

Epidemiology of Platelet Transfusions in Hospitalized Children: A Pediatric Hospital Information System Database Study

Emily A. Lang, MD,^a Anjile An, MPH,^b Sarah Finn, MHA,^c Fisnik Prishtina, MBA,^c Robert A. DeSimone, MD,^d Marianne E. Nellis, MD, MS^e

ABSTRACT

OBJECTIVES: To describe the epidemiology and complications of platelet transfusions among hospitalized pediatric patients during 2010 to 2019.

METHODS: We performed a retrospective cohort study of hospitalized children within the Pediatric Health Information System database. Pediatric encounters receiving at least one platelet transfusion during hospitalization from 2010 to 2019 were identified. Data regarding demographics, diagnoses, procedures required during hospitalization, complications, and outcomes were extracted for eligible encounters.

RESULTS: Within the Pediatric Health Information System database, 6 284 264 hospitalizations occurred from 2010 to 2019. A total of 244 464 hospitalizations required at least one platelet transfusion, yielding a prevalence of 3.89% (95% confidence interval [CI], 3.87%–3.91%). Transfusion prevalence did not change significantly across the decade (P value = .152). Two-thirds of children receiving platelet transfusions were in their first 6 years of life, and the majority identified as male (55%). Recipients most commonly had diseases of the circulatory system (21%, 52 008 of 244 979), perinatal disorders (16%, 38 054 of 244 979), or diseases of the hematologic/immune systems (15%, 37 466 of 244 979). When adjusted for age, support by extracorporeal membrane oxygenation, mechanical ventilation, surgical intervention, and diagnostic category, the odds of thrombosis, infection, and mortality increased by 2% (odds ratio [OR], 1.02; 95% CI, 1.016–1.020), 3% (OR, 1.03; 95% CI, 1.028–1.033), and 7% (OR, 1.07; 95% CI, 1.067–1.071), respectively, with each additional transfusion.

CONCLUSIONS: The prevalence of platelet transfusions among pediatric inpatients remained consistent across the decade. Our finding that increasing numbers of transfusions may be associated with elevated morbidity and mortality is consistent with other observation and experimental studies, highlighting the need to be thoughtful in weighing risks and benefits when prescribing repeated platelet transfusions to hospitalized children.



^aDoctoral Program, and
^bDivision of Biostatistics,
Departments of
Population Health
Sciences and ^dPathology
and Laboratory Medicine,
Weill Cornell Medicine,
New York, New York;
^cMorgan Stanley
Children's Hospital
Administration, New York-
Presbyterian Morgan
Stanley Children's
Hospital, New York, New
York; and ^eDivision of
Pediatric Critical Care
Medicine, Department of
Pediatrics, New York
Presbyterian Hospital-
Weill Cornell, New York,
New York

www.hospitalpediatrics.org

DOI: <https://doi.org/10.1542/hpeds.2022-006832>

Copyright © 2023 by the American Academy of Pediatrics

Address correspondence to Marianne Nellis, MD, MS, Division of Pediatric Critical Care Medicine, New York Presbyterian Hospital–Weill Cornell Medical Center, 525 East 68th St, New York, NY 10065. E-mail: man9026@med.cornell.edu

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FUNDING: No external funding.

CONFLICT OF INTEREST DISCLOSURES: The authors have indicated they have no conflicts of interest relevant to this article to disclose.

Platelet transfusions are frequently prescribed to children; according to a survey by the American Association of Blood Banks, ~48 000 children received apheresis platelets in 2015.¹ In a large database study of children admitted to both community and academic hospitals in 2016, 0.35% of hospitalized children received at least 1 platelet transfusion.² More recently, a study of children admitted to 11 academic hospitals in the United States found that platelets were transfused in ~3.9% of pediatric admissions.³ Platelet transfusions are commonly given to prevent, as well as treat, bleeding.^{4–6}

