


Outcomes of critically ill children with pre-existing mental health conditions

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ABSTRACT

Importance: Critically ill children with pre-existing mental health conditions may have an increased risk of poor health outcomes.

Objective: We aimed to evaluate if pre-existing mental health conditions in critically ill pediatric patients would be associated with worse clinical outcomes, compared to children with no documented mental health conditions.

Methods: This retrospective observational cohort study utilized the TriNetX electronic health record database of critically ill subjects aged 12–18 years. Data were analyzed for demographics, pre-existing conditions, diagnostic, medication, procedural codes, and mortality.

Results: From a dataset of 102 027 critically ill children, we analyzed 1999 subjects (284 [14.2%] with a pre-existing mental health condition and 1715 [85.8%] with no pre-existing mental health condition). Multivariable analysis demonstrated that death within one year was associated with the presence of pre-existing mental health conditions (odds ratio 8.97 [3.48–23.15], $P < 0.001$), even after controlling for the presence of a complex chronic condition.

Interpretation: The present study demonstrates that the presence of pre-existing mental health conditions was associated with higher odds of death within 1 year after receiving critical care. However, the confidence interval was wide and hence, the findings are inconclusive. Future studies with a larger sample size may be necessary to evaluate the true long-term impact of children with pre-existing mental health conditions who require critical care services.

KEYWORDS

Critical care, Psychiatry, Psychology, Public health

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INTRODUCTION

Mental health conditions are prevalent in the United States. For reasons that are multifactorial, these conditions are associated with physical illnesses.^{1,2} Because of this and due to various challenges in caring for patients with mental health conditions, when a physical illness occurs it is associated with increased hospitalizations, nonpsychiatric emergency department visits, healthcare utilization, and death.³ This continues to be a major public challenge in this vulnerable patient population worldwide.^{4,5} In addition to adults, children can be impacted by psychiatric conditions. Due to adverse childhood experiences, genetics, psychosocial risk factors, and comorbid medical illnesses, children can develop depression, post-traumatic stress disorder, schizophrenia, or anxiety.^{2,6–10} When unrecognized or untreated, it can place the child at risk for complications from the psychiatric illness itself as well as the conditions that develop in association with it during childhood and/or adulthood.¹¹ Therefore, it is important to not only identify and treat the mental health conditions in children but also understand their impact on outcomes in this patient population.

Children with chronic medical conditions are at particular risk for developing mental health diseases.^{12,13} These conditions may arise in association with an underlying disorder with poor prognosis,^{13–15} the stress of hospitalization, or the inability to participate in normal life situations. Because this patient population may require future hospitalizations, including the need for pediatric critical care services, there is a risk that the patient's pre-existing mental health condition may be exacerbated and the psychiatric illness itself may potentially be a significant barrier in the recovery of the patient's underlying chronic condition.^{16–19} This, however, is understudied in children. An understanding of how pre-existing mental health conditions impact critical care management in children may result in improved care and clinical decision-making to minimize its effects in this vulnerable patient population, both in the acute phase and also after discharge.

The objectives of this study are to utilize an electronic health record database to evaluate the (1) clinical characteristics, (2) frequency of critical care services required (i.e., mechanical ventilation, vasoactive medications, and haloperidol usage), and (3) odds of death within 1 year in critically ill pediatric subjects with a pre-existing mental health condition (depression, schizophrenia, bipolar disorder, anxiety, and post-traumatic stress disorder). We hypothesized that a majority would have a co-existing pediatric complex chronic condition, more critical care services would be required, and higher odds of death within 1 year would be associated with children within this patient population.

METHODS

Ethical approval

No protected health information is provided by TriNetX, thus our university's Institutional Review Board pre-determined this study to be non-human research.

Study design

This is a retrospective observational cohort study utilizing the TriNetX electronic health record (EHR) database of pediatric subjects aged 12 to 18 years who were reported to have received 3 consecutive days of pediatric critical care services and survived at least 30 days after the first day of pediatric critical care services.

