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Hospitalization Outcomes of Full-Term and Premature Children Aged Less Than 2 Years Hospitalized With RSV

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Abstract

BACKGROUND: Prematurity may place young children at increased risk for severe respiratory syncytial virus (RSV) disease because of differences in lung development. We describe characteristics of children aged less than 2 years hospitalized with RSV by prematurity and bronchopulmonary dysplasia (BPD) status and examine both as risk factors for severe in-hospital outcomes.

METHODS: During 2016–2023, population-based surveillance was conducted at 7 medical centers for hospitalizations with RSV-associated acute respiratory illness in children. Poisson regression with robust variance was used to estimate adjusted relative risks (aRRs) of prolonged hospitalization (≥3 days), intensive care unit (ICU) admission, and assisted ventilation by age in children with prematurity without and with BPD compared with term children after adjustment for surveillance site and palivizumab receipt.

RESULTS: Among 5844 children, 4626 (79.2%) were term and 1218 (20.8%) were premature, including 1138 (93.4%) without BPD and 80 (6.6%) with BPD. Compared with term children, all premature children had greater risks for prolonged hospitalization (aRR = 1.3; 95% CI, 1.2–1.5), ICU admission (aRR = 1.4; 95% CI, 1.2–1.6), and assisted ventilation (aRR = 2.0; 95% CI, 1.4–2.8) at chronological age less than 6 months. Premature children with BPD also had greater risk for prolonged hospitalization at all ages through 23 months.

CONCLUSIONS: Premature children accounted for 1 in 5 hospitalizations among children aged less than 2 years hospitalized with RSV. Compared with term children, all premature children had increased risk for severe in-hospital outcomes in early infancy, and those with BPD remained at increased risk of prolonged hospitalization through age 23 months.

INTRODUCTION

Respiratory syncytial virus (RSV) is a major cause of hospitalization in children globally, resulting in an estimated 3.6 million RSV-associated lower respiratory tract infection hospitalizations per year among children.[1] One-quarter of global RSV-associated hospitalizations among infants are estimated to occur among infants born prematurely (defined as birth at <37 gestational weeks),[2] whereas the global prevalence of preterm birth is approximately 10%.[3] In the United States, RSV is the leading cause of hospitalization in infants.[4,5]

Prematurity places young children at increased risk for severe outcomes from acute respiratory illnesses (ARIs) compared with term children because of differences in lung

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development resulting in smaller airways and reduced lung volumes. Prior studies have identified prematurity as a risk factor for RSV infection and RSV-associated hospitalization with some studies demonstrating varying risk by gestational age and by chronological age among children with prematurity.[2,6] Some studies have also found that certain underlying conditions that are more prevalent at lower gestational ages, such as bronchopulmonary dysplasia (BPD) and hemodynamically significant congenital heart disease, may confer a greater risk of severe outcomes from ARI than prematurity alone.[2,7,8] However, few studies have examined in-hospital outcomes among premature children hospitalized with RSV or the association between prematurity and risk of severe in-hospital outcomes. Using data from 2016 to 2023, we describe demographic and clinical characteristics of children aged less than 2 years hospitalized with RSV by prematurity status, compare the risk of severe in-hospital outcomes among premature vs term children by chronological age, and examine whether the risk for severe in-hospital outcomes differs among premature children with BPD.

METHODS

New Vaccine Surveillance Network Study Design and Data Collection

The New Vaccine Surveillance Network (NVSN) is a population-based, prospective surveillance platform for ARI in children aged less than 18 years.[9,10] The network includes 7 pediatric medical centers in the United States: Cincinnati Children's Hospital Medical Center (Cincinnati, Ohio), Texas Children's Hospital (Houston, Texas), Children's Mercy Hospital (Kansas City, Missouri), Monroe Carell Jr. Children's Hospital at Vanderbilt (Nashville, Tennessee), UPMC Children's Hospital of Pittsburgh (Pittsburgh, Pennsylvania), UR-Medicine Golisano Children's Hospital (Rochester, New York), and Seattle Children's Hospital (Seattle, Washington). These counties represent 4.5% of the United States' pediatric population.

Children were eligible for enrollment if they had an illness duration of less than 14 days, were enrolled within 48 hours of hospitalization, had at least 1 qualifying ARI sign or symptom (eg, cough, fever, nasal congestion, or wheezing), or apparent life-threatening event or brief resolved unexplained event. Children were excluded if they had a known nonrespiratory cause for hospitalization, had fever and neutropenia from chemotherapy, were admitted less than 5 days after a prior hospitalization, were transferred from another hospital within more than 48 hours of hospitalization, were a newborn who had never been discharged from the hospital, or were previously enrolled in the NVSN in the preceding 14 days.

