COVID-19 in Children—Learning From the Past, Planning for the Future

Kathleen Chiotos, MD, MSCE; Julie C. Fitzgerald, MD, PhD, MSCE

As of April 2023, over 39 million children worldwide have been infected with SARS-CoV-2.¹ Now entering the fourth year after COVID-19 was declared a pandemic in March 2020, children have been at the forefront of dialogues around school closures, mask mandates, and vaccination campaigns. Fundamental to these discussions lies a need to quantify the impact of COVID-19 on children—and in order to optimize child health now and in the future, we must learn from our past.

In this issue of JAMA Pediatrics, Ward and colleagues² present a multiyear study characterizing the epidemiology of hospital and pediatric intensive care unit (PICU) admissions among children and young people with COVID-19 and pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (Paediatric Inflammatory Multisystem Syndrome [PIMS-TS], also referred to as multisystem inflammatory syndrome in children in England). Using national data reflecting 98% of hospitalizations and leveraging several linked data sources to systematically capture SARS-CoV-2 testing, PICU admissions, deaths, and prior COVID-19 vaccination or infection, the authors identified 10,540 hospitalizations between February 2020 and January 2022 in which COVID-19 was the primary reason for hospitalization. Of these, 448 children were admitted to the PICU (4.3%) and 48 died within 28 days of admission (0.46%). An additional 997 children with PIMS-TS were identified and nearly half (437 patients [44%]) necessitated PICU admission, while no children with PIMS-TS died. Based on these findings, the authors concluded that PICU utilization and mortality among children with SARS-CoV-2 infection are low in this comprehensive, nationally representative sample. Beyond this, this study captures several epidemiologic nuances with implications for public health, pandemic preparedness, and clinical care for children with COVID-19.

First, while severe illness was rare in children overall, a salient finding from this work² is that the need for PICU admission among children hospitalized with COVID-19 declined over the course of the pandemic with PICU admission occurring in nearly 10% of hospitalized pediatric patients during the wild-type period, 3.4% in the Delta period, and 1.7% in the Omicron period. Similar declines in PICU admissions during the Omicron period relative to earlier variants have been reported in other countries, including in series from the US, Canada, and South Africa.³ ⁷ The consistency of this association across settings increases confidence that there has been true attenuation in illness severity over time, a finding strengthened by the nationally representative data presented in the current study. Furthermore, while the direct contribution of vaccination to the declining trajectory of critical illness is not measurable in this study given that COVID-19 vaccinations were not widely available to children younger than 12 years old during the study period, other reports have demonstrated that vaccination is protective against critical illness due to COVID-19, including studies conducted during the Omicron period.⁸ Collectively, these findings suggest that at this stage in the pandemic, critical illness due to COVID-19 is extremely rare—and is fortunately largely preventable with vaccines.

Second, while declining rates of PICU admission among infected and hospitalized children are certainly reason for optimism, this measure has limitations. To start, estimates of the frequency of PICU admission among hospitalized children vary across studies. For example, using data from COVID-NET, a network of hospitals in 14 US states used to conduct population-based surveillance, 21% of hospitalized children aged 0 to 4 years and 19% of hospitalized children aged 5 to 11 years who tested positive for SARS-CoV-2 required PICU admission during the Omicron wave, estimates nearly 15-fold higher than the same age groups in the present study.³ ⁴ There are several possible reasons for these variable findings, including differences in PICU admission threshold across settings, differences in case mix at hospitals participating in surveillance networks vs the nationally representative sample presented in the current study, and variability in inclusion criteria defining the denominator of patients with COVID-19. More objective measures of illness severity, such as a need for mechanical ventilation or vasoressors, may partially improve uniformity in classification of critical illness and therefore prove complementary to quantify PICU resource utilization.

Additionally, and particularly for public health and preparedness efforts, population-based estimates of hospitalization and PICU admission rates have additional utility, as these measures reflect changes in absolute numbers of patients requiring hospital-based resources. While population-based estimates (ie, hospitalizations per 100,000 population) were not directly reported in the present study, the absolute number of children aged 0 to 4 years requiring hospitalization in January 2021, the peak of the Omicron phase, was approximately 3-fold and 4-fold higher than the monthly peaks during the Delta and wild-type periods, respectively. Similar trends are borne out in the COVID-NET data, which estimated a 5-fold greater hospitalization rate per 100,000 population during the Omicron phase relative to the Delta phase, while the PICU admission rates were 3.5 times higher.⁴ Thus, while reassuring that a smaller proportion of infected children developed severe illness, the larger absolute number of children requiring hospitalization or PICU admission may nevertheless strain the
pediatric health care system, contribute to excess health care costs, and result in lost wages for caregivers.