Data source

TriNetX is a global federated research network that was developed to collect and organize aggregated EHR data elements (i.e., diagnoses, procedures, laboratory values) of approximately 68 million patients in 56 large healthcare organizations predominantly in the United States in real-time. If a subject has multiple encounters within a healthcare system that participates in TriNetX, all the EHR data elements are available for analysis allowing for a longitudinal evaluation of a subject before and after a code of interest. A description of this database, and a description of how it maintains the privacy and security of healthcare data and data availability has been previously described.²⁰

Data collection

The data used in this study was collected on July 10, 2022, from the TriNetX Research Network and included subjects who received critical care services from July 24, 2003, up to May 22, 2022. After the dataset was received, we identified the index date as the first day a subject was reported to have received critical care services. We then analyzed the following EHR data: age, sex, race, ethnicity, International Classification of Diseases, 9 (ICD-9) and 10th edition diagnostic codes (ICD-10), medication, and procedural codes. The data was de-identified and no date of birth was provided, therefore, ages are approximate (within one year). For example, a subject born in 2012 reported to have received pediatric critical care services [Common Procedural Terminology Code 99291] on January 1st, 2022, was determined to be 10 years of age. ICD-9 codes were mapped to ICD-10 codes as defined by the TriNetX database [i.e. Major depressive affective disorder, recurrent episode, mild (ICD-9, 296.31) and deemed equivalent to Major depressive disorder, recurrent, mild (ICD-10, F33.0)]. Diagnostic codes were categorized for the overall cohort as defined by the

Pediatric Clinical Classification System.²¹ The procedure codes evaluated were mechanical ventilation. Medication categories evaluated were psychedelic and medications utilized for inotropic and vasoactive cardiovascular support in the pediatric critical care setting (epinephrine, norepinephrine, vasopressin, milrinone, dopamine, dobutamine, and phenylephrine). Because delirium may not be reported as a diagnostic code, we utilized the presence of a medication code associated with haloperidol (an agent typically utilized for delirium) as a surrogate.²²

Study population

From the entire population of pediatric subjects aged 12–18 years who were reported to have received 3 consecutive days of pediatric critical care services and survived at least 30 days after the first day of pediatric critical care services, the study population was divided into two cohorts (pre-existing mental health condition group and no pre-existing mental health condition group) and analyzed. Subjects were identified as having a pre-existing mental health condition if the following diagnoses were present (depression, schizophrenia, bipolar disorder, anxiety, and post-traumatic stress disorder) any time prior to receiving pediatric critical care services for the first time in their database history. This was based on previous studies where these conditions were associated with worse outcomes.^{23–25} To ensure the subject reported to have a pre-existing mental health condition had this disorder, we only included subjects who were also receiving a medication classified as antidepressants (N06A) and psycholeptics (N05) in the Anatomical Therapeutic Chemical classification system any time prior to receiving critical care services.²⁶ Subjects who were reported to have only a diagnostic code or only a medication code associated with treatment of a psychiatric condition, but not both, were excluded. We ensured that the cohort without a pre-existing mental health condition did not have a diagnostic code or medication code associated with the treatment of a psychiatric condition before receiving pediatric critical care services. Exact death dates were not provided by the TriNetX database for patient privacy reasons. Thus, time to mortality following critical care services was calculated by using the estimated date of death minus the first recording of critical care services. Because one of the focuses of this study was to evaluate long-term outcomes after receiving critical care services, only survivors (death dates that occurred more than 30 days after critical care services) were included in the analysis. Using ICD-9, ICD-10, and ICD-10 Procedure Coding System (ICD-10-PCS) codes prior to the first date of critical care services, pediatric complex chronic conditions (PCCC) were identified and categorized using the R PCCC package.^{27,28}

Statistical analysis

By the presence and absence of pre-existing mental health conditions, we reported patient demographic characteristics, critical care services, and pediatric complex conditions using summary statistics. We conducted a two-sample *t*-test to compare the patient age between those with and those without pre-existing mental health conditions, and we applied Fisher's exact test to compare the categorical demographic factors, the presence of different types of critical care services, and the presence and categories of complex chronic conditions between the mental health condition groups.

Univariable and multivariable logistic regressions were conducted to explore the association between the mortality within one year and the mental health status. In our analysis, we removed one observation with missing data for "sex", but we kept the "unknown" category in "race" and "ethnicity" at a separate level due to their relatively high proportions in the data. Additionally, we combined the "Asian", "American Indian or Alaska Native", and "Native Hawaiian or Other Pacific Islander" categories in "race" into an "Other" category due to their small proportions in the sample. We first fit univariable regression models for sex, race, ethnicity, age, the status of pediatric complex chronic condition, and the status of mental health condition to estimate the unadjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs). We then fit a multivariable model including all the factors above to explore the covariate effects controlling for other characteristics. The adjusted ORs with 95% CIs were paralleled to the univariable output described in the results section.