Demographic and clinical data, including prematurity status, gestational age at birth, underlying conditions, and parent-reported race and ethnicity were systematically collected through parent/guardian interviews and medical record abstraction; underlying conditions were abstracted from clinical notes in patients' medical records. As available, palivizumab receipt was verified from inpatient medical records or state immunization information systems or, if necessary, by reviewing primary health care provider records.

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All enrolled children had midturbinate nasal swabs or throat swabs collected and tested for RSV by real-time reverse transcription polymerase chain reaction in laboratories that support the NVSN.[11] For patients from whom specimens could not be obtained for this surveillance activity, clinically obtained respiratory specimens were salvaged for surveillance testing.

Children were included in this analysis if they were younger than age 2 years and were hospitalized with RSV confirmed by surveillance or clinical testing in a surveillance hospital from December 1, 2016, to July 31, 2023. Children were excluded from this analysis if data were not available on gestational age at birth.

Study Definitions and Statistical Analysis

Prematurity was defined as birth at less than 37 weeks gestation. Prematurity subgroups were defined according to established criteria as extremely preterm (22 to <28 weeks), very preterm (28 to <32 weeks), and moderate to late preterm (32 to <37 weeks).[3] The moderate and late preterm subgroups were initially assessed separately and then aggregated for final analyses because the results for the 2 subgroups were similar. Underlying conditions of interest identified a priori included congenital heart disease, Down syndrome, BPD, and chronic lung disease other than BPD. BPD was defined as chronic lung disease of prematurity or chronic obstructive lung disease (eg, BPD or bronchiolitis obliterans). Congenital heart disease was defined as any of the following: septal defects; abnormalities of the aortic arch; hypoplastic left heart syndrome; pulmonary atresia, tricuspid atresia, or tetralogy of Fallot; transposition of the great arteries; other abnormalities of heart valves; dextrocardia; double outlet right ventricle; or other congenital cardiac malformations. Isolated patent ductus arteriosus or patent foramen ovale was not included in the definition of congenital heart disease.

Demographic characteristics, underlying conditions of interest, and palivizumab receipt among children hospitalized with RSV-associated ARI were summarized with descriptive statistics and compared by prematurity status (born premature vs term) and by prematurity subgroups (vs term) using the chi-square test or Fisher exact test for categorical variables and the Mann-Whitney U test for median age. Testing was 2-sided and conducted at the 5% level of significance. Race and ethnicity categories were selected based on the Office of Management and Budget Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity. Data on race and ethnicity were collected by the NVSN to characterize the representativeness of the analytic population and allow for evaluation of disparities in care or health outcomes.

Poisson regression with robust variance was used to estimate adjusted relative risks (aRRs) and 95% CIs. The aRRs of severe in-hospital outcomes were estimated by prematurity status for all age groups combined and by chronological age and prematurity subgroups using term children as the referent group. Separate models also compared risks in premature children without or with BPD compared with term children; term children with BPD were excluded from these analyses. Models were adjusted for surveillance site, palivizumab receipt, chronological age group (all age analyses only), and underlying conditions of interest as a composite variable (excluding in BPD models). Severe in-hospital outcomes included (1) prolonged hospitalization at least 3 days (defined based on a median length

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of hospitalization of 2 days; IQR, 1–4 days), (2) intensive care unit (ICU) admission, and (3) assisted ventilation, defined as intubation or noninvasive ventilation with continuous positive airway pressure or bilevel positive airway pressure. SAS software version 9.4 (SAS Institute, Cary, NC) was used for data analysis, Microsoft Excel and RStudio Desktop version 2024.04.1+738 were used for figures.

Ethics Statement

A parent or guardian provided informed consent before the child's enrollment. NVSN activities during 2016–2022 were reviewed and approved by the institutional review boards at the US Centers for Disease Control and Prevention (CDC) and each participating site (45 CFR part 46 and 21 CFR part 56). NVSN activities during 2023 were reviewed by the CDC, deemed not research, and were conducted consistent with applicable federal law and CDC policy (45 CFR part 46.102(l)(2) and 21 CFR part 56; 42 USC §241(d); 5 USC §552a; and 44 USC §3501 et seq).

RESULTS

Baseline Characteristics of Enrolled Children

Overall, 5844 children aged less than 2 years hospitalized with RSV were enrolled, of whom 1218 (20.8%) were premature and 4626 (79.2%) were born at term (Table 1; Supplemental Figure 1). Among all enrolled children, the median age was 4 months (IQR, 2–11 months); 3256 (55.7%) were aged less than 6 months, and 3304 (56.5%) were male. Overall, 285 of 5844 (4.9%) children had an underlying condition of interest, including 195 (3.3%) with congenital heart disease, 82 (1.4%) with BPD and 43 (0.7%) with Down syndrome, and 5 (<0.1%) with other chronic lung disease.

