The Impact of Strict Public Health Restrictions on Pediatric Critical Illness*

OBJECTIVES: To characterize the impact of public health interventions on the volume and characteristics of admissions to the PICU.

DESIGN: Multicenter retrospective cohort study.

SETTING: Six U.S. referral PICUs during February 15, 2020–May 14, 2020, compared with the same months during 2017–2019 (baseline).

PATIENTS: PICU admissions excluding admissions for illnesses due to severe acute respiratory syndrome coronavirus 2 and readmissions during the same hospitalization.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Primary outcome was admission volumes during the period of stay-at-home orders (March 15, 2020-May 14, 2020) compared with baseline. Secondary outcomes were hospitalization characteristics including advanced support (e.g., invasive mechanical ventilation), PICU and hospital lengths of stay, and mortality. We used generalized linear mixed modeling to compare patient and admission characteristics during the stay-at-home orders period to baseline. We evaluated 7,960 admissions including 1,327 during March 15, 2020-May 14, 2020. Daily admissions and patients days were lower during the period of stay-at-home orders compared with baseline: median admissions 21 (interquartile range, 17–25) versus 36 (interquartile range, 30–42) (p < 0.001) and median patient days 93.0 (interguartile range, 55.9-136.7) versus 143.6 (interguartile range, 108.5–189.2) (p < 0.001). Admissions during the period of stay-at-home orders were less common in young children and for respiratory and infectious illnesses and more common for poisonings, endocrinopathies and for children with race/ethnicity categorized as other/unspecified. There were no differences in hospitalization characteristics except fewer patients received noninvasive ventilation during the period of stay-at-home orders.

CONCLUSIONS: Reductions in PICU admissions suggest that much of pediatric critical illness in younger children and for respiratory and infectious illnesses may be preventable through targeted public health strategies.

KEY WORDS: epidemiology; intensive care units, pediatric; patient admission; primary prevention; respiratory tract infections; severe acute respiratory syndrome coronavirus 2

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic fundamentally altered the way children work, play, and learn. In the United States, transmission events of SARS-CoV-2 were first identified in January of 2020. By March 16, 2020, all 50 states declared states of emergency, allowing enactment of stay-at-home orders alongside closure of schools, parks, and businesses (1). Universal mask wearing was also encouraged or mandated in many places. These sweeping public health interventions aimed at slowing the spread of the virus likely had significant unintended effects on the activities and health of children, the ripples of which have been

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observed in reports of decreased admission volumes to PICUs in the United States, Latin America, and Europe (2–6). This natural experiment raises the question of whether a substantial fraction of pediatric critical illness is preventable.

To better understand the proportion of pediatric critical illness that may be preventable, we studied the impact of United States public health interventions on the volume and characteristics of non-coronavirus disease (COVID) PICU admissions during a 2-month period early in the pandemic when most states enacted stay-at-home orders (7). We hypothesized that infectious diseases, primarily affecting younger children, decreased in response to pandemic measures.

MATERIALS AND METHODS

We conducted a retrospective, multicenter study across six U.S. pediatric regional referral centers in the Midwest, West, and South. The sites range in size from 12 to 84 beds, baseline annual PICU admission volumes were 650 to 4,000 patients, and all have active pediatric training programs. No site reported significant changes in referral patterns or PICU capacity between 2019 and 2020, and no site diverted pediatric admissions to repurpose beds for adult admissions.

We included PICU admissions during the study period February 15-May 14 during 2017-2020. Each site's state began limiting gatherings and activities between March 10, 2020, and March 14, 2020, and each site was under a stay-at-home order by March 24, 2020, until at least May 8, 2020 (8) (Supplemental Table 1, http://links.lww.com/CCM/G594). We excluded repeat PICU readmissions during the same hospitalization and admissions for COVID. The primary analyses compared admissions during the stay-at-home order period, defined as March 15, 2020-May 14, 2020, to the same time period, March 15–May 14, during years 2017-2019 (baseline). We also compared daily admission volumes during February 15, 2020-March 14, 2020, to the same period during the baseline years (2017 - 2019).