We used R v.4.2.2 for data preprocessing, statistical tests, and logistic regression analyses. *P*-values of less than or equal to 0.05 were regarded as statistically significant.²⁹

RESULTS

Overview

A total of 1999 subjects (284 [14.2%] with a pre-existing mental health diagnosis and 1715 [85.8%] with no pre-existing mental health diagnosis) were included (Figure 1). Subject demographics are summarized in Table 1.

Pre-existing mental health conditions

Of the subjects with pre-existing mental health conditions, a majority consisted of anxiety (232 [81.7%]), followed by major depressive disorder (119 [41.9%]), posttraumatic stress disorder (24 [8.5%]), schizophrenia and other psychotic disorder (16 [5.6%]), bipolar disorder (13 [4.6%]), and manic episodes (5 [1.8%]) (Table 1).

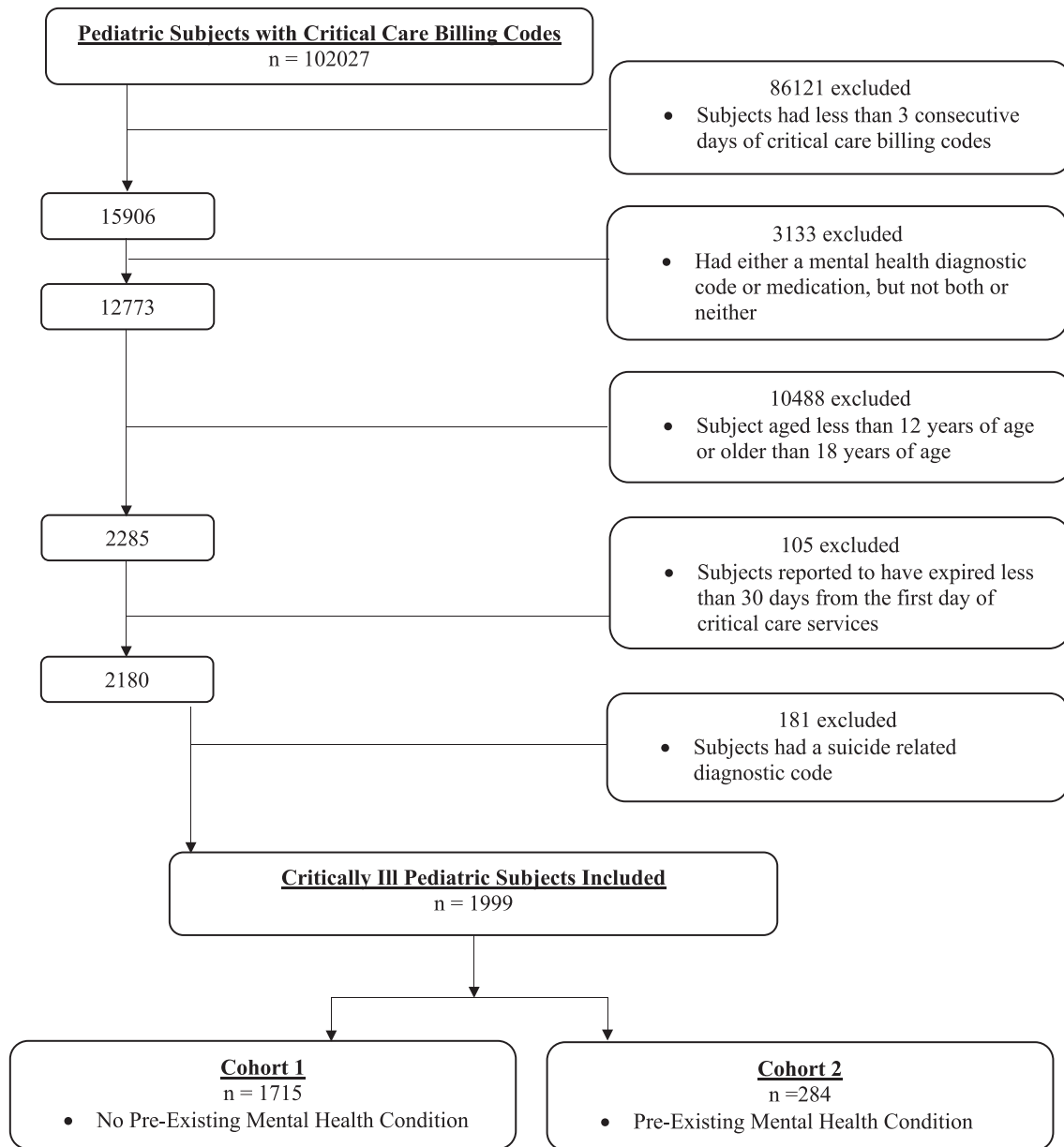


FIGURE 1 Flow chart of subjects in each cohort after applying inclusion and exclusion criteria.

Critical care services

There was no difference noted in the presence of mechanical ventilation code and inotropic/vasoactive support. Subjects in the pre-existing mental health cohort, however, had a higher frequency of haloperidol administration (18 [6.3%] vs. 54 [3.1%], $P = 0.014$) when compared to subjects without a pre-existing mental health condition (Table 2).

Pediatric complex chronic conditions

Subjects with pre-existing mental health conditions had a higher proportion of any pediatric complex chronic con-

dition (244 [85.9%] vs. 556 [32.4%], $P < 0.001$) when compared to the cohort without a pre-existing mental health condition. Overall, complex chronic conditions were higher in the mental health group. Cardiovascular conditions were the most frequent pediatric complex chronic condition category present with a significantly higher proportion noted in the pre-existing mental health condition group (135 [47.5%] vs. 301 [17.6%], $P < 0.001$) (Table 3).