Compared with children born at term, those with prematurity were older (median age 6 vs 4 months, $P < .001$); similarly, a higher proportion of premature children were aged 12–23 months (27.3% vs 21.1%) (Table 1). Premature children accounted for an increasing proportion of hospitalized children with RSV as chronological age at hospitalization increased from 8.8% of children aged less than 1 month to 30.1% of children aged 23 months (Figure 1). Similarly, children in more severe prematurity subgroups accounted for a larger proportion of hospitalized premature children and all hospitalized children as chronological age at hospitalization increased.

A larger proportion of children with prematurity had congenital heart disease (6.3% vs 2.6%, $P = .08$) or BPD (6.6% vs <0.1%, $P < .001$) compared with children born at term, although results did not reach statistical significance for congenital heart disease. Small proportions of term and premature children had Down syndrome (1.1% vs 0.6%, $P = .10$) and other chronic lung conditions (0.1% vs 0.2%, $P = .30$). Among premature children hospitalized with RSV, congenital heart disease, BPD, and other chronic lung conditions were more frequent among children in more severe prematurity subgroups than in children with moderate to late prematurity. For example, 13.4% of extremely premature children had congenital heart disease compared with 5.1% of children with moderate/late prematurity (Supplemental Table 1). Similarly, 50.4% of extremely premature children had BPD compared with <1%

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of children with moderate/late prematurity. Premature children with BPD made up an increasing proportion of children hospitalized with RSV with increasing chronological age at hospitalization (from 0% of children aged <1 month to 4.8% of children aged 23 months) (Figure 2).

Risk of Severe In-Hospital Outcomes

Premature children hospitalized with RSV had a significantly higher risk of prolonged hospitalization (aRR, 1.3; 95% CI, 1.2–1.4), ICU admission (aRR, 1.2; 95% CI, 1.1–1.4), and assisted ventilation (aRR, 1.8; 95% CI, 1.3–2.4) compared with term children (Figure 3); there were no in-hospital deaths among premature or term children. Risks for each outcome were also largely increased across prematurity subgroups compared with children born at term (Supplemental Figure 2 and Supplemental Table 2). When risks were examined by chronological age at hospitalization, premature children had a higher risk of prolonged hospitalization (aRR, 1.3; 95% CI, 1.2–1.5), ICU admission (aRR, 1.4; 95% CI, 1.2–1.6), and assisted ventilation (aRR, 2.0; 95% CI, 1.4–2.8) than children born at term at younger than age 6 months, but not at ages 6–11 months or 12–23 months, with the exception of risk for prolonged hospitalization, which was also increased among children aged 12–23 months (Figure 3; Supplemental Table 3).

Among all children aged less than 2 years, premature children without BPD had significantly greater risks of prolonged hospitalization (aRR, 1.3; 95% CI, 1.2–1.4), ICU admission (aRR, 1.2; 95% CI, 1.1–1.4), and assisted ventilation (aRR, 1.7; 95% CI, 1.3–2.3) compared with term children (Figure 3 and Supplemental Table 4). However, when risks were examined by chronological age at hospitalization, premature children without BPD had greater risks for prolonged hospitalization and ICU admission at age less than 6 months (aRR, 1.3; 95% CI, 1.2–1.5; aRR, 1.4; 95% CI, –1.6, respectively) when compared with term children, but the risks for both outcomes were largely similar for children aged at least 6 months.

Among all children aged less than 2 years, premature children with BPD also had greater risks of prolonged hospitalization (aRR, 2.0; 95% CI, 1.7–2.4) and ICU admission (aRR, 1.7; 95% CI, 1.2–2.3). When risks were stratified by chronological age at hospitalization, premature children with BPD had increased risk for prolonged hospitalization across all age groups (<6 months: 1.8, 95% CI, 1.1–3.1; 6–11 months: 1.7, 95% CI, 1.3–2.3; 12–23 months: 2.1, 95% CI, 1.6–2.6) (Figure 3).

DISCUSSION

In this multicenter analysis of more than 5000 children aged less than 2 years hospitalized with RSV-associated ARI, children born prematurely accounted for 1 in 5 hospitalizations. By comparison, approximately 1 in 10 children in the United States are born prematurely.[12] Premature children, particularly those born at earlier gestational ages and those with BPD, accounted for an increasing proportion of all RSV-associated hospitalizations as chronologic age at hospitalization increased. All premature children (with and without BPD) had higher risks of prolonged hospitalization, critical illness, and assisted ventilation when hospitalized at age less than 6 months. Those with BPD continued to be at increased risk for prolonged

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hospitalization through age 23 months, as observed in other studies.[13] Collectively, these findings document the disproportionate burden of RSV-associated hospitalizations and related complications in premature children and the importance of BPD as a risk factor for severe disease outcomes beyond infancy.