Multiple studies have characterized the prevalence of platelet transfusions, in particular subsets of pediatric patients, such as those with oncologic diagnoses, those who are critically ill, and those supported by extracorporeal membrane oxygenation (ECMO).^{4,5,7,8} However, few studies have described the epidemiology of pediatric platelet transfusions across a wide variety of hospital settings or across a significant period of time. Because platelet transfusions are associated with an increased risk of morbidity, such as infection, thrombosis, and transfusion-related acute lung injury,^{9–12} as well as increased mortality,^{4,9–11,13} a broader understanding of the prevalence and settings of platelet transfusions in pediatric inpatients is critical for the refinement of transfusion guidelines. A greater understanding of which children most commonly receive platelet transfusions will allow transfusion medicine specialists and pediatric researchers to focus blood management programs and research priorities in these areas.

We sought to use a large administrative database to describe the patterns and epidemiologic trends in the use of platelet transfusions in children hospitalized in tertiary care centers, as well as to report their clinical outcomes.

METHODS

We performed a retrospective cohort study of hospitalized children within the

Pediatric Health Information System (PHIS) database. PHIS is an administrative database composed of inpatient, emergency department, ambulatory surgery, and observation unit encounters from ~52 freestanding children's hospitals affiliated with the Children's Hospital Association.¹⁴ Participating hospitals provide demographic, diagnosis, complication, and resource utilization data for each encounter. The study was approved by the institutional review board at Weill Cornell Medicine.

Pediatric encounters (age 0–18 years) receiving at least 1 platelet transfusion during hospitalization from January 1, 2010, to December 31, 2019, at participating PHIS hospitals were included. In addition, the total number of admissions per year was extracted and used to calculate prevalence of platelet transfusion. Birth encounters were included. All encounters involving a platelet transfusion were identified by Clinical Transaction Classification billing codes specific for platelet transfusion (ie, 354060, 354061, 354062, 354063, 354082, 354083). Demographic data, as well as information regarding diagnoses, complex chronic conditions, the use of mechanical ventilation, ECMO, or surgical procedures, and clinical outcomes (ie, mortality, length of stay, and hospitalization cost) were extracted for all eligible encounters. Surgical interventions were identified through the presence of a flag for an operating room charge within PHIS. Race was entered into the database at each participating hospital on the basis of parental report. Admitting diagnosis was defined by All Patient Refined Diagnosis Group codes and described by Major Diagnostic Categories (used across multiple data sets and formed by dividing all possible principal diagnoses into 25 mutually exclusive diagnosis areas). The presence of complex chronic conditions was defined by Pediatric Medical Complexity Algorithm categories. Complications, such as thrombosis and nosocomial infections, were identified by International Classification of Diseases, Ninth Edition, and International Classification of Diseases, 10th Edition,

codes (Supplemental Table 6), and extracted for relevant hospitalizations. Thrombosis included codes for deep vein thrombosis, pulmonary embolism, and ischemic stroke. A subset of the data was validated through manual chart review to confirm the accuracy of encounter identification and associated data before extraction of all eligible encounters from the PHIS database. Approximately 6% of all unique admissions (300 platelet transfusions administered to 82 unique hospitalized children) from Cornell within the PHIS database were reviewed for accuracy of data. All data fields reported from PHIS were compared with the electronic medical record (EMR). PHIS data were considered accurate when the rate of matching between PHIS and the was > 85%. Ethnicity was the only recorded variable determined to be inaccurate using the validation cohort, and therefore is not reported here. The Strengthening the Reporting of Observational Studies in Epidemiology guidelines for reporting in cross-sectional studies were used.

Descriptive statistics were used to characterize the study sample with respect to clinical and demographic factors of interest. Continuous variables are represented as median (interquartile range [IQR]), mean (SD), and range. Categorical variables are represented as *n* (%). The Mann-Kendall test was used to assess the trend in prevalence of transfusions across the time period. A multivariable logistic regression model was used to evaluate the independent effect of total administered transfusions on developing a thrombus, nosocomial infection, and mortality. Variables included in the model were age, ECMO flag, mechanical ventilation flag, operating room flag, Pediatric Medical Complexity Algorithm category and Major Diagnostic Category. Multicollinearity between variables was assessed and determined not to be an issue. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the multivariable models. All *P* values are 2-sided with statistical significance evaluated at the .05 α level. All analyses were performed in