We collected patient and admission characteristics including age, sex, race/ethnicity, admission source, primary diagnosis, preexisting medical conditions, severity of illness scores (Pediatric Risk of Mortality [PRISM] III score, Pediatric Index of Mortality risk of mortality), and elective admission status (9–11) (**Supplemental Table 2**, http://links.lww.com/CCM/G594). Hospitalization characteristics collected included use of continuous renal replacement therapy (CRRT), extracorporeal membrane oxygenation (ECMO), noninvasive ventilation (NIV) and invasive mechanical ventilation (including duration), PICU and hospital lengths of stay, and inhospital mortality.

Our primary outcome was volume of PICU admissions defined as number of admissions during the study period. Secondary outcomes included utilization of advanced support (CRRT, ECMO, NIV, invasive mechanical ventilation), PICU and hospital lengths of stay, and mortality.

Definitions

Primary diagnoses were grouped using Virtual (VPS)-defined Pediatric Systems categories (Supplemental Table 3, http://links.lww.com/CCM/ G594). "Infectious" diagnoses include infectious diseases (e.g., septic shock) not primarily focused on the respiratory tract or CNS. The "Poisoning/adverse effects" category was primarily representative of drug intoxication. Primary diagnosis categories representing fewer than 3% of total admissions were combined and categorized as "Other." Preexisting chronic conditions were classified as complex chronic conditions, noncomplex chronic conditions, or not a chronic condition based on the Pediatric Medical Complexity Algorithm 3.0 using a process derived from previously published work (Supplemental Tables 4 and 5, http:// links.lww.com/CCM/G594) (12, 13). A "complicated PICU stay" was defined by receipt of either CRRT, ECMO, or invasive mechanical ventilation. A complete list of variable definitions is available in Supplemental Table 2 (http://links.lww.com/CCM/G594).

Statistical Analyses

Summary statistics were stratified by year of admission and reported as median and interquartile range (IQR) for continuous variables and frequency (percentage) for categorical variables. We compared median daily admission volumes and patient days across predefined time periods using the Wilcoxon rank-sum test. We used generalized linear mixed modeling to test for characteristics associated with admission during March 15, 2020–May 14, 2020, compared with the same months during 2017–2019 (baseline). We chose

this analysis to account for sources of variability (e.g., site effects) not incorporated when reporting raw rates. We evaluated patient, admission, and hospitalization characteristics in univariate analyses. Continuous independent variables were scaled with mean zero and sD of one to facilitate model convergence. Categorical independent variables with more than two levels were assessed for overall significance using a likelihood ratio test. A random intercept was included for hospital to account for correlation. Very few subjects had repeated admissions within the study period (n = 421 [5.6%])and a sensitivity analysis with a random intercept for subject showed negligible differences. Thus, we did not include a random intercept for subject. A multivariable model was developed by including independent variables associated with admission in 2020 (p < 0.1) with final variables selected using backward selection based on Akaike information criterion. There was not an interaction between diagnosis category and age nor evidence of collinearity. We used two-sided tests and a significance level of 0.05. Analyses were conducted using R Version 4.0.2 (2020-06-22; Vienna, Austria). This study was reviewed and approved by each site's Institutional Review Board.

RESULTS

We evaluated 13,103 admissions during 2017–2020 between the dates of February 15 and May 14. We excluded 59 admissions for COVID and 601 PICU readmissions (**Supplemental Fig. 1**, http://links.lww. com/CCM/G594). Of the included admissions, 7,960 occurred between March 15 and May 14 (**Table 1**). Admission characteristics of the site contributing data extracted from the electronic health record (EHR) differed from the remaining VPS sites in the distribution of primary diagnoses and elective admissions (**Supplemental Table 6**, http://links.lww.com/CCM/G594).

Admission volumes were markedly lower during the 2020 period of stay-at-home orders compared with baseline (**Fig. 1**). Daily admission volumes decreased 41.7% to a median 21 (IQR, 17–25) during the stay-at-home period from 36 (IQR, 30–42) during the baseline period (p < 0.001). Similarly, daily patient days decreased by 35.2% to a median 93.0 (IQR, 55.9–136.7) from 143.6 (IQR, 108.5–189.2) (p < 0.001). These differences were primarily reflected in lower volumes

of respiratory diagnoses with median 4 (IQR, 2–6) daily admissions versus 13 (IQR, 10–16.5) (p < 0.001) and infectious diagnoses with median 1 (IQR, 1–2) daily admission versus 3 (IQR, 2–4) (p < 0.001) during the stay-at-home period compared with baseline, respectively.