Prior studies, including published reports from the NVSN,[14,15] found that premature children born at less than 29 weeks gestation are at increased risk of RSV-associated hospitalization compared with term infants. However, findings in premature children born at greater than or equal to 29 weeks have been mixed.[13,16,17] Most US studies examining prematurity as a risk factor for severe RSV disease were conducted more than a decade ago and were retrospective analyses of medical claims or electronic health record data that may be subject to ascertainment biases from inconsistent clinical testing for RSV.[16] Fewer US studies have examined the association between prematurity and severe in-hospital outcomes once children are hospitalized with RSV. This analysis expands on prior studies[13–17] by providing evidence from more recent seasons that premature children continue to account for a large fraction of RSV-associated hospitalizations in children aged less than 2 years. Additionally, this study documents that premature children, including those born at greater than or equal to 29 weeks, are at increased risk of severe in-hospital outcomes at age less than 6 months irrespective of BPD status and that prematurity with BPD remains a risk factor for some outcomes through at least age 23 months.

BPD is one of the most common complications of premature birth and occurs with increasing frequency at younger gestational ages and lower birth weights.[18] A recent meta-analysis found that RSV-associated hospitalization rates were approximately 20 times higher in children with BPD than in those without BPD at age less than 5 years. The same analysis also found that children with BPD hospitalized with RSV had a higher likelihood of ICU admission, oxygen supplementation, assisted ventilation, and in-hospital death, although results related to in-hospital outcomes were based on a small number of studies.[19] Children with BPD who are hospitalized with critical illness from respiratory tract infections also have higher risks of long-term sequelae, such as reductions in lung function. Our findings corroborate prior reports[19] that BPD increases the risk for severe outcomes among children hospitalized with RSV and underscore the importance of RSV prevention with nirsevimab for premature children with BPD who are entering their second RSV season, as is currently recommended in the United States.[20]

From 2014 through June 2023, the American Academy of Pediatrics stated that palivizumab, the only available RSV prevention product, could be considered for premature infants born at <29 weeks gestation in their first RSV season and children with BPD requiring medical support in their second season. In 2023, maternal RSV vaccine and nirsevimab were approved and recommended to protect all US infants aged less than 8 months entering or born during their first RSV season, including premature infants born at any gestational age, and clesrovimab was approved and recommended in 2025 as an additional option to protect all infants in this age group. Nirsevimab is also recommended to protect certain children aged 8–19 months in their second season, including children with BPD.[20] Maternal RSV vaccine, nirsevimab, and clesrovimab all reduce the risk of severe RSV disease in infants,[20–24] and nirsevimab efficacy has been evaluated in prelicensure trials specifically in moderate

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to late premature infants.[25] In this analysis, findings that premature children account for a sizeable proportion of RSV-associated hospitalizations in children aged less than 2 years and are at increased risk for prolonged hospitalization, critical illness, and assisted ventilation suggest that preventing RSV-associated hospitalizations in premature children might have substantial impact on reducing the overall burden of complications in US children and the associated economic costs. Further, premature children account for an increasing proportion of RSV-associated hospitalizations with increasing chronologic age; therefore, efforts to ensure that age-eligible children born prematurely before their first RSV season receive nirsevimab or clesrovimab before season start will be important to protect this vulnerable group.

Strengths of this analysis include the use of prospective surveillance with a standardized case definition and systematic molecular testing for RSV at geographically and demographically diverse US sites. However, several limitations should be considered when interpreting findings. First, NVSN sites are academic medical centers that are not necessarily nationally representative. Second, data were not collected on indicators of BPD severity, such as chronic corticosteroid or diuretic therapy and home oxygen use, precluding analysis of subgroups of children with more severe BPD. Third, we limited this analysis to BPD because there was a significant difference in RSV-associated hospitalization by prematurity status and did not explore other underlying conditions that may be of importance but did not differ by prematurity status (ie, congenital heart disease, Down syndrome, and other chronic lung diseases). Fourth, unmeasured confounding may have been present in multivariable analyses.

Among a large cohort of children aged less than 2 years hospitalized with RSV-associated ARI during 2016–2023, premature children were disproportionately represented. All premature infants were at increased risk of prolonged hospitalization, critical illness, and assisted ventilation compared with term children during their first 6 months of life. Prematurity with BPD remained a risk factor for some severe in-hospital outcomes through age 23 months. Currently recommended RSV prevention products, including maternal RSV vaccine, nirsevimab, and clesrovimab, offer effective options for protecting premature infants, including those who were previously ineligible for palivizumab.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

ARI	acute respiratory illness

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aRR	adjusted relative risk
BPD	bronchopulmonary dysplasia
CDC	US Centers for Disease Control and Prevention
ICU	intensive care unit
NVSN	New Vaccine Surveillance Network
RSV	respiratory syncytial virus

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WHAT'S KNOWN ON THIS SUBJECT:

Prematurity is a risk factor for respiratory syncytial virus (RSV) infection and RSV hospitalization, with some studies demonstrating varying risk by gestational age and chronological age. Few studies have examined the association between prematurity and risk of severe in-hospital outcomes.