RESULTS

Within the PHIS database from 2010 to 2019, there were 6 284 264 total hospital admissions composed of 4 025 830 unique children. Of these admissions, 145 218 unique children received at least 1 platelet transfusion during 244 464 hospitalizations, yielding a transfusion prevalence of 3.89% (95% CI, 3.87–3.91). The prevalence of platelet transfusions varied slightly each year, ranging from 3.69% (95% CI, 3.64–3.74) in 2010 and 2019 to 4.28% (95% CI, 4.23–4.33) in 2016. Although the proportion of patients who received transfusions was slightly higher at the end versus the beginning of the study period, this difference was not significant ($\tau = 0.378$, P value = .152; Fig 1). The number of children undergoing procedures in the operating room, receiving invasive mechanical ventilation, and being supported by ECMO all significantly increased during the study period (Supplemental Figs 2–4). When given, platelets were transfused a median (IQR) of 1 (1–3) separate times during a hospitalization (range, 1–374).

Two-thirds (153 859 of 244 464) of platelet transfusions were given to children in their first 6 years of life, with over half of those children being <1 year of age. The median (IQR) age of the recipient was 3.0 (0.0–11.0) years. There was a slight male predominance in the cohort (55%). The racial background of the recipients was varied, with the majority of patients (61%) identifying as white (Table 1).

The Major Diagnostic Coding for each admission is presented in Table 2. Of note, some children had >1 diagnostic code listed for each hospitalization. Recipients were most commonly diagnosed with diseases of the circulatory system (21%, 52 008 of 244 979), were newborns/neonates with perinatal disorders (16%, 38 054 of 244 979), or had diseases of the blood, blood-forming organs, or immunologic systems (15%, 37 466 of 244 979). The majority of children who were transfused platelets had complex

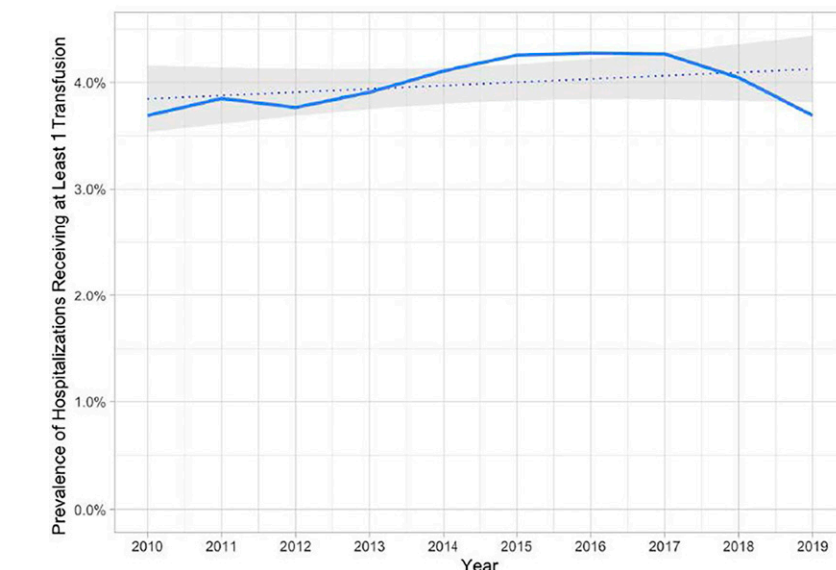


FIGURE 1 Prevalence of hospitalizations requiring at least 1 platelet transfusion from 2010 to 2019. There was no statistically significant change in prevalence of platelet transfusion across the decade ($\tau = 0.378$, 2-sided P value = .152).

chronic conditions (91%, 223 180 of 244 464). During the hospitalization, 44% (107 478 of 244 464) of transfused children were mechanically ventilated, 53% (129 765 of 244 464) underwent a procedure in the operating room, and 5% (12 546 of 244 464) were supported by ECMO.