To ensure that 2020 was not an unusual year prior to the initiation of stay-at-home orders, we also compared admission volumes during the month leading up to the stay-at-home orders (February 15–March 14) with the same month during 2017–2019 (Fig. 1). Admission volumes during this period were similar in 2020 compared with 2017–2019: median daily admissions 44 (IQR, 36–47) versus 38.5 (IQR, 32–45.3) (p = 0.069) and daily patient days 162.3 (IQR, 142.4– 214.2) versus 148.1 (IQR, 121.1–227.0) (p = 0.181).

In univariate analyses, younger patients and patients of White race/ethnicity compared with patients categorized as "other" were less likely to be admitted in 2020 versus the baseline period (Supplemental Fig. 2, http://links.lww.com/CCM/G594). The distribution of patients with preexisting chronic conditions did not differ between 2020 and baseline. Admissions were less likely from the ward or operating room compared with admission from the emergency department/direct admission. Admission for a primary respiratory or infectious diagnosis was less frequent in 2020 compared with the baseline period. Conversely, admissions with primary diagnosis categories of neurologic, injury, poisoning/adverse events, and endocrine were more likely in 2020. Patients admitted in 2020 had higher PRISM III scores compared with the baseline period.

In multivariable analyses, younger patients and patients of White race/ethnicity compared with patients categorized as "other" were less likely to be admitted in 2020 versus the baseline period (**Fig. 2**). Admissions were less likely to be from the operating room compared with admission from the emergency department/direct admission. Primary respiratory (odds ratio [OR], 0.56; 95% CI, 0.47–0.66; p < 0.001) and infectious diagnoses (OR, 0.54; 95% CI, 0.41–0.71; p < 0.001) were less likely in 2020 compared with the baseline period. Poisoning/adverse effects (OR, 1.42; 95% CI, 1.07–1.88; p = 0.02) and endocrinopathies (OR, 1.65; 95% CI, 1.24–2.19; p = 0.001) were more common in 2020.

Next, we compared hospitalization characteristics between 2020 and the baseline period (**Supplemental**

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TABLE 1. Patient and Admission Characteristics Based on Year of Admission: March 15 to May 14

Characteristic	2017 (<i>n</i> = 2,079)	2018 (n = 2,092)	2019 (<i>n</i> = 2,462)	2020 (<i>n</i> = 1,327)
Age category, n (%)				
< 5 yr	1,032 (49.6)	1,053 (50.3)	1,273 (51.7)	551 (41.5)
5–10 yr	376 (18.1)	347 (16.6)	393 (16.0)	223 (16.8)
10–18 yr	553 (26.6)	576 (27.5)	666 (27.1)	458 (34.5)
> 18 yr	118 (5.6)	116 (5.5)	130 (5.3)	95 (7.2)
Female sex, n (%)	949 (45.6)	939 (44.9)	1,136 (46.1)	607 (45.7)
Preexisting chronic conditions by Pediatric Medical Complexity Algorithm, n (%) ^a				
No chronic conditions	1,036 (49.8)	978 (46.7)	1,191 (48.4)	636 (47.9)
Complex chronic condition(s)	510 (24.5)	568 (27.2)	712 (28.9)	354 (26.7)
Noncomplex chronic condition(s)	193 (9.3)	171 (8.2)	213 (8.7)	142 (10.7)
Race/ethnicity, <i>n</i> (%)ª				
White	862 (41.5)	844 (40.3)	991 (40.3)	517 (39.0)
Hispanic or Latino	370 (17.8)	382 (18.3)	493 (20.0)	256 (19.3)
Black or African American	284 (13.7)	248 (11.9)	335 (13.6)	152 (11.5)
Other/unspecified	213 (10.2)	242 (11.6)	296 (12.0)	203 (15.3)
Admission source, <i>n</i> (%) ^a				
Emergency department/direct admit	1,013 (48.7)	978 (46.7)	1,279 (51.9)	703 (53.0)
Operating room	396 (19.0)	365 (17.4)	457 (18.6)	234 (17.6)
Ward	283 (13.6)	314 (15.0)	320 (13.0)	159 (12.0)
Another ICU	50 (2.4)	60 (2.9)	61 (2.5)	36 (2.7)
Elective admission, <i>n</i> (%)	397 (19.1)	387 (18.5)	484 (20.0)	255 (19.2)
Primary diagnosis, <i>n</i> (%)				
Respiratory	722 (34.7)	723 (34.6)	1,021 (41.5)	304 (22.9)
Neurologic	241 (11.6)	280 (13.4)	309 (12.6)	207 (15.6)
Infectious	207 (10.0)	208 (9.9)	180 (7.3)	95 (7.2)
Injury	142 (6.8)	115 (5.5)	137 (5.6)	107 (8.1)
Oncologic	100 (4.8)	83 (4.0)	113 (4.6)	78 (5.9)
Poisoning/adverse effects	90 (4.3)	78 (3.7)	102 (4.1)	112 (8.4)
Cardiovascular	86 (4.1)	94 (4.5)	78 (3.2)	59 (4.4)
Endocrine	64 (3.1)	59 (2.8)	87 (3.5)	90 (6.8)
Other	288 (13.9)	309 (14.8)	325 (13.2)	205 (15.4)
Undetermined	139 (6.7)	143 (6.8)	110 (4.5)	70 (5.3)
Pediatric Risk of Mortality III, median (IQR)^{a}	2 (0-5)	2 (0-5)	2 (0-5)	3 (0-6)
Pediatric Index of Mortality risk of mortality (%), median (IQR)ª	0.78 (0.25-2.9)	0.83 (0.24–2.87)	0.79 (0.25–2.52)	0.82 (0.33-2.96)

