–34 wGA infants relative to term infants in RSV seasons after 2014 vs before [8–10]. Krilov et al showed that RSVH and BH severity was higher in 2014–2017 vs 2011–2014 among 29–34 wGA infants, especially those aged <3 months [10]. However, these studies are limited due to a large proportion of children aged <1 year with missing information on date of birth or who were enrolled short-term [25]. Consistent with these studies, the current analyses demonstrate that RSVH increased significantly among 29–34 wGA infants after the 2014 AAP guidance revisions, offering evidence that the guidance change affected the burden of RSV disease in different settings. Differences in RSV disease severity were also observed to be significant in this wGA category with increases in the percentage of patients admitted to ICU, median length of stay, and median adjusted estimated cost. In the adjusted model that included sex, race, comorbidity, and cluster (hospital), only the change in the percentage of patients admitted to ICU was found to be statistically significantly greater. The significant increase in ICU admissions for RSVH and BH is a notable finding confirming the impact of

decreased palivizumab use in 29–34 wGA infants. The results are consistent with a recently published retrospective claims analysis that reported an association between decreased outpatient palivizumab use and increased ICU admissions after the 2014 AAP guidance change among 29–34 wGA infants aged <6 months [10].

Statistically significant differences in the median length of stay and median adjusted cost were not observed. Nevertheless, the significant increases in the proportions of hospitalizations among 29–34 wGA infants after 2014 (nearly 2-fold) dramatically increased the total cost associated with RSVH in the PHIS system from $37 million to nearly $60 million. A recent study assessed healthcare utilization and costs in the 12 months subsequent to RSVH or unspecified bronchiolitis hospitalization among infants identified in the Truven Health MarketScan Medicaid and commercial databases [26]. The study investigators reported that both early- and late-preterm infants had higher costs than term infants, following RSVH or unspecified bronchiolitis hospitalization. In the commercially insured population, incremental follow-up costs after discharge from RSVH ranged from $1403 for healthy term infants up to $37 417 for infants born at <29 wGA. The true costs associated with RSVH and BH for 29–34 wGA infants are expected to be greater than the costs observed in the current study.

It is possible that comorbidities such as CHD and chronic respiratory disease arising in the perinatal period among 29–34 wGA infants affected the length of stay and adjusted estimated cost for RSVH. Studies have documented that BPD/CLDP and hs-CHD significantly affect RSVH and associated disease severity [20, 27–29]. In the current study, the comorbidities of CHD and CLDP were combined and reported in 13.1% and 15.7% of RSVH before and after the guidance change, respectively. Perhaps in future investigations, each comorbid condition should be considered individually and not under the broad grouping of CHD and CLDP if the sample size allows for finer granularity.

The overall cohort included 67 570 RSVH, of which wGA was known for 22 937 patients. Infants with missing wGA coding were not included in the analyses. In the PHIS database, missing wGA coding was more likely among infants aged 4–6 months, whites, and non-Hispanics. Bias may have resulted if older, white infants were more likely to become infected with RSV. However, this is not the case, as the scientific literature suggests that younger, nonwhite children are more likely to develop an RSV illness.

The strengths of this study include the large study size, design (stratification across different wGA categories), and the multiple-hospital approach based on data from the robust PHIS database. Moreover, infants were not selected based on their disease status and outcome status, and participation selection was not biased toward including only patients with the most severe RSV outcomes. All infants who met the eligibility criteria were included, indicating minimal selection bias.

There are some limitations to note for the current study. First, the population was limited only to those infants hospitalized in PHIS-affiliated children's hospitals and who had sufficient data to be included in this study. The PHIS data set has not been designed to be a representative sample of all children's hospitals and cannot be used to generate national estimates for the United States. This is observed by 60% of patients hospitalized for RSV being identified as white in the race category, but in the US, the Census Bureau reported that more than 50% of infants aged <1 year were minorities as of 1 July 2011 [30]. Second, this study may have underestimated or overestimated severe RSV disease because of reliance on the diagnosis codes for RSV disease and all-cause bronchiolitis. The results of diagnostic testing were not recorded in the PHIS data set. An *ICD* code for RSV only indicates that an RSV test was performed and not the results of that test. Hence, it is possible that a large number of patients hospitalized for all-cause bronchiolitis should have been specified as RSVH. Because RSV testing is not consistent and cases are often missed, the true prevalence of RSVH is likely to be underestimated; case ascertainment for RSV is passive [27, 31]. Third, evaluation was limited to the inpatient setting. This may also underestimate the true burden of RSV disease because many moderately severe RSV cases are managed in the emergency department or outpatient settings and may not be coded as RSV diagnosis [3, 4]. Fourth, a large proportion of infants in the PHIS database did not have a wGA recorded. This may have biased our results, as specific categories of wGA were more likely to be missing than other categories, especially if they were also related to time period of episode. However, only about 10% of births in the US are classified as premature and it is likely that those with missing wGA data were full-term infants, thereby minimizing the likelihood of bias [32]. In addition, preterm and full-term as measured by wGA were identified through the presence of *ICD-9-CM* or *ICD-10-CM* diagnosis codes; it is possible that misclassification of wGA may have occurred.

Notably, the first RSV season after the AAP's revised recommendations in 2014 may have included delays in the adoption of the new guidance by hospitals. Quantifying the extent of this phenomenon is outside the scope of this study owing to the data limitations within the PHIS database. With the updated policy recommendations, outpatient use of palivizumab was expected to drop significantly in the 2014–2015 RSV season. Conversely, slower uptake of the 2014 AAP revised recommendations in hospitals could have also affected disease severity and RSVH and BH. However, the PHIS database does not contain any data on outpatient palivizumab use. The extent of palivizumab's coverage among predischarge inpatients across RSV seasons will need to be explored in additional investigations once the data become available.

In conclusion, our analyses show that 29–34 wGA infants experienced a higher proportion of hospitalization due to respiratory illness after 2014. Continued and systematic evaluations of RSVH/BH of the PHIS data set are needed to further examine how revisions to the AAP RSV immunoprophylaxis guidance affect RSV disease severity and healthcare utilization for 29–34 wGA infants.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Author contributions. J. F., T. G., and J. P. F. contributed to the design and execution of the historical, observational cohort study, including data collection and organization. X. J. performed the statistical analysis of the data. J. F., T. G., J. P. F., and M. S. assisted in analyzing and interpreting the data. M. S. developed the first draft of the manuscript, and J. P. F., X. J., J. F., and T. G. made significant contributions to the final version of the manuscript.

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Potential conflicts of interest. J. F. has received grant/research support from AstraZeneca/MedImmune and is a member of the AstraZeneca and Sobi speaker's bureaus. M. S., X. J., and J. P. F. are employees of EpidStrategies. T. G. is an employee of Sobi, Inc. EpidStrategies received funding from AstraZeneca and Sobi, Inc for this research.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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