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Characteristics and Clinical Outcomes of Vaccine-Eligible US Children Under-5 Years Hospitalized for Acute COVID-19 in a National Network

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Abstract

Background and objectives: In June 2022, the mRNA COVID-19 vaccination was recommended for young children. We examined clinical characteristics and factors associated with vaccination status among vaccine-eligible young children hospitalized for acute COVID-19.

Methods: We enrolled inpatients 8 months to <5 years of age with acute community-acquired COVID-19 across 28 US pediatric hospitals from September 20, 2022 to May 31, 2023. We assessed demographic and clinical factors, including the highest level of respiratory support, and vaccination status defined as unvaccinated, incomplete, or complete primary series [at least 2 (Moderna) or 3 (Pfizer-BioNTech) mRNA vaccine doses 14 days before hospitalization].

Results: Among 597 children, 174 (29.1%) patients were admitted to the intensive care unit and 75 (12.6%) had a life-threatening illness, including 51 (8.5%) requiring invasive mechanical ventilation. Children with underlying respiratory and neurologic/neuromuscular conditions more frequently received higher respiratory support. Only 4.5% of children hospitalized for COVID-19 (n = 27) had completed their primary COVID-19 vaccination series and 7.0% (n = 42) of children initiated but did not complete their primary series. Among 528 unvaccinated children, nearly half (n = 251) were previously healthy, 3 of them required extracorporeal membrane oxygenation for acute COVID-19 and 1 died.

Conclusions: Most young children hospitalized for acute COVID-19, including most children admitted to the intensive care unit and with life-threatening illness, had not initiated COVID-19 vaccination despite being eligible. Nearly half of these children had no underlying conditions. Of the small percentage of children who initiated a COVID-19 primary series, most had not completed it before hospitalization.

Keywords

COVID-19; vaccination; vaccine coverage; under-5 years; clinical outcomes

During the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron B.1.1.529 peak in winter 2021–2022 in the United States (US), children 6 months to younger than 5 years old comprised the highest incidence of pediatric hospitalizations attributed to acute coronavirus disease 2019 (COVID-19).^{1,2} On June 18, 2022, the messenger RNA (mRNA) vaccines by Pfizer-BioNTech and Moderna were recommended for use in US children 6 months of age.^{3,4} On December 9, 2022, recommendations were updated to include either a bivalent booster dose 2 months after completing a 2-dose series (Moderna) or to receive a bivalent dose among those completing a 3-dose series (Pfizer-BioNTech).⁵ Real-world evaluations among children 5–18 years of age have demonstrated Pfizer-BioNTech's BNT162b2 vaccine to be highly effective at reducing hospitalizations and deaths attributed to COVID-19,^{6,7} but data are limited on the prevention of COVID-19-related hospitalization in children under 5 years of age and on pediatric vaccine effectiveness attributed to the Moderna vaccine. Real-world vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection and outpatient symptomatic COVID-19 in 3–5-year-olds has been demonstrated.^{8,9}

In children with previous infection, vaccination induces higher neutralizing antibody titers that are cross-reactive across known SARS-CoV-2 variants, while antibodies produced from previous infection from prior variants alone do not demonstrably neutralize Omicron subvariants.¹⁰ Immunologic studies among young children from trial data have also demonstrated that two 25 µg doses of the Moderna series among children 6 months through 5 years of age, and three 3 µg doses of the Pfizer-BioNTech series among children 6 months through 4 years old, elicited noninferior immune responses compared with adolescents and young adults.^{11,12} Different inter-dose intervals are recommended for these vaccine series. The minimum time required to complete the initially recommended primary series is 11 weeks for Pfizer-BioNTech and 4 weeks for Moderna.¹³

Despite reports of severe COVID-19-related outcomes in young children and demonstrated efficacy of mRNA COVID-19 vaccination in older children and adults, data on vaccination status and clinical course of children <5 years of age hospitalized for acute COVID-19 are limited. Our objectives were to describe patient characteristics and clinical course, including the highest level of COVID-19-related respiratory support and COVID-19 vaccination status, among vaccine-eligible children <5 years of age hospitalized for COVID-19.

METHODS

Study Design and Population

We evaluated the clinical characteristics and outcomes of vaccine-eligible children 8 months to <5 years of age hospitalized through May 31, 2023, at 28 US pediatric hospitals participating in the Overcoming COVID-19 network, with acute COVID-19 as the primary reason for hospital admission.¹⁴ All patients had a positive nucleic acid amplification test or antigen test either during hospitalization or at a healthcare facility before hospitalization. In accordance with Centers for Disease Control and Prevention recommendations for COVID-19 vaccinations among children 6 months to <5 years old,³ we used 8 months as the minimum age at which a child could plausibly have completed an mRNA primary vaccination series, with 6 months being the earliest possible age at first dose, plus up to