WHAT THIS STUDY ADDS:

Premature children, including those born at later gestational ages, are at increased risk of severe in-hospital outcomes at less than 6 months irrespective of bronchopulmonary dysplasia (BPD) status; prematurity with BPD remains a risk factor for prolonged hospitalization through 23 months.

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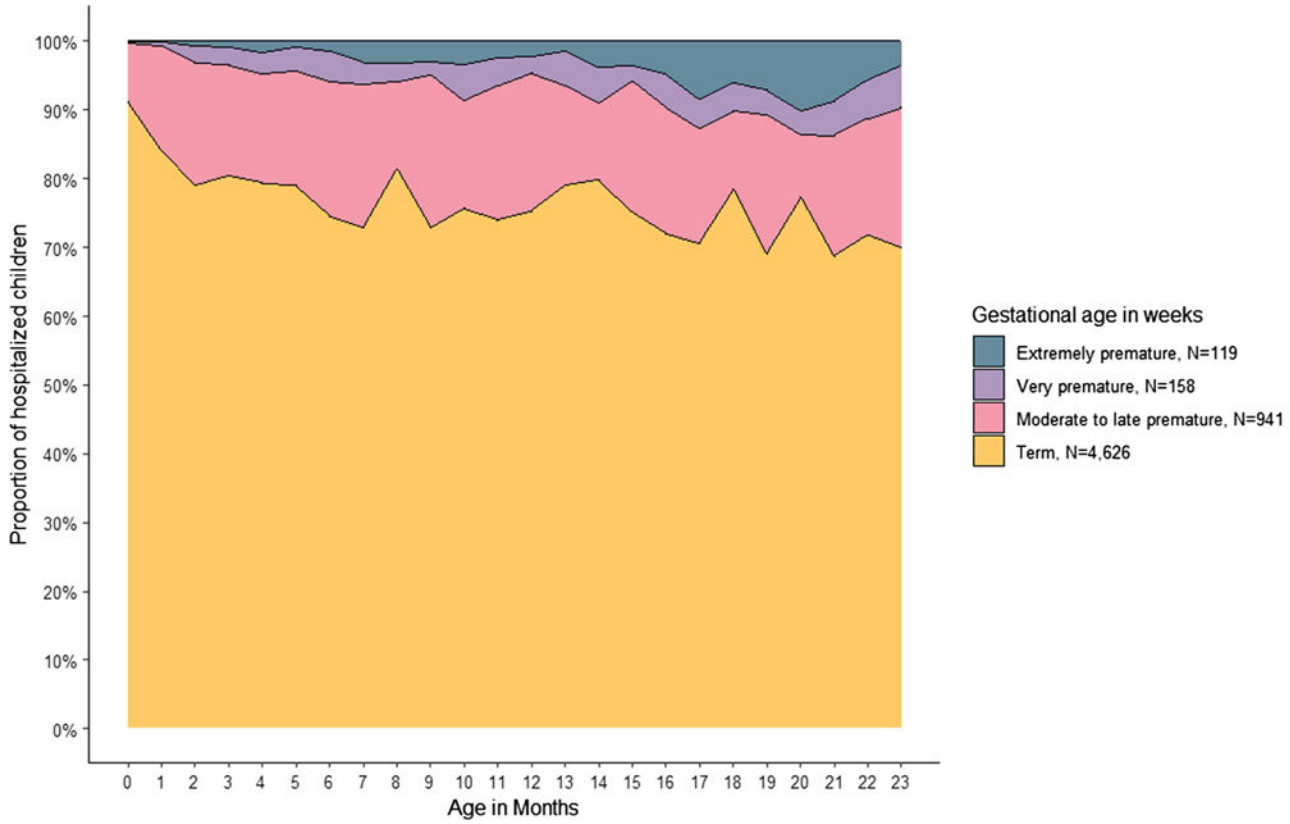


FIGURE 1.

Distribution of term or prematurity status by month of chronological age among children aged younger than 2 years hospitalized with respiratory syncytial virus, New Vaccine Surveillance Network, December 1, 2016, to July 31, 2024, N = 5844. “Term” was defined as birth at more than or equal to 37 weeks gestation. Prematurity subgroups were defined according to the established criteria as extremely premature (22 to <28 weeks gestation), very premature (28 to <32 weeks gestation), and moderate to late premature (32 to <37 weeks gestation). Extremely premature children often have prolonged hospitalizations during the first months of life, which limits detection in the New Vaccine Surveillance Network.