Mortality outcomes within 1 year

After surviving 30 days from the first day of pediatric critical care services, a higher frequency of death within 1

TABLE 1 Demographics of subjects who have received pediatric critical care services divided by the presence and absence of a pre-existing mental health condition

Variables	Pre-existing mental health condition (<i>n</i> = 284)	No mental health condition (<i>n</i> = 1715)	<i>P</i> -value
Sex			0.172
Male	149 (52.5)	1003 (58.5)	
Female	135 (47.5)	711 (41.5)	
Unknown	0 (0.0)	1 (0.0)	
Race			0.027
White	184 (64.8)	939 (54.8)	
Black or African American	54 (19.0)	441 (25.7)	
Asian	5 (1.8)	44 (2.6)	
American Indian or Alaska Native	2 (0.7)	7 (0.4)	
Native Hawaiian or other pacific islander	1 (0.4)	4 (0.2)	
Unknown	38 (13.4)	280 (16.3)	
Ethnicity			<0.001
Hispanic or Latino	45 (15.8)	408 (23.8)	
Not Hispanic or Latino	228 (80.3)	1081 (63.0)	
Unknown	11 (3.9)	226 (13.2)	
Age (year)	14.5 ± 1.71	14.3 ± 1.77	0.144
Death within 365 days from the first day of critical care services	17 (6.0)	11 (0.6)	<0.001
Mental health conditions ^a			-
Anxiety	232 (81.7)	-	
Major depressive disorder	119 (41.9)	-	
Posttraumatic stress disorder	24 (8.5)	-	
Schizophrenia and other psychotic disorders	16 (5.6)	-	
Bipolar disorder	13 (4.6)	-	
Manic disorder	5 (1.8)	-	

Data are presented as *n* (%) or mean ± standard deviation

^aMental health conditions were not mutually exclusive.

TABLE 2 Critical care services provided in subjects with and without a pre-existing mental health condition [*n* (%)]