4 weeks required to complete the 2-dose Moderna primary series, plus 14 days between time since last dose and hospitalization. Because June 21, 2022, was the initial date when vaccines became available for children under 5 years of age, we began enrollment on September 20, 2022, to account for the maximum time interval required to complete the initial recommended primary series (ie, 11 weeks for the 3-dose Pfizer-BioNTech primary series) and 2 weeks to develop immunity after the last vaccination. We excluded patients hospitalized for acute COVID-19 within the previous 60 days of the study hospital admission date and those whose vaccination status could not be verified. The surveillance protocol was reviewed by the Centers for Disease Control and Prevention and other participating institutions and was determined to be public health surveillance and not subject to informed consent requirements per 45 Code of Federal Regulations §46.101(b)(4). This report adheres to the STrengthening the Reporting of OBServational studies in Epidemiology reporting guidelines for cross-sectional studies.¹⁵

Vaccine Verification

Study personnel verified vaccination status by searching electronic medical records, viewing COVID-19 vaccination cards, and through state immunization information systems. We classified vaccination status as follows: (1) Unvaccinated (no recorded vaccination before hospitalization); (2) Initiated but incomplete primary series (not all doses received at least 14 days before hospitalization); or (3) Complete primary series (at least 2 doses of the Moderna series or at least 3 doses of the Pfizer-BioNTech series at least 14 days before hospitalization). We also calculated the time at which a primary series dose was considered overdue for children initiating the Pfizer-BioNTech or Moderna vaccination series and compared the proportion of children with an incomplete primary series between manufacturers and the timing of hospitalization relative to the last dose. We determined whether a child was overdue for a primary series dose or was hospitalized in between recommended dosing intervals.

Data were captured by chart review and through parent interviews. Patient data included demographics (age, sex, race and ethnicity, and census region), comorbidities, available clinical information on respiratory viral co-detections (where additional viral testing was performed), and clinical outcomes. Prespecified primary outcomes included: (1) the highest level of respiratory support (no or low-flow oxygen, high-flow nasal cannula, continuous positive airway pressure, bilevel positive airway pressure and invasive mechanical ventilation (IMV)) and (2) life-threatening illness, including receipt of IMV, vasopressors, or extracorporeal membrane oxygenation (ECMO) and/or death.

Statistical Analyses

Descriptive statistics included frequency (proportion) for categorical/binomial variables and median [interquartile range (IQR)] for continuous variables. Fisher exact and Wilcoxon rank-sum tests were used to compare binomial and continuous demographic and clinical variables, respectively, by age group, clinical outcomes (such as highest level of respiratory support), vaccination status (unvaccinated, initiated but incomplete primary series or completed primary series/booster dose). Patients who initiated but did not complete their primary series were further categorized by whether they were overdue for their next dose

(overdue for 2nd or 3rd Pfizer-BioNTech dose or overdue for 2nd Moderna dose) or were hospitalized for COVID-19 in between recommended doses.

RESULTS

We enrolled 597 infants and young children with acute COVID-19 with verifiable documentation of vaccination status, of whom 371 (62.1%) were 8 months to <2 years of age and 226 (37.9%) were 2 to <5 years of age (Fig. 1 and Table 1). Table 1 shows the demographic and clinical characteristics of these children by age group. The largest percentage of children were enrolled in the South and the lowest number in the Northeast, compared with the West and Midwest census regions. The proportion of patients with at least one underlying condition differed by age group: among children <2 years of age, 44.7% had at least one underlying medical condition, compared with 69.9% of those 2 to <5 years old ($P < 0.001$). Among these children, the most common underlying conditions were respiratory or neurologic/neuromuscular. Over 80% of children ($n = 499/597$, 83.6%) were tested for at least 1 non-SARS-CoV-2 respiratory virus, all of whom were tested for influenza, and 490 (82.1%) were tested for respiratory syncytial virus (RSV) (Table 1). Among the 499 children with any other viral testing, 188 (37.7%) tested positive for any virus. Co-detection of influenza virus was infrequent (1.2%). RSV was co-detected in 11.4% of children <5 years old tested during the study period.

Clinical outcomes by age group are shown in Table 2. Median length of hospital stay was 2 days (IQR: 1–4 days) among children 8 months to <2 years and 3 days (IQR: 2–5 days) in children 2 to <5 years. Over one-third ($n = 228$, 38.2%) of children received respiratory support above low-flow oxygen, with high-flow nasal cannula (21.8%) being the most common, followed by IMV (8.5%) and bilevel positive airway pressure or continuous positive airway pressure (7.9%). There were 174 (29.1%) patients admitted to the intensive care unit (ICU); 75 (12.6%) had a life-threatening illness. Three patients with no underlying medical conditions required ECMO and one of these patients died. Except for longer length of stay, outcomes were similar among children 8 months to <2 years and 2 to <5 years of age.