IQR = interquartile range.

^aData element available from five sites (n = 6,708 admissions).

Number of patients with data available: n = 1,742 (2017), n = 1,717 (2018), n = 2,117 (2019), and n = 1,132 (2020). Percentages may not sum to 100 due to rounding.

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Figure 1. Moving 7-d average of daily PICU admissions during the baseline (averaged over 2017–2019) and 2020 study periods. Stayat-home orders were initiated at all sites by March 24, 2020.

Table 7, http://links.lww.com/CCM/G594). In univariate regression, there were no differences in the distribution of subjects supported with CRRT, ECMO, invasive mechanical ventilation, or those with a complicated PICU stay (**Fig. 3**). Fewer patients in 2020 were supported with NIV compared with the baseline period. There was no difference in duration of invasive mechanical ventilation, PICU or hospital lengths of stay, or mortality.

DISCUSSION

These findings clearly demonstrate that the implementation of public health measures intended to decrease SARS-CoV-2 transmission was associated with significant changes in the patterns of pediatric critical illness observed across a geographically diverse sample of U.S. pediatric centers. These findings are consistent with previous reports that stay-at-home orders affected the distribution of lower acuity pediatric acute care visits (14–27). In our cohort, decreasing social interaction was associated with fewer life-threatening illnesses in younger children and due to infectious diseases. Conversely, these measures were associated with more critical illnesses due to poisonings and endocrinopathies.

The decreased volume of pediatric critical illness is striking. We observed a 41.7% reduction in PICU admissions and a 35.2% reduction in patient days associated with stay-at-home orders. This observation implies that a significant portion of life-threatening illness in children could be prevented with public healthrelated behavioral modifications. Based on previously published U.S. healthcare cost data, these findings imply potentially preventable hospitalization costs in the billions of dollars annually for critically ill children (28, 29). Importantly, the similar rates of protection of patients with preexisting conditions suggest that some of the costliest PICU stays are avoidable (29, 30). While stay-at-home orders have many undesirable social and economic consequences, these observations suggest that further analysis to determine the most effective components of the public health measures and to identify less intrusive, sustainable strategies could result in large medical and financial benefits.

Adult studies have suggested that decreased hospitalizations may reflect an increased proportion of patients being managed at home (31, 32). This explanation is unlikely to account for the observed changes

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Figure 2. Multivariable model of patient and admission factors independently associated with admission during March 15, 2020–May 14, 2020, versus the same time period during the baseline period (2017–2019). Model includes data from 6,688 admissions across five hospitals. ^aOdds ratios (ORs) for continuous variables are per sp (age = 6.6 yr, Pediatric Risk of Mortality [PRISM] III score = 5.5 points). ^bReference: White, non-Hispanic (largest group). ^cReference: emergency department/direct admit. ^dReference: any other diagnosis.