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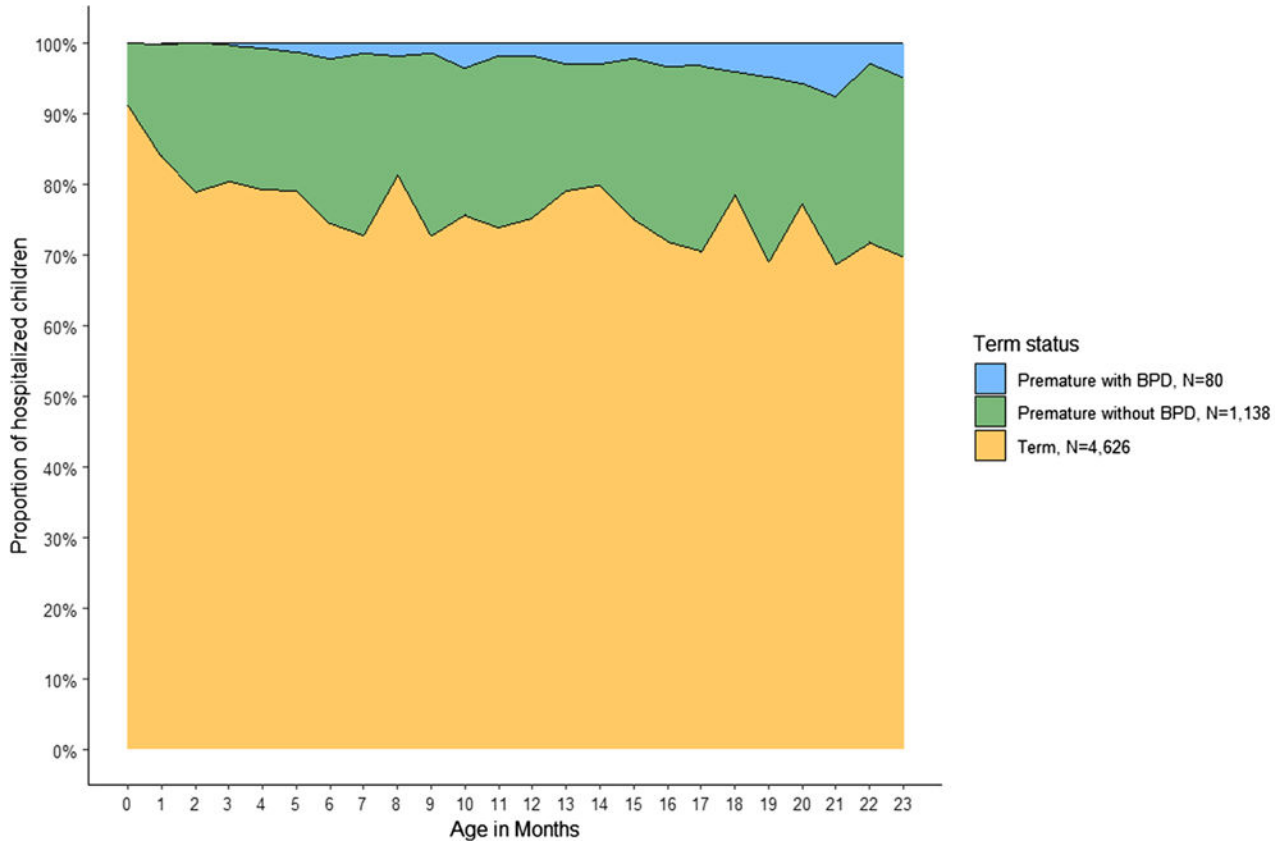


FIGURE 2.

Distribution of term or premature children with and without BPD among children aged younger than 2 years hospitalized with respiratory syncytial virus, New Vaccine Surveillance Network, December 1, 2016, to July 31, 2023, N = 5,844. “Term” was defined as birth at greater than or equal to 37 weeks gestational age. “Premature” was defined as birth at less than 37 weeks gestational age.

Abbreviation: BPD, bronchopulmonary dysplasia.