Figure 2 shows the demographic and clinical characteristics of children with acute COVID-19 categorized by the highest levels of respiratory support (none or low-flow oxygen only to IMV) by percentage of patients. Of 51 children requiring IMV, approximately half (25, 49.0%) were non-Hispanic White and 33 (64.7%) had underlying medical conditions (Figure 2, Supplemental Digital Content 2, <http://links.lww.com/INF/F364>), most commonly cardiorespiratory or neurologic/ neuromuscular disease. Of those children with no underlying medical conditions, 63.7% required no respiratory support or low-flow oxygen supplementation only; however, this declined to 48.4% and 53.3% of patients with underlying respiratory and neurologic conditions, respectively (Fig. 2). Nearly 60% of children requiring IMV who had any other viral testing had only SARS-CoV-2 detected, with no detection of a second virus (Table, Supplemental Digital Content 2, <http://links.lww.com/INF/F364>). Among 86 patients who required noninvasive or IMV and received additional testing, 40 (46.5%) had no viral co-detections, 46 (53.5%) had at least 1 viral co-detection and 6 (7.0%) had multiple viral co-detections (Table, Supplemental

Digital Content 2, <http://links.lww.com/INF/F364>). Among the 3 children requiring ECMO, 2 had coinfection with human metapneumovirus, including the 1 patient who died (Table, Supplemental Digital Content 3, <http://links.lww.com/INF/F365>).

Most children (n = 528, 88.4%) hospitalized with acute COVID-19 were not vaccinated against COVID-19 despite being eligible for vaccination. Only 27 (4.5%) patients had received their primary series [3 doses of Pfizer-BioNTech (n = 8) or 2 doses of Moderna (n = 19)]. White non-Hispanic patients comprised most patients who completed the primary series (n = 20, 74.1%). Completion of a primary mRNA vaccination series was low across all regions but was highest in the Northeast (11/90, 12.2%) and lowest in the South (3/205, 1.5%). Most children with critical illness were unvaccinated or had not completed their primary series, including 164/174 (94.3%) children with COVID-19 who were admitted to the ICU, 45/51 (88.2%) who received IMV, and 69/75 (92.0%) with life-threatening COVID-19. This included all 3 patients who required ECMO (1 died) and all 29 patients who required vasopressors (Table 3). All 6 patients who completed their primary series and were hospitalized with a life-threatening illness had at least 1 underlying respiratory or neurologic condition, including 4 patients who had both (Table, Supplemental Digital Content 4, <http://links.lww.com/INF/F366>).

Some patients initiated but did not complete the COVID-19 primary vaccination series before hospitalization (n = 42, 7.0%). Of these, 33 were overdue for a vaccine dose at the time of hospitalization while 9 were hospitalized between doses but were not overdue for their next dose (Figure 3). Overdue doses were common among those who initiated the Pfizer-BioNTech primary series [n = 27 (81.8%)] compared with those who initiated the Moderna primary series [n = 6 (18.2%)]. Likewise, among the 9 nonoverdue patients who were hospitalized in between primary series doses, 8 initiated the Pfizer-BioNTech primary series.

DISCUSSION

Across 28 centers in 21 states from September 20, 2022 to May 31, 2023, we identified 597 children between 8 months and <5 years of age hospitalized for COVID-19. Nearly half were previously healthy with no underlying conditions. Over a quarter of these hospitalized children required ICU admission, and life-threatening COVID-19 occurred in over 1 in 10. All 3 of the children who required ECMO for acute COVID-19 were previously healthy, and none of these children nor the 29 children requiring vasopressors were vaccinated, and 1 died. Vaccine coverage in this cohort was very low despite being eligible, including among those developing severe and life-threatening disease. Furthermore, over 60% of those hospitalized for acute COVID-19 who had initiated vaccination had not completed their primary series prior to hospitalization. Given the low overall vaccination coverage among these patients, it is imperative to understand the underlying reasons for such limited vaccine uptake in this age group.

Vaccine efficacy has primarily been ascertained through immunogenicity studies that were not designed to assess protection against severe clinical outcomes, which occurred rarely among these trial cohorts. Our platform is designed specifically to enroll hospitalized

patients; however, fewer than 5% of children hospitalized for acute COVID-19 and approximately 7% of SARS-CoV-2 negative patients enrolled through this same network had completed the primary COVID-19 vaccination series before admission, precluding real-world evaluation of vaccine effectiveness against severe COVID-19 illness. This low coverage stands in contrast to influenza vaccine uptake in this age group. In previous reports of influenza vaccine effectiveness among children <5 years of age hospitalized for acute respiratory infection within the New Vaccine Surveillance Network and the Pediatric Intensive Care Influenza Network, between 30% and 40% of children <9 years of age hospitalized for influenza and 50%–70% of hospitalized influenza negative controls had received a seasonal influenza vaccine.^{16–18} Notably, over the first 4 months following the rollout of the Pfizer-BioNTech and Moderna monovalent primary series in this age group, US real-world vaccine effectiveness against outpatient symptomatic SARS-CoV-2 infection among children 3–5 years old was demonstrated to be 31% and 36% effective, respectively.⁸ In Singapore, vaccine effectiveness against outpatient symptomatic SARS-CoV-2 infection among infection-naïve children 1–4 years of age was 63%.⁹ Vaccine effectiveness should be continuously monitored, given the recent incorporation of doses targeting the Omicron subvariant XBB.1.5, into all primary mRNA vaccination series.

