

Letters

RESEARCH LETTER

Incidence Rates and Clinical Outcomes of SARS-CoV-2 Infection With the Omicron and Delta Variants in Children Younger Than 5 Years in the US

With the Omicron variant (B.1.1.529), SARS-CoV-2 infections and hospitalizations reached record levels.¹ Children younger than 5 years may be especially vulnerable because they are not eligible for COVID-19 vaccination.² We examined incidence rates and clinical outcomes of Omicron infection before and after Omicron became the predominant variant in the US.



[Supplemental content](#)

Methods | This cohort study (September 1, 2021-January 31, 2022) was approved by the MetroHealth System institutional review board (IRB); the need for informed consent was waived owing to use of deidentified patient data. We used the TriNetX Analytics Platform to access aggregated and deidentified electronic health records of 90 million patients from 66 health care organizations. TriNetX built-in analytic functions permit patient-level analyses while only reporting population-level data. Patients represented 28% of the US population from 50 states covering diverse geographic, age, race, income, and insurance groups.³ Self-identified race and ethnicity were included owing to their association with SARS-CoV-2 infection risk and outcomes.

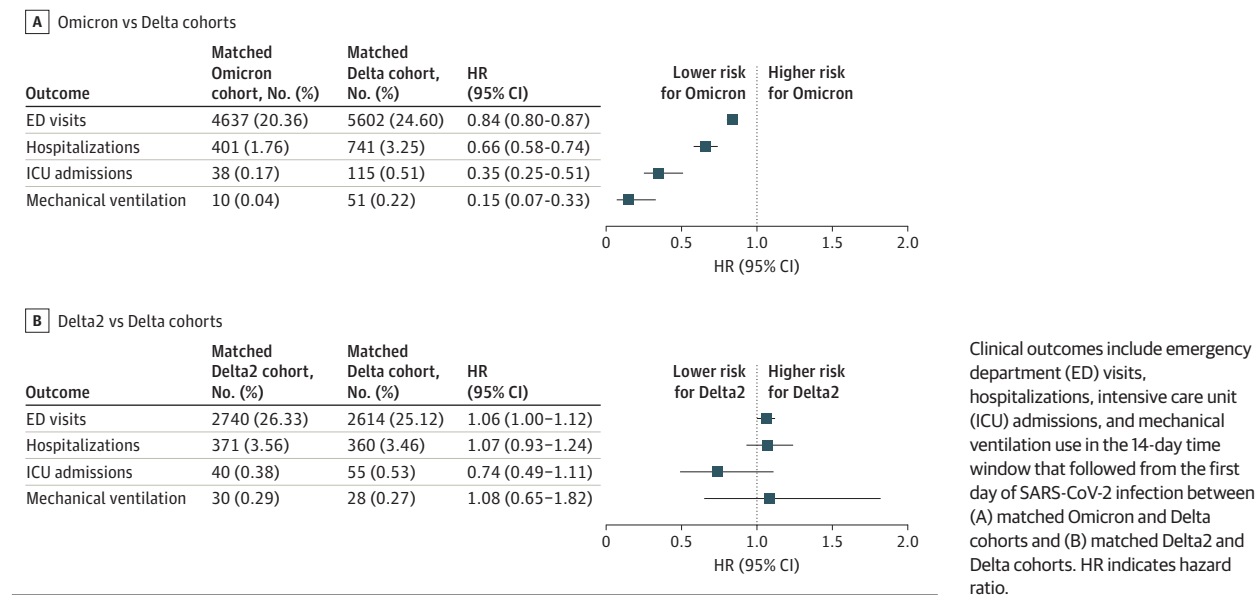
Table. Characteristics of the Omicron Cohort and the Delta Cohort Before and After Propensity Matching^a