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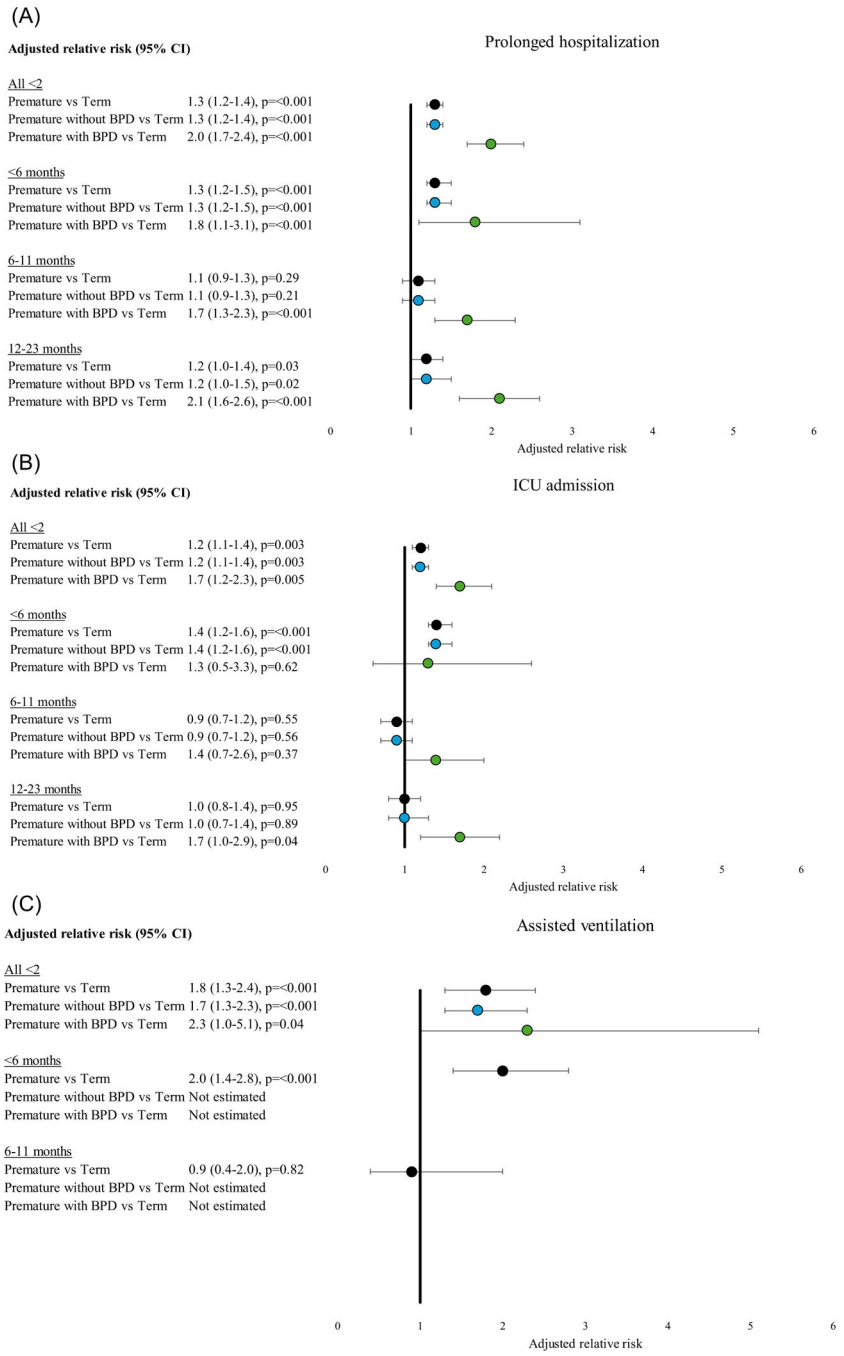


FIGURE 3.

aRR of severe in-hospital outcomes among premature vs. term children aged less than 2 years hospitalized with respiratory syncytial virus-associated acute respiratory illness, New Vaccine Surveillance Network, December 1, 2015-July 31, 2023, N = 5844 for (A) prolonged hospitalization, (B) intensive care unit admission, and (C) assisted ventilation. aRR comparing the risk among premature children with term children: the “All children” model adjusts for study site, chronological age group, presence of underlying conditions, and palivizumab receipt. Each chronological age subgroup model adjusts for study site,

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presence of underlying conditions, and palivizumab receipt. aRR comparing the risk among premature children without BPD and premature children with BPD with term infants: the “All children” model adjusts for study site, age in months, and palivizumab receipt. Chronological age subgroup models adjust for study site and palivizumab receipt. The aRR for assisted ventilation could not be estimated for children hospitalized at age 12–23 months because of small sample size. aRR of assisted ventilation was not estimated separately among premature children with and without BPD because of low numbers.
Abbreviations: aRR, adjusted relative risk; BPD, bronchopulmonary dysplasia; ICU, intensive care unit.

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TABLE 1.