This investigation highlights the need to improve COVID-19 vaccination coverage and awareness of severe COVID-19 illness in young children. Despite an observed decrease in the proportion of hospitalized children <5 years of age requiring ICU admission during the period of Omicron predominance, similar proportions are still requiring IMV.¹⁹ In this analysis, those children with underlying respiratory or neurologic conditions developed more severe COVID-19, requiring higher levels of respiratory support. Although children with these conditions are known to be at higher risk for COVID-19-related complications,²⁰ only a few were vaccinated. Among the small percentage of children who were fully vaccinated, 70% were non-Hispanic White, and the highest proportion of children completing their primary series reside in the Northeast census region. Disparities in vaccination coverage by race and ethnicity and geographic region comport with previous findings in this age group, likewise finding disproportionately higher vaccine coverage among non-Hispanic White children and those residing in the Northeast.²¹

Low vaccine coverage in this age group may indicate logistical barriers to provision of COVID-19 vaccine to very young children, which include (1) challenges in vaccine distribution (where doses may be available only in pediatric hospitals or large pediatric practices), (2) reliance on pediatricians and hospitals over pharmacies to administer doses to very young or medically complex children and (3) the relative complexity of the Pfizer-BioNTech primary series (three doses, with different inter-dose intervals), which may reduce parental compliance with the primary series schedule. Reflecting this, we noted that a higher proportion of patients initiated but did not complete the Pfizer-BioNTech primary series compared with those who initiated the Moderna primary series. While nearly 70% of those who completed the primary series initiated the Moderna series, over 80% of children who did not complete their primary series initiated the Pfizer-BioNTech primary series. The longer timeframe required to complete the 3-dose Pfizer-BioNTech primary series may also allow for more opportunities for infection during inter-dose intervals. In addition, caregiver perceptions of COVID-19 severity and vaccine safety may predict COVID-19 vaccination

intention for children <5 years. In the early months of eligibility in this age group, there was substantial evidence of parental hesitancy and low vaccine confidence.²² Despite this, pre- and early post-marketing monitoring for severe adverse events indicated that COVID-19 vaccination was overwhelmingly safe and effective among children 6 months to <5 years of age, with adverse events rarely reported.^{11,12,23,24} Of note, 73% of US children have completed their routine pediatric vaccines, all consisting of multidose series, and 17% have initiated but not completed one or more of their routine series. While these figures highlight a need for promotion and programmatic optimization to improve routine pediatric vaccine uptake, COVID-19 vaccination coverage in young children remains far below coverage of routine pediatric vaccination.²⁵ Expanded efforts to address gaps in vaccine access and additional caregiver outreach may help promote adherence to COVID-19 vaccination schedules.

Strengths of this investigation include representative enrollment of hospitalized COVID-19 patients by site, wide geographic breadth of included sites covering 28 pediatric hospitals in 21 states, rigorous vaccine verification procedures, and timing of patient enrollment that aligned with vaccine eligibility in this age group. This investigation, however, was subject to several limitations. First, even with simultaneous enrollment of a separate population of hospitalized SARS-CoV-2-negative patients, vaccine coverage in this population was too low to evaluate vaccine effectiveness. Second, we did not universally test all patients for other respiratory viruses; rather, clinical data on viral co-detections were obtained solely through medical records abstraction. Influenza affected relatively few patients, but it is possible that RSV, human metapneumovirus or other respiratory viral co-detections influenced disease severity. Third, we could not reliably differentiate between patients who received low-flow oxygen supplementation compared with those who received no oxygen support, as low-flow oxygen supplementation is frequently transient and challenging to ascertain through retrospective medical record abstraction. Finally, patients were enrolled largely from tertiary referral pediatric centers, so while participating sites represented geographic breadth, the findings from this investigation may not be generalizable to all patients 8 months to 5 years hospitalized for severe COVID-19 illness in the community.