Variables	Pre-existing mental health condition (<i>n</i> = 284)	No pre-existing mental health condition (<i>n</i> = 1715)	<i>P</i> -value
Mechanical ventilation	82 (28.9)	515 (30.0)	0.727
Inotropic and/or vasoactive cardiovascular support	80 (28.2)	443 (25.8)	0.422
Haloperidol use	18 (6.3)	54 (3.1)	0.014

year was observed in the pre-existing mental health condition group (17 [6.0%] vs. 11 [0.6%], $P < 0.001$) when compared to the no pre-existing mental health condition group. The univariable analysis demonstrated that death within 1 year was associated with lower odds of being female (OR 0.37 [95% CI: 0.15–0.91], $P = 0.030$), higher odds of having a pediatric complex chronic condition (OR 3.21 [95% CI: 1.45–7.14], $P = 0.004$) and a higher odds

of having a pre-existing mental health condition (OR 9.86 [95% CI: 4.57–21.27], $P < 0.001$) (Table 4). When controlling for other factors in a multivariable analysis, only being female (OR 0.31 [95% CI: 0.12–0.79], $P = 0.014$) and having a mental health condition (OR 8.97 [95% CI: 3.48–23.15], $P < 0.001$) remained significantly associated with 1-year mortality. The univariate association with death and the presence of a pediatric complex chronic condition

TABLE 3 Frequency of pediatric complex conditions in subjects with and without pre-existing mental health conditions (*n* [%])

Variables	Pre-existing mental health condition (<i>n</i> = 284)	No pre-existing mental health condition (<i>n</i> = 1715)	<i>P</i> -value
Any pediatric complex chronic condition	244 (85.9)	556 (32.4)	<0.001
Pediatric complex chronic condition categories			
Congenital and/or genetic conditions	103 (36.3)	131 (7.6)	<0.001
Cardiovascular conditions	135 (47.5)	301 (17.6)	<0.001
Gastrointestinal conditions	83 (29.2)	85 (5.0)	<0.001
Hematologic and/or immunologic conditions	80 (28.2)	74 (4.3)	<0.001
Malignancy	81 (28.5)	85 (5.0)	<0.001
Metabolic conditions	123 (43.3)	120 (7.0)	<0.001
Neuromuscular conditions	96 (33.8)	137 (8.0)	<0.001
Renal conditions	73 (25.7)	39 (2.3)	<0.001
Respiratory conditions	31 (10.9)	43 (2.5)	<0.001

TABLE 4 Univariable and multivariable analysis for 1-year mortality of critically ill pediatric patients

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
Sex (Ref: Male)				
Female	0.37 (0.15–0.91)	0.030	0.31 (0.12–0.79)	0.014
Race (Ref: White)				
Black or African American	0.93 (0.38–2.26)	0.877	1.05 (0.42–2.63)	0.925
Other	2.13 (0.48–9.43)	0.319	2.61 (0.56–12.27)	0.223
Unknown	0.41 (0.09–1.79)	0.236	0.74 (0.16–3.54)	0.698
Ethnicity (Ref: Not Hispanic or Latino)				
Hispanic or Latino	0.48 (0.16–1.38)	0.172	0.61 (0.19–1.95)	0.408
Unknown	-	-	-	-
Age				
1-year increase	0.88 (0.70–1.10)	0.256	0.86 (0.68–1.08)	0.190
Any pediatric complex chronic condition (Ref: Absence)				
Presence	3.21 (1.45–7.14)	0.004	1.12 (0.42–2.98)	0.821
Any mental health disorder (Ref: Absence)				
Presence	9.86 (4.57–21.27)	<0.001	8.97 (3.48–23.15)	<0.001

Abbreviations: Ref, reference; OR, odds ratio; CI, confidence interval.

was no longer significant (OR 1.12 [95% CI: 0.42–2.98], *P* = 0.821) (Table 4).

DISCUSSION

In this present study, we hypothesized that in critically ill pediatric subjects with a pre-existing mental health condition, a majority would have a co-existing pediatric complex chronic condition, more critical care services would be required, and odds of death within 1 year would be higher when compared to children without a pre-existing mental health condition. We found that

while there was a higher frequency of pediatric complex chronic conditions in children with a pre-existing mental health condition, there was no difference in mechanical ventilation and inotropic/vasoactive use. In survivors of those who received pediatric critical care services, however, higher odds of death within 1 year were noted. The confidence interval, however, was wide, hence these findings are inconclusive. While future studies with a larger sample size are needed, these preliminary findings may highlight the potential health burdens this vulnerable patient population faces after receiving critical care services.

Due to various different reasons including psychosocial and genetic, children can develop a mental health condition.^{2,6-10} In the United States, the incidence has been increasing and because of this, it stands to reason that when children require hospitalization for a physical illness, a pre-existing mental health condition may be present.³⁰ In addition, its presence in hospitalized children may have consequences. Studies performed in this patient population have demonstrated an association with a longer length of stay, higher hospital costs, and a higher likelihood of hospital re-admission.³¹ Thus, understanding how pre-existing mental health conditions impact hospitalized children is essential to improving their care.