Figure 3. Univariate models of hospitalization outcomes associated with admission during March 15, 2020–May 14, 2020, versus the same time period during the baseline period (2017–2019). ^aOdds ratios (ORs) for continuous variables are per 1 sp (duration of invasive mechanical ventilation = 7.9 d, PICU length of stay [LOS] = 10.4 d, hospital LOS = 30.3 d). ^bVariable available from five centers (n = 6,708 admissions). Remainder from six centers (n = 7,960 admissions). ^cComplicated PICU stay includes: continuous renal replacement therapy (CRRT), extracorporeal membrane oxygenation (ECMO), or invasive mechanical ventilation. NIV = noninvasive ventilation.

in our data. With very limited exceptions, pediatric critical illnesses are not amenable to management at home. In support of this assertion, when comparing 2020 with the baseline period, we found similar proportions of patients with a complicated PICU stay, lengths of PICU and hospital stays, and overall mortality rates. This finding suggests that PICU admissions were decreased across the spectrum of illness severity, rather than only for those with less severe disease. Recent

reports have also described excess overall mortality during the COVID pandemic, raising concerns that the pandemic has led to hospital avoidance and delayed presentations (33-37). To date, however, the 2020 mortality rate in individuals younger than 20 years old has remained similar or lower than expected, and our data do not provide evidence of widespread delays in seeking care (38). Taking these findings together, we conclude that the decreased PICU admission volume during the study period is the result of a lower frequency of life-threatening illness in children.

Our results suggest that the lower volume is primarily attributable to a reduction in rates of respiratory illnesses, which has been reported across pediatric hospitalizations globally (2–4, 6, 14, 15, 23, 26, 39). This finding is also consistent with adult data showing a decline in non-COVID respiratory illness (40). In both age ranges, the likely cause is decreased transmission of common infectious diseases. For

example, U.S. influenza transmission abruptly ended in mid-March 2020 as public health restrictions were being implemented (41). While our data do not rule out alternate explanations for this observation such as virus-virus competition or other epidemiologic factors, the strong temporal association with the implementation of activity restrictions is highly suggestive that those interventions were causative of reduced non-COVID respiratory disease transmission.

We also found that the stay-at-home period was associated with a higher risk of pediatric critical illness due to both poisoning/adverse events and endocrinopathies. The Centers for Disease Control and Prevention reported increased visits for mental health illnesses associated with the public health restrictions across all age groups (21). Our data are consistent with this report given that most admissions in the Poisonings/adverse events category are related to intentional ingestions, suggesting that this increase represents mental illness exacerbated by social isolation or reduced access to mental health services (42). Similarly, our study suggests an increase in endocrinopathy admissions, primarily diabetic ketoacidosis. This finding is consistent with other reports of increased rates and more severe presentations of diabetic ketoacidosis attributed to SARS-CoV-2 infections (43, 44).

Our study is strengthened by inclusion of a multicenter cohort of referral PICUs admitting patients from geographically and ethnically diverse urban and rural regions throughout the United States and by the observation that all of the centers saw similar impacts from stay-at-home orders and physical distancing measures. However, our study has several limitations. This study relies on appropriate designation of diagnoses by data entry personnel, which may not always be accurate. One of the six centers collected data from the EHR rather than VPS, limiting the uniformity of the data particularly related to determination of primary diagnosis and elective admissions. Additionally, EHR data extraction was limited and led to missing data elements such as illness severity scores and durations of mechanical ventilation. However, inclusion of this site increased the generalizability of our results, strengthening the study overall. Also, fluctuations in admission volumes may be in part a result of minor changes in operations or referral patterns at individual sites. We anticipate that the 3-year baseline period, geographic site diversity, and statistical design accounted for these factors. Finally, our population is likely representative of the broad catchment area of these six PICUs during the study period evaluated, however, generalizability beyond these sites, across seasons, and during the period following the stay-at-home orders requires further study.

CONCLUSIONS

The physical distancing measures put in place to decrease transmission of SARS-CoV-2 were associated with widespread and substantial reductions in PICU admissions, suggesting that a considerable portion of pediatric critical illness may be preventable, particularly those due to respiratory and infectious illnesses. These findings may have important implications for child health and public policy. Further study is warranted to identify which strategies most effectively decrease transmission of childhood infections while avoiding the negative consequences of social isolation.

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