Despite eligibility, most children hospitalized for COVID-19, including most children with underlying medical conditions, had not initiated their COVID-19 mRNA primary vaccination series before their hospitalization. Of the children who had initiated vaccination, particularly those initiating the Pfizer-BioNTech primary series, most had not completed their primary series by the time they were hospitalized. Our investigation shows that some young children, including those who are otherwise previously healthy, are at risk of developing severe COVID-19. Strategies to reduce barriers to vaccine access among young children, as well as caregiver education, are vital components of efforts to expand coverage and promote completion of all recommended COVID-19 mRNA vaccine doses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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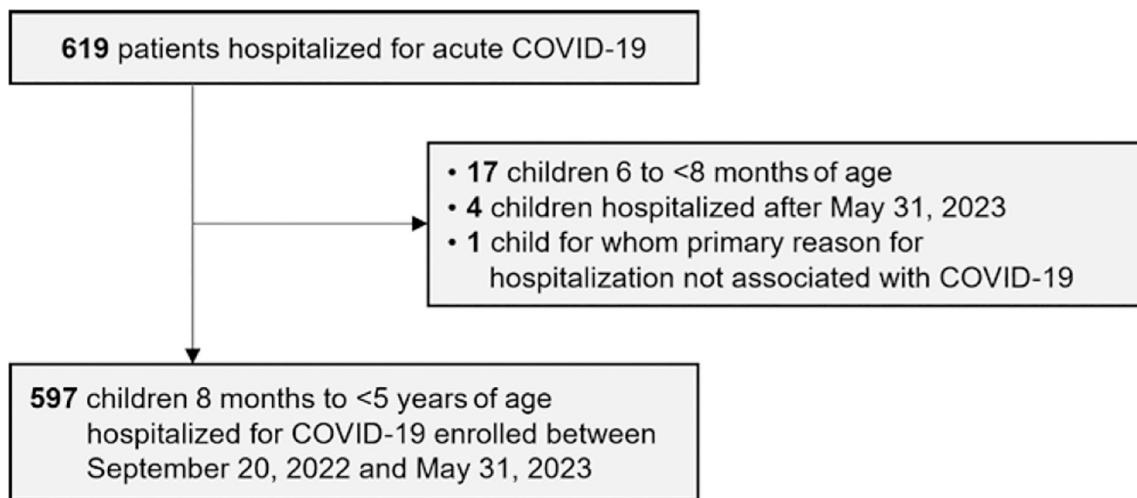


Figure 1. Patient enrollment and exclusion criteria among children under 5 years of age hospitalized for acute COVID-19 within the Overcoming COVID-19 network.

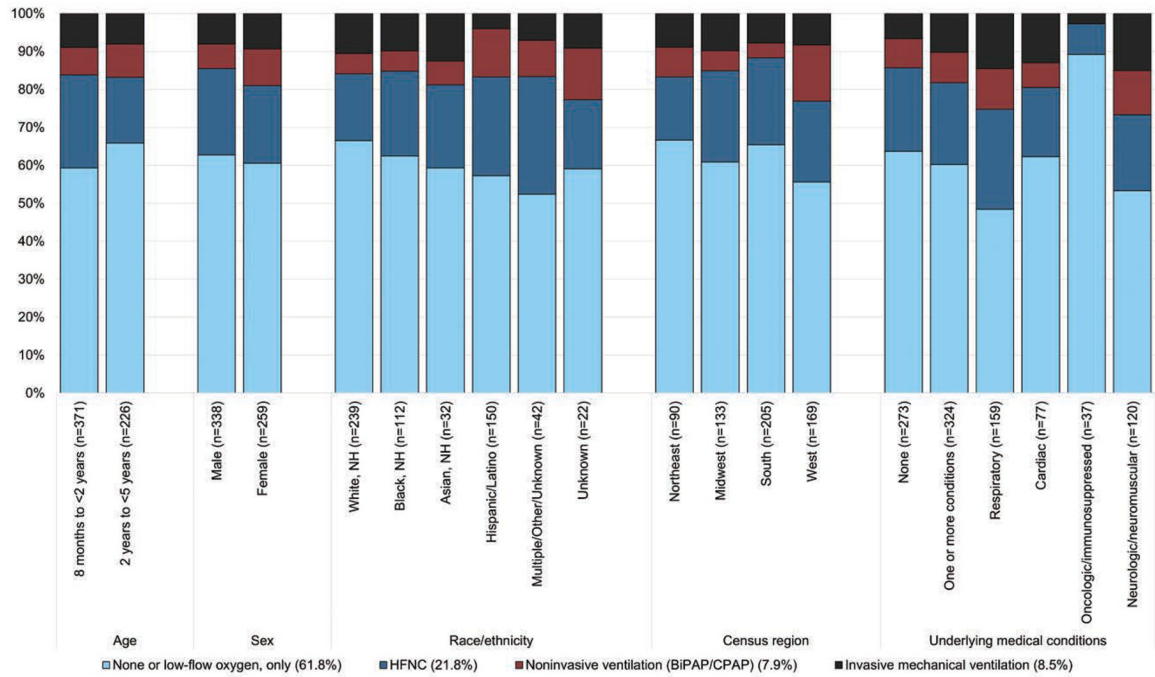


Figure 2. Proportion of patients hospitalized for COVID-19 requiring various levels of respiratory support, by demographic characteristic, and presence of underlying medical conditions.