Among children who received at least 1 platelet transfusion, 3% (8112 of 244 464) had a thrombus and 1% (3250 of 244 464) were diagnosed with a nosocomial infection. The median (IQR) length of stay for children who were transfused platelets was 10 (4–28) days. The median (IQR) cost of each hospitalization involving at least 1 transfusion was \$57 120 (\$18 903–\$142 299). During their hospitalization, 18 499 children who received platelets died, yielding a hospital mortality rate of 8%.

The results of the multivariable regression are displayed in Tables 3–5. Among patients who received platelet transfusions, each additional transfusion was associated with increased risk of thrombus, nosocomial infection, and mortality when adjusted for age, ECMO support, mechanical ventilation, need for surgical intervention, presence of chronic or complex chronic condition, and Major

Diagnostic Category (all P values < .001). For each additional transfusion, the odds of thrombosis, infection, and mortality increased by 1% (OR, 1.011; 95% CI, 1.009–1.013), 2% (OR, 1.022; 95% CI, 1.019–1.024), and 6% (OR, 1.067; 95% CI, 1.064–1.069), respectively.

TABLE 1 Demographics Characteristics of Platelet Transfusion Recipients

Recipient Characteristics	N (%)
Biologic sex	
Male	135 247 (55)
Female	109 125 (45)
Unknown	92 (<0.1)
Age categories, y	
<1	79 511 (33)
1–6	74 348 (30)
7–13	52 563 (22)
14–18	38 042 (16)
Race	
White	149 012 (61)
Black	29 986 (12)
Asian American/Pacific Islander	11 475 (5)
American Indian	3470 (1)
Other/unknown	50 521 (21)

TABLE 2 Admitting Diagnoses of Platelet Transfusion Recipients

Major Diagnostic Category	N (%)
Diseases and disorders of the circulatory system	52 008 (21)
Newborns and other neonates with conditions originating in the perinatal period	38 054 (16)
Diseases and disorders of blood, blood-forming organs, and immunologic disorders	37 466 (15)
Lymphatic, hematopoietic, other malignancies, chemotherapy, and radiotherapy	31 206 (13)
Other	23 244 (10)
Infectious and parasitic diseases, systemic, or unspecified sites	12 326 (5)
Transplant	10 739 (4)
Diseases and disorders of the nervous system	6892 (3)
Diseases and disorders of the digestive system	5440 (2)
Diseases and disorders of the musculoskeletal system and connective tissue	4929 (2)
Endocrine, nutritional, and metabolic diseases and disorders	3986 (2)
Ear, nose, mouth, throat, and craniofacial diseases and disorders	3721 (2)
Diseases and disorders of the respiratory system	3628 (2)
Diseases and disorders of the hepatobiliary system and pancreas	2974 (1)
Diseases and disorders of the kidney and urinary tract	2280 (1)
Rehabilitation, aftercare, other factors influencing health status and other health service contacts	2052 (<1)
Multiple significant trauma	1377 (<1)
Diseases and disorders of the skin, subcutaneous tissue and breast	965 (<1)
Poisonings, toxic effects, other injuries, and other complications of treatment	854 (<1)
Diseases and disorders of the eye	278 (<1)
Diseases and disorders of the female reproductive system	244 (<0.1)
Diseases and disorders of the male reproductive system	149 (<0.1)
Burns	68 (<0.1)
Mental diseases and disorders	45 (<0.1)
HIV infections	25 (<0.1)
Pregnancy, childbirth, and the puerperium	19 (<0.1)
Alcohol/drug use and alcohol/drug induced organic mental disorders	10 (<0.1)

DISCUSSION

We present the first large-scale database study that examines the epidemiology and complications of platelet transfusions in hospitalized children in freestanding children's hospitals across a decade. Nearly 4% of children were transfused platelets and this remained consistent over time. The most commonly transfused children were those with diseases of the circulatory system, perinatal disorders, or diagnoses of the hematologic and/or immune systems, indicating patient populations that can be targeted for pediatric blood management programs. The receipt of multiple platelet transfusions within 1 admission may put a child at risk for the development of thrombus, nosocomial infection, and increased

mortality, though the relationship should be further investigated.