Characteristic	Before matching			After matching		
	Cohort, No. (%)		SMD	Cohort, No. (%)		SMD
	Omicron	Delta		Omicron	Delta	
Total No. of infected children <5 y	22 772	66 692		22 769	22 769	
Age, mean (SD), y	1.5 (1.42)	1.7 (1.39)	0.14	1.5 (1.42)	1.5 (1.42)	0.005
Sex						
Female	10 780 (47.3)	30 978 (46.4)	0.02	10 780 (47.3)	10 802 (47.4)	0.002
Male	11 987 (52.6)	35 689 (53.5)	0.02	11 984 (52.6)	11 958 (52.5)	0.002
Ethnicity						
Hispanic/Latinx	2972 (13.1)	10 562 (15.8)	0.08	2972 (13.1)	2977 (13.1)	<.001
Not Hispanic/Latinx	9025 (39.6)	36 136 (54.2)	0.29	9025 (39.6)	9080 (39.9)	0.005
Unknown	10 775 (47.3)	19 994 (30.0)	0.36	10 772 (47.3)	10 712 (47.0)	0.005
Race						
Asian	518 (2.3)	1595 (2.4)	0.01	518 (2.3)	536 (2.4)	0.005
Black	4388 (19.3)	12 483 (18.7)	0.01	4387 (19.3)	4313 (18.9)	0.008
White	10 826 (47.5)	31 291 (46.9)	0.01	10 824 (47.5)	10 837 (47.6)	0.001
Unknown	6935 (30.5)	21 019 (31.5)	0.02	6935 (30.5)	6975 (30.6)	0.004
Adverse social determinants of health	352 (1.5)	1750 (2.6)	0.08	352 (1.5)	311 (1.4)	0.02
Comorbidities						
Cancer	434 (1.9)	1641 (2.5)	0.04	432 (1.9)	420 (1.8)	0.004
Congenital heart diseases	520 (2.3)	1930 (2.9)	0.04	520 (2.3)	511 (2.2)	0.003
Diabetes						
Type 1	10 (0.04)	34 (0.05)	0.003	10 (0.04)	10 (0.04)	<.001
Type 2	11 (0.05)	34 (0.05)	0.001	10 (0.05)	10 (0.04)	<.001
Asthma	474 (2.1)	2385 (3.6)	0.09	474 (2.1)	438 (1.9)	0.01
Blood disorders including anemia, neutropenia, coagulation disorders	664 (2.9)	2999 (4.5)	0.08	664 (2.9)	666 (2.9)	<.001
BMI, percentile for age						
≥95th	118 (0.5)	718 (1.1)	0.06	118 (0.5)	106 (0.5)	0.008
Between 85th-95th	106 (0.5)	602 (0.9)	0.04	106 (0.5)	91 (0.4)	0.01
<5th	66 (0.3)	326 (0.5)	0.03	66 (0.3)	66 (0.3)	<.001
Autistic disorder	89 (0.4)	456 (0.7)	0.04	89 (0.4)	93 (0.4)	0.003
Attention-deficit hyperactivity disorders	30 (0.1)	116 (0.2)	0.01	30 (0.1)	28 (0.1)	0.003

Abbreviations: BMI, body mass index; SMD, standardized mean difference.

^a Cohorts were propensity-score matched 1:1 using greedy nearest-neighbor matching with a caliper of 0.25 × SD.

Figure. Comparison of Risks of Clinical Outcomes of SARS-CoV-2 Infection in Children Younger Than 5 Years



The study population contained 3 cohorts of children younger than 5 years with no prior SARS-CoV-2 infection: (1) Omicron cohort, who contracted SARS-CoV-2 infection between December 26, 2021, and January 25, 2022⁴; (2) Delta (B.1.617.2) cohort, who contracted SARS-CoV-2 infection between September 1, 2021, and November 15, 2021⁴; and (3) Delta2 cohort, who contracted SARS-CoV-2 infection between November 16 and November 30, 2021.⁴ Delta2 cohort was developed to control for later time periods and shorter infection window.

We examined monthly incidence rates of SARS-CoV-2 infection (new cases per 1000 persons per day) between September 1, 2021, and January 31, 2022, among children without prior infections, stratified by 2 age groups (0-2 and 3-4 years). We tested whether severe clinical outcomes differed between Omicron and Delta cohorts and between Delta2 and Delta cohorts. Cohorts were propensity-score matched for demographics (Table). Risk of death, emergency department visits, hospitalizations, intensive care unit (ICU) admissions, and the need for mechanical ventilation within 14 days after initial SARS-CoV-2 infection were compared between matched cohorts using hazard ratios (HRs) and 95% CIs. Statistical tests were conducted within the TriNetX Analytics Platform with significance set at a 2-sided *P* value < .05. TriNetX database and statistical analyses are in the eMethods in the Supplement. This study followed STROBE reporting guidelines.

Results | This cohort study included a total of 651 640 children younger than 5 years: (1) Omicron cohort, 22 772 children; (2) Delta cohort, 66 692 children; and (3) Delta2 cohort, 10 496 children. The monthly incidence rate of SARS-CoV-2 infections was mostly stable (1.0-1.5 cases per 1000 persons per day) between September and November 2021 (Delta-predominant period) but rapidly increased to 2.4 to 5.6 cases per 1000 persons per day in December 2021, coincident with the emergence

of Omicron variant. Monthly incidence rate of SARS-CoV-2 infections peaked at 8.6 cases per 1000 persons per day in the first half of January 2022 (Omicron-predominant period) and 8.2 in the second half of January 2022. Incidence rate of Omicron infection was higher in children aged 0 to 2 years than in those aged 3 to 4 years. Omicron cohort was younger and with fewer comorbidities than Delta cohort, but differences were eliminated after matching (Table). Risks for severe clinical outcomes in children infected with Omicron variant were significantly lower than those in the matched Delta cohort (Figure, A), whereas the risks for severe clinical outcomes in Delta2 cohort did not differ from those in Delta cohort (Figure, B). There were fewer than 10 deaths in all cohorts.

Discussion | Results of this cohort study suggest that the incidence rate of SARS-CoV-2 infection with Omicron variant was 6 to 8 times that of Delta variant in children younger than 5 years, but severe clinical outcomes were less frequent than with Delta variant. Study limitations include potential biases introduced by the observational and retrospective analyses of electronic health records and the need for validation of the results from other data. Study findings may inform risk-benefit considerations about in-person school attendance, mask use, and vaccination implementation for young children.

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