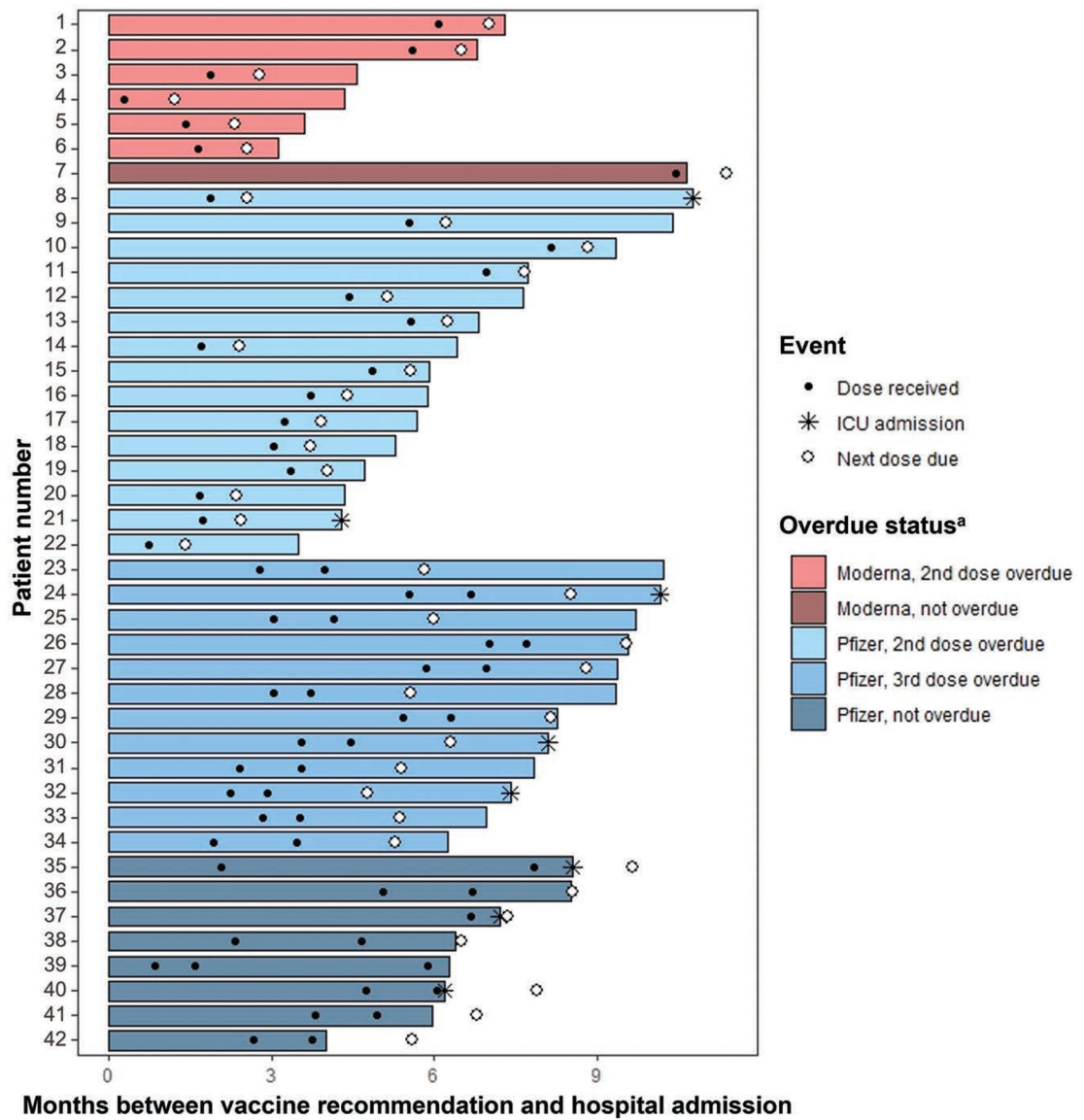


Figure 3. Timing of hospitalization relative to vaccination course among 42 pediatric patients hospitalized for COVID-19 with an incomplete vaccine series.

Table 1. Demographic and Clinical Characteristics and Outcomes Among Children 8 Months–4 Years of Age Hospitalized with Laboratory-confirmed COVID-19—Overcoming COVID-19 Vaccine Effectiveness Network, 28 hospital sites, September 20, 2022–May 31, 2023