Our prevalence of platelet transfusion is consistent with existing published literature. When examining the use of platelet transfusions from 2013 to 2016 in 11 academic children's hospitals in the United States, Nellis and colleagues reported a prevalence rate of 3.9%.³ In contrast, a report on 2016 data from the Kids' Inpatient Database (KID) (which includes both community and academic hospitals that care for children) described a platelet transfusion prevalence of 0.35%.² This discrepancy may be explained by the increasing complexity of patients typically cared for at academic centers, where greater illness severity may require more aggressive therapies. There are

several databases of hospitalized children which may be queried for epidemiologic studies. KID, the largest of the administrative data sources, includes data on discharges from 4121 hospitals from 44 states. However, it is limited in the information available on interventions for critically ill children.¹⁵ PHIS includes data from a subset of the members of the Children's Hospital Association and includes revenue codes linked to care of the critically ill child. Therefore, the KID likely has less-complex patients included in their cohort, and thus a lower prevalence of platelet transfusion.

Our cohort of children receiving platelet transfusions included those largely under the age of 6 with neonatal, cardiac, and hematologic/oncologic diagnoses. These

TABLE 3 Multivariable Logistic Regression Model Describing the Independent Association Between Repeated Platelet Transfusions and the Development of Thrombus

Development of Thrombus Characteristic	OR	95% CI	P
Number of platelet transfusions	1.01	1.009–1.013	<.001
Age, y	1.01	1.004–1.014	<.001
PMCA category			
Nonchronic	Ref	—	—
Noncomplex chronic	1.06	0.835–1.343	.660
Complex chronic	2.45	1.999–3.033	<.001
ECMO, yes/no	1.69	1.569–1.810	<.001
Mechanical ventilation, yes/no	4.78	4.431–5.153	<.001
Surgical intervention, yes/no	1.43	1.348–1.522	<.001
Diagnostic category, “diseases and disorders of”			
Burns	0.86	0.227–2.717	.810
Blood, blood-forming organs, and immunologic	0.29	0.158–0.593	<.001
Circulatory system	0.28	0.157–0.580	<.001
Digestive system	0.58	0.311–1.196	.110
Female reproductive system	0.35	0.053–1.349	.180
Hepatobiliary system and pancreas	0.67	0.356–1.400	.240
Kidney and urinary tract	1.65	0.889–3.415	.140
Male reproductive system	0.24	0.013–1.286	.180
Musculoskeletal and connective tissue	0.32	0.166–0.663	<.001
Nervous system	0.94	0.512–1.920	.840
Respiratory system	0.85	0.460–1.744	.620
Skin, subcutaneous tissue, and breast	0.43	0.178–1.058	.061
ENT/craniofacial	0.25	0.124–0.548	<.001
Endocrine, nutritional, and metabolic	0.51	0.266–1.077	.056
HIV	1.64	0.237–7.046	.550
Infectious and parasitic diseases	0.84	0.463–1.720	.600
Lymphatic, hematopoietic, and other malignancies	0.55	0.305–1.133	.075
Mental disease and disorders	1.19	0.175–4.928	.830
Multiple significant trauma	0.58	0.304–1.227	.120
Newborns and perinatal conditions	0.56	0.307–1.136	.076
Other	0.43	0.239–0.892	.012
Poisonings, toxins, and other injuries	0.69	0.338–1.525	.330
Rehabilitation/aftercare	0.55	0.277–1.187	.100
Tracheostomy with long-term ventilation	1.48	0.812–3.027	.240
Transplant	0.82	0.452–1.673	.550

Please note that not all confounding variables (measured and unmeasured) can be included in the model. ENT, ear, nose, and throat; PMCA, Pediatric Medical Complexity Algorithm; Ref, reference. —, not available.