Characteristics of Children Aged Less Than 2 Years Hospitalized With Respiratory Syncytial Virus–Associated Acute Respiratory Illness by Term or Premature Status, New Vaccine Surveillance Network, December 1, 2016–July 31, 2023, N = 5844

Characteristics	All Children (N = 5844)		Term (≥37 wGA) (n = 4626)		Premature (<37 wGA) (n = 1218)		*P* Value[a]
	n	%	n	%	n	%	
Age at hospitalization							
<1 month	510	8.7	465	10.1	45	3.7	<0.001
1–2 months	884	15.1	743	16.1	141	11.6	-
2–5 months	1862	31.9	1480	32.0	382	31.4	-
6–11 months	1280	21.9	963	20.8	317	26.0	-
12–17 months	804	13.8	608	13.1	196	16.1	-
18–23 months	504	8.6	367	7.9	137	11.2	-
Median (IQR), months	4.0 (2.0–11.0)		4.0 (1.0–10.0)		6.0 (2.0–12.0)		<0.001
Sex, n (%)							
Male	3304	56.5	2621	56.7	683	56.1	0.82
Female	2539	43.4	2004	43.3	535	43.9	-
Race and ethnicity							
White, NH	2766	47.3	2256	48.8	510	41.9	<0.001
Black, NH	955	16.3	687	14.9	268	22.0	-
Hispanic	1497	25.6	1179	25.5	318	26.1	-
Native Hawaiian/other Pacific Islander	36	0.6	30	0.6	6	0.5	-
American Indian/Alaska Native, NH	51	0.9	44	1.0	7	0.6	-
Asian, NH	214	3.7	173	3.7	41	3.4	-
Multiple race or other, NH	279	4.8	219	4.7	60	4.9	-
Unknown	46	0.8	38	0.8	8	0.7	-
Premature subgroup							
Moderate/late premature (32 to <37 weeks)	-	-	-	-	941	77.3	-
Very premature (28 to <32 weeks)	-	-	-	-	158	13.0	-
Extremely premature (<28 weeks)	-	-	-	-	119	9.8	-
Palivizumab receipt							

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Characteristics	All Children (N = 5844)		Term (≥37 wGA) (n = 4626)		Premature (<37 wGA) (n = 1218)		*P* Value[a]
	n	%	n	%	n	%	
Yes	117	2.0	26	0.6	91	7.5	<0.001
No	4587	78.5	3700	80.0	887	72.8	-
Missing[b]	1140	19.51	900	19.4	240	19.7	-
Underlying conditions							
>=1 condition[c]	285	4.9	136	2.9	149	12.2	<0.001
Congenital heart disease[d]	195	3.3	118	2.6	77	6.3	0.08
Down syndrome	43	0.7	30	0.6	13	1.1	0.10
BPD	82	1.4	2	0.0	80	6.6	<0.001[e]
Other lung condition[f]	5	0.1	3	0.1	2	0.2	0.30[e]
Viral coinfections[g]							
Yes	779	13.3	628	13.6	151	12.4	0.28
No	5065	86.7	3998	86.4	1067	87.6	-

Abbreviations: BPD, bronchopulmonary dysplasia; NH, non-Hispanic; wGA, weeks gestational age.

[a] P values were derived from Pearson chi-squared or Fisher exact tests when the expected values were <5 for categorical variables.

[b] Data for palivizumab receipt were considered missing if complete medical records were unavailable to verify palivizumab receipt status.

[c] At least 1 underlying condition of interest was defined as congenital heart malformation, Down syndrome, BPD, or other lung condition besides BPD.

[d] Includes atrial septal defect, ventricular septal defect, atrioventricular septal defect, or atrioventricular canal and abnormalities of the aortic arch (coarctation of aorta, double aortic arch, interrupted aortic arch, hypoplastic aortic arch, right-sided aortic arch, or truncus arteriosus), hypoplastic left heart syndrome, pulmonary atresia, tricuspid atresia or tetralogy of Fallot, transposition of the great arteries, or partial or total anomalous pulmonary venous return. This also includes other abnormalities of the heart valves, such as aortic valve stenosis, dysplasia, or insufficiency; Ebstein anomaly of tricuspid valve or tricuspid stenosis, dysplasia, or insufficiency; mitral valve atresia, stenosis, dysplasia, or insufficiency; pulmonary valve stenosis, dysplasia, or insufficiency; and dextrocardia, double outlet right ventricle, or other congenital heart malformations.

[e] Fisher exact test.

[f] Includes chronic respiratory failure with continuous positive airway pressure/bilevel positive airway pressure/ventilator dependence, chronic restrictive lung disease owing to any cause (eg, scoliosis, cerebral palsy, or autoimmune or neuromuscular disease), or pulmonary hypertension (neonatal, primary, or secondary). This also includes chronic aspiration pneumonia, interstitial lung disease (eg, interstitial pneumonitis or parenchymal disease), agenesis, hypoplasia, or other congenital lung deformities, including congenital diaphragmatic hernia, chronic bronchiectasis from cystic fibrosis, or other lung diseases.

[g] In addition to respiratory syncytial virus, the New Vaccine Surveillance Network routinely conducts surveillance testing for influenza viruses; adenoviruses; SARS-CoV-2 (since 2020); human coronaviruses 229E, NL63, OC43, and HKU1 (HCOV); enterovirus D68; human metapneumovirus; parainfluenza viruses 1–4; and rhinovirus/enterovirus.