Characteristic	Total (n = 597)	8 Months to <2 Years (n = 371)	2 Years to <5 Years (n = 226)	P Value
Sex				
Male	338 (56.6)	211 (56.9)	127 (56.2)	0.87
Female	259 (43.4)	160 (43.1)	99 (43.8)	
Race/ethnicity				
White, non-Hispanic	239 (40.0)	160 (43.1)	79 (35.0)	0.01 ^{‡*}
Black, non-Hispanic	112 (18.8)	62 (16.7)	50 (22.1)	
Asian, non-Hispanic	32 (5.4)	13 (3.5)	19 (8.4)	
Hispanic/Latino	150 (25.1)	94 (25.3)	56 (24.8)	
Multiple/other, non-Hispanic	42 (7.0)	24 (6.5)	18 (8.0)	
Unknown	22 (3.7)	18 (4.9)	4 (1.8)	
Census region				
Northeast	90 (15.1)	48 (12.9)	42 (18.6)	0.24
Midwest	133 (22.3)	83 (22.4)	50 (22.1)	
South	205 (34.3)	135 (36.4)	70 (31.0)	
West	169 (28.3)	105 (28.3)	64 (28.3)	
Underlying medical conditions				
None	273 (45.7)	205 (55.3)	68 (30.1)	<0.001
One or more underlying medical condition	324 (54.3)	166 (44.7)	158 (69.9)	
Multiple underlying medical conditions				
Cardiorespiratory	112 (18.8)	55 (14.8)	57 (25.2)	0.002
Respiratory	204 (34.2)	109 (29.4)	95 (42.0)	0.002
Cardiac	159 (26.6)	80 (21.6)	79 (35.0)	<0.001
Oncologic or immunosuppressed	77 (12.9)	49 (13.2)	28 (12.4)	0.77
Non-oncologic immunosuppressive disorder	37 (6.2)	10 (2.7)	27 (11.9)	<0.001
Oncologic	16 (2.7)	7 (1.9)	9 (4.0)	0.12
Neurologic/neuromuscular	21 (3.5)	3 (0.8)	18 (8.0)	<0.001 ^{‡*}
	120 (20.1)	58 (15.6)	62 (27.4)	<0.001

Characteristic	Total (n = 597)	8 Months to <2 Years (n = 371)	2 Years to <5 Years (n = 226)	P Value
Endocrine*	31 (5.2)	15 (4.0)	16 (7.1)	0.10
Respiratory viral co-detection [†]				
Any respiratory viral co-detection	188/499 (37.7)	108/310 (34.8)	80/189 (42.3)	0.09
Multiple co-detections	26/499 (5.2)	15/310 (4.8)	11/189 (5.8)	0.63
Influenza	6/499 (1.2)	2/310 (0.6)	4/189 (2.1)	0.21 [‡]
Respiratory syncytial virus	56/490 (11.4)	25/305 (8.2)	31/185 (16.8)	0.004
Other respiratory virus [§]	137/353 (38.8)	85/215 (39.5)	52/138 (37.7)	0.73

* No children were noted to have diabetes. Obesity is not defined in children <2 years of age and height was missing for 112 (18.8%) of patients, including 44 (19.5%) of patients 2 years of age or older; there were 47 (7.9%) children in the 95th weight-for-age percentile.

[†]We collected information regarding testing for the following non-SARS-CoV-2 respiratory viruses: influenza, respiratory syncytial virus (RSV), parainfluenza (types 1, 2, 3 and 4), human metapneumovirus, adenovirus or rhinovirus/enterovirus. All 499 patients were tested for influenza, 490 were tested for RSV and 353 were tested for the other viruses.

[‡]Fisher exact tests were performed where cell sizes were <5.

[§]Other respiratory viruses include those for which we specifically collected data on the case report form: parainfluenza (types 1, 2, 3 and 4), human metapneumovirus, adenovirus and rhinovirus/enterovirus. Overall detections for these viruses were 17/353 (4.8%), 34/353 (9.6%), 24/351 (6.8%) and 82/353 (23.2%), respectively.

Table 2. Clinical Outcomes and Highest Level of Respiratory Support Among Children 8 Months–4 Years of Age Hospitalized With Laboratory-confirmed COVID-19 —Overcoming COVID-19 Vaccine Effectiveness Network, 28 hospital sites, September 20, 2022–May 31, 2023

Hospitalization and Clinical Outcomes	Total (n = 597)	8 Months to <2 years (n = 371)	2 Years to <5 Years (n = 226)	P Value*
Length of hospital stay, days, median (IQR) †	3 (1–4)	2 (1–4)	3 (2–5)	0.01
ICU admission	174 (29.1)	116 (31.3)	58 (25.7)	0.14
Life-threatening illness ‡	75 (12.6)	51 (13.7)	24 (10.6)	0.26
Any respiratory support (above low-flow oxygen) §	228 (38.2)	151 (40.7)	77 (34.1)	0.11
Highest level of respiratory support				
High flow nasal cannula	130 (21.8)	91 (24.5)	39 (17.3)	0.17
BiPAP/CPAP	47 (7.9)	27 (7.3)	20 (8.8)	
Invasive mechanical ventilation	51 (8.5)	33 (8.9)	18 (8.0)	
Vasoactive infusions	29 (4.9)	20 (5.4)	9 (4.0)	0.44
ECMO	3 (0.5)	1 (0.3)	2 (0.9)	0.56*
In-hospital death ¶	1 (0.2)	0	1 (0.4)	0.38*

* Fisher exact tests were performed where cell sizes were <5; Wilcoxon Rank Sum test used for continuous variables.

† Length of hospital stay was determined as the days between the earliest hospital admission date (either the admission date at the study hospital or the admission date of an external hospital, if patient was transferred) and the date of hospital discharge or death.