Studies in the critical care population, however, are to our knowledge limited to only adults. In this patient population, the potential role of pre-existing mental health conditions on critical illness has been increasingly recognized.³² Wunsch et al.³³ found that prior psychiatric diagnoses are more common in critically ill patients, a potential pre-disposing factor. In another study examining critically ill acute respiratory distress syndrome patients who have developed depression, when both these conditions are present, it was associated with an increased 2-year all-cause mortality.³⁴ Another study evaluating critically ill patients with pre-existing psychiatric disorders found that patients who were admitted for reasons other than self-harm had a higher intensive care unit mortality rate when compared to those admitted for deliberate self-harm.¹⁸ Based on these limited, retrospective data, mental health conditions may be associated with worse outcomes in children as well. Further research, however, is needed to evaluate if underlying psychiatric diagnoses also impact critically ill children in a similar way.

In our study, we found that a majority of subjects with pre-existing mental health conditions also had an associated pediatric chronic complex condition. These findings are consistent with what is reported in the literature thus far. Because of advances in healthcare, children with chronic conditions may live longer but their quality of life as well as other factors can be impacted.^{35,36} They may require medications that require adherence to a specific schedule, frequent hospitalizations, invasive procedures, and/or follow-up diagnostic testing for monitoring.³⁷ This patient population may also have pain or a disability that limits their ability to participate in various activities.³⁷ Thus, children with complex chronic conditions may develop psychiatric conditions prior to presentation for critical care services.

Despite the presence of a pediatric clinical complex condition, when controlled for in the multivariable analysis, children with pre-existing mental health conditions had higher odds of 1-year all-cause mortality. Additionally, both

cohorts had a similar mechanical ventilator and vasoactive use. While these findings should be interpreted with caution and further study is needed, there could be several reasons for these results. It is possible that the underlying psychiatric diagnosis was exacerbated or caused the development of a new psychiatric condition that impacted recovery from critical illness. Patients with mental health conditions may have psychosocial issues that influence medication adherence, compliance with therapy, recovery, and/or ability to follow up. Finally, many mental health conditions have a strong family history and thus may be seen in parents who are also the patient's caretakers.³⁸ Parents may also be stressed by the child's recent illness which may be a factor in a child's successful recovery from this illness. Future studies should confirm our findings, evaluate the health burdens this patient population and their families face after an intensive care stay, and whether closer monitoring is necessary to improve their care.

This study had several limitations. While this study demonstrated that pre-existing mental health diagnoses are associated with 1 year all-cause mortality, the overall number of deaths in both cohorts was low impacting the confidence level. Future studies, with a larger sample size, may be necessary to evaluate the true long-term impact of children with pre-existing mental health conditions who require critical care services. Exact death dates were not provided by this database due to patient privacy reasons. Additionally, death was also more likely to be reported if the patient was hospitalized, thus mortality may have been underreported. We limited the study to subjects that had both a medication code and diagnostic code consistent with a psychiatric diagnosis. This approach was conservative as it may have excluded subjects who have a psychiatric diagnosis and no reported medication prescription and vice versa, but it was chosen to demonstrate a more distinct group of children ensuring that there was an absence or presence of a pre-existing mental health condition. Due to database limitations, the accuracy of the critical care services as well as other important history (psychiatric as well as cause of death) could not be confirmed with supporting clinical documentation (which was not available). It is not known if there were other diagnoses and/or procedures present that were not coded. EHR data is restricted to institutions part of the TriNetX network, thus if subjects have received care (in particular, prescriptions and psychiatric diagnoses) in an institution outside the network, we were not able to include them in this analysis, and consequently selection bias was likely present. Finally, certain data (i.e., characteristics of healthcare organizations, and primary reasons for admission to critical care) were not available for all subjects at the time of our initial query.

Critically ill pediatric patients can have pre-existing mental health conditions. In our study, we found that its presence

was associated with a higher odds of death within 1 year after receiving critical care. Future study is needed to understand the health burdens this patient population faces after an intensive care stay and whether closer monitoring is necessary to improve their care.

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CONFLICT OF INTEREST

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