Third, by any measure, the direct impact of COVID-19 has uniquely affected children with comorbid medical conditions, who have accounted for a disproportionate fraction of hospitalizations and PICU admissions, as well as the overwhelming majority of mortalities from COVID-19.3,4,9 In the current report,2 children with comorbidities experienced a nearly 8-fold greater odds of PICU admission relative to those without comorbidities, and in particular, presence of multiple comorbid medical conditions and a life-limiting neurodisability conferred the greatest odds of PICU admission, a finding consistent with other reports.9 Unfortunately, and a limitation of this study and others using similar designs, it is not known whether the need for PICU admission was the result of the underlying comorbid medical condition itself, a lowered threshold for PICU admission in children perceived to be medically fragile, the direct effects of COVID-19, or some combination of these factors. Furthermore, while the relative risk of PICU admission is high among children with comorbidities relative to those without, the absolute risk of PICU admission may still be quite low. Defining the populations at sufficiently high absolute risk for severe outcomes from COVID-19 is critical to identify patients likely to derive significant benefit from SARS-CoV-2-directed outpatient therapies, particularly at a stage of the pandemic where illness severity is attenuated and vaccination is widely available to most age groups. This consideration is particularly timely, as nirmatrelvir-ritonavir (Paxlovid) will likely become more readily available in the near future, as the drug was approved by the US Food and Drug Administration for use in high-risk adults in May 2023, with pediatric studies ongoing (NCT05261139). Continued availability of evidence-based guidelines informing patient selection for antiviral therapies, such as those put forth by the National Institutes of Health, will be critical, as will future comparative and cost-effectiveness studies evaluating the benefit of these therapies in children.10

Fourth, PIMS-TS warrants special consideration, given the striking differences in the epidemiology relative to primary COVID-19 and high illness severity necessitating PICU admission in a large proportion of children, including in nearly 50% of cases in the current report.11 In contrast to hospitalizations due to primary COVID-19, the peak in PIMS-TS hospitalizations per 100 000 infections occurred early in 2021, with a substantial decline in both hospitalizations and PICU admissions thereafter, despite high numbers of SARS-CoV-2 infections during the Omicron era. This decrement in both number of PIMS-TS cases, as well as illness severity, has been reported in other studies and is likely driven by both host and pathogen factors—that is, the genetic mutations in the Omicron variant may stimulate less hyperinflammation, while the host response is attenuated as a result of prior exposure to SARS-CoV-2 through natural infection or immunization.12,13 Overall, while pediatricians should be reassured that a once dreaded complication of SARS-CoV-2 appears to be largely behind us, the mysterious emergence of PIMS-TS in April 2020 highlights the potential for unexpectedly severe complications of novel diseases, even in apparently healthy children, and the importance of high-quality surveillance and real-time learning networks to define epidemiology and optimal treatment of emerging diseases.

Lastly, at a stage of the pandemic where severe illness from SARS-CoV-2 is fortunately exceedingly rare in children, it is perhaps that which is not measured in this report that represents our greatest imperative: addressing the decrement in child physical and mental health indirectly related to the COVID-19 pandemic and the resulting mitigation strategies.14,15 Overcoming these secondary pandemic effects will require complex solutions, including expanding child mental health services, promoting access to routine child vaccinations and preventive health care, and investments in community and public school-based programs, particularly those focused on sociodemographically disadvantaged groups, who have been impacted by widened health care disparities during the pandemic. We must now look beyond counts of pediatric COVID-19 cases to understand, measure, and reduce the deleterious indirect impacts of the COVID-19 pandemic on children—and at a time when many have declared the COVID-19 pandemic “over,” our efforts to overcome these secondary pandemic effects have only just begun.

ARTICLE INFORMATION
Author Affiliations: Division of Critical Care Medicine, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania (Chiotos, Fitzgerald); Division of Infectious Diseases, Children’s Hospital of Philadelphia, Philadelphia, Pennsylvania (Chiotos); Department of Anesthesiology and Critical Care Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia (Chiotos, Fitzgerald).
Corresponding Author: Kathleen Chiotos, MD, MSCE, Children’s Hospital of Philadelphia, 3401 Civic Center Blvd, 9th Floor Main Hospital, 9NW29, Philadelphia, PA 19104 (chiotos@chop.edu).
Published Online: July 31, 2023, doi:10.1001/jamapediatrics.2023.2354
Conflict of Interest Disclosures: Dr Fitzgerald reported grants from the National Institutes of Health outside the submitted work. No other disclosures were reported.

REFERENCES