‡ Life-threatening illness was defined as those receiving invasive mechanical ventilation, vasoactive infusions, ECMO, or illness resulting in death.

§ Of 597 patients, 369 (61.8%) either received no oxygen support or low-flow oxygen support only.

¶ The patient who died also received invasive mechanical ventilation and ECMO.

BiPAP indicates bilevel positive airway pressure; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation.

Table 3.

Demographic and Clinical Characteristics and Outcomes Among Children 8 Months - 4 Years of Age Hospitalized with Laboratory-confirmed COVID-19, by Vaccination Status*

Characteristic	Total N	Unvaccinated n (%)	Initiated But Incomplete Primary Series n (%)	Completed Primary Series 14 Days Prior to Hospitalization		
				Primary Series or Booster [†] n (%)	Pfizer-BioNTech	Moderna
All patients	597	528 (88.4)	42 (7.0)	27 (4.5)	8	19
Age group						
8 months to <2 years	371	330 (88.9)	27 (7.3)	14 (3.8)	4	10
2 years to <5 years	226	198 (87.6)	15 (6.6)	13 (5.7)	4	9
Sex						
Male	338	296 (87.6)	30 (8.9)	12 (3.6)	5	7
Female	259	232 (89.6)	12 (4.6)	15 (5.8)	3	12
Race/ethnicity						
White, non-Hispanic	239	199 (83.3)	20 (8.4)	20 (8.3)	6	14
Black, non-Hispanic	112	108 (96.4)	3 (2.7)	1 (0.9)	0	1
Hispanic/Latino	150	136 (90.7)	13 (8.7)	1 (0.7)	0	1
Multiple/Other & Unknown [‡]	96	85 (88.5)	6 (6.3)	5 (5.2)	2	3
Census region						
Northeast	90	74 (82.2)	5 (5.6)	11 (12.2)	3	8
Midwest	133	116 (87.2)	10 (7.5)	7 (5.3)	3	4
South	205	193 (94.1)	9 (4.4)	3 (1.5)	0	3
West	169	145 (85.8)	18 (10.7)	6 (3.6)	2	4
Underlying medical conditions [§]						
None	273	251 (91.9)	13 (4.8)	9 (3.3)	2	7
One or more underlying medical condition	324	277 (85.5)	29 (9.0)	18 (5.5)	6	12
Multiple underlying medical conditions	112	94 (83.9)	9 (8.0)	9 (8.0)	3	6
Cardiorespiratory	204	173 (84.8)	17 (8.3)	14 (6.9)	3	11
Respiratory	159	132 (83.0)	14 (8.8)	13 (8.2)	3	10
Cardiac	77	71 (92.2)	3 (3.9)	3 (3.9)	1	2
Neurologic/neuromuscular	120	104 (86.7)	8 (6.7)	8 (6.7)	3	5

Characteristic	Total N	Unvaccinated n (%)	Initiated But Incomplete Primary Series n (%)	Completed Primary Series 14 Days Prior to Hospitalization		
				Primary Series or Booster [†] n (%)	Pfizer-BioNTech	Moderna
Hospitalization outcome						
Length of hospital stay, median (IQR) [‡]	597	2 (1–4)	3 (2–5)	3 (1–4)	4 (3–4)	2 (1–5)
ICU admission	174	156 (89.7)	8 (4.6)	10 (5.7)	4	6
Life-threatening illness [§]	75	66 (88.0)	3 (4.0)	6 (8.0)	3	3
Any respiratory support	228	197 (86.4)	19 (8.3)	12 (5.3)	5	7
Highest level of respiratory support						
High flow nasal cannula	130	116 (89.2)	9 (6.9)	5 (3.8)	2	3
BiPAP/CPAP	47	38 (80.9)	8 (17.0)	1 (2.1)	0	1
Invasive mechanical ventilation	51	43 (84.3)	2 (3.9)	6 (11.8)	3	3
Vasoactive infusions	29	27 (93.1)	2 (6.9)	0	0	0
ECMO	3	3 (100.0)	0	0	0	0
In-hospital death	1	1 (100.0)	0	0	0	0

* Vaccination status is computed as row percentages to portray vaccination coverage among each subgroup.

[†] Includes two patients who received an mRNA booster dose. The remaining 25 patients had completed a primary series only.

[‡] Given limited sample size, 32 patients of Asian descent and 22 patients with unknown race/ethnicity were combined into this group.

[§] There were 31 patients diagnosed with an endocrine disorder, and none were noted to have diabetes (Type 1 or Type 2).

[¶] Length of hospital stay was determined as the days between the earliest hospital admission date (either the admission date at the study hospital or the admission date of an external hospital, if patient was transferred) and the date of hospital discharge.

^{||} Life-threatening illness was defined as those receiving invasive mechanical ventilation, vasoactive infusions, ECMO, or illness resulting in death.