characteristics are also consistent with previously published reports. Nearly one-sixth of our transfused cohort was grouped into a major diagnostic category of “Newborns and Other Neonates with Conditions Originating in the Perinatal Period.” Although it is unclear if our results truly reflect transfusion practices specifically within the NICU, work within

the Recipient Epidemiology and Donor Evaluation Study-III suggests one-third of neonates <27 weeks’ gestational age receive at least 1 platelet transfusion.⁸ Recipient Epidemiology and Donor Evaluation Study-III analyses have also examined children with underlying oncologic diagnoses and found that nearly one-quarter of the admissions for these

children involve at least 1 platelet transfusion.¹⁶ In addition, previous findings have suggested that children with underlying oncologic diagnoses receive nearly half of platelets prescribed by pediatric intensivists,¹⁷ and that patients undergoing cardiac repairs or being supported by ECMO are at an increased risk of requiring platelet transfusions.^{3,5,9,18} The consistent use of platelet transfusions in these patients suggests that further development of transfusion guidelines should focus specifically on these particular populations.

The need for consideration of more restrictive transfusion practices is highlighted by recent literature reporting increased morbidity and mortality associated with platelet transfusions.^{4,9,11,13,19–23} Among critically ill children, platelet transfusions have been associated with an increased risk of transfusion-related acute lung injury, febrile nonhemolytic transfusion reactions, and organ failure.^{11,13} Other studies examining the effects of platelet transfusion in children being supported by ECMO or undergoing cardiopulmonary bypass found that transfusions were associated with longer length of stay in the PICU and increased number of days on mechanical ventilation, as well as increased risk of thrombosis, bleeding, and acute hepatic injury.^{9,19,20} Platelet transfusions have also been independently associated with increased mortality among pediatric patients,^{4,9,11,13,21–23} a finding particularly emphasized by a recent trial demonstrating decreased morbidity and mortality among neonates who were transfused at more restrictive thresholds.²³ Though we were unable to account for all confounding bias, we report similar associations with repeated platelet transfusions. Our rates of thrombus and nosocomial infection in children who receive platelet transfusions are higher than national rates for all hospitalized children reported by the Children’s Hospitals’ Solutions for Patient Safety.²⁴ In addition, after controlling for illness severity by adjusting for age, ECMO, mechanical ventilation, surgical

TABLE 4 Multivariable Logistic Regression Model Describing the Independent Association Between Repeated Platelet Transfusions and the Development of Nosocomial Infections

Development of Nosocomial Infection Characteristic	OR	95% CI	P
Number of platelet transfusions	1.02	1.019–1.024	<.001
Age, y	0.96	0.960–0.970	<.001
PMCA category			
Nonchronic	Ref	—	—
Noncomplex chronic	2.06	1.209–3.754	.012
Complex chronic	5.35	3.328–9.348	<.001
ECMO, yes/no	0.99	0.867–1.1433	.960
Mechanical ventilation, yes/no	1.46	1.329–1.603	<.001
Surgical intervention, yes/no	2.18	1.996–2.381	<.001
Diagnostic category, “diseases and disorders of”			
Burns	7.74	1.46–57.20	.020
Blood, blood-forming organs, and immunologic	0.71	0.22–4.302	.630
Circulatory system	0.34	0.107–2.039	.130
Digestive system	1.51	0.468–9.234	.570
Female reproductive system	0.92	0.042–9.655	.940
Hepatobiliary system and pancreas	1.37	0.412–8.518	.660
Kidney and urinary tract	1.40	0.411–8.736	.650
Musculoskeletal and connective tissue	0.69	0.202–4.354	.620
Nervous system	1.26	0.392–7.710	.750
Respiratory system	2.15	0.666–13.15	.290
Skin, subcutaneous tissue, and breast	0.99	0.212–6.977	.999
ENT/craniofacial	0.36	0.093–2.386	.200
Endocrine, nutritional, and metabolic	0.88	0.259–5.535	.870
Infectious and parasitic diseases	9.29	2.969–56.19	.002
Lymphatic, hematopoietic, and other malignancies	1.69	0.539–10.23	.460
Multiple significant trauma	3.89	1.178–24.04	.063
Newborns and perinatal conditions	0.91	0.289–5.499	.890
Other	1.12	0.355–6.816	.870
Poisonings, toxins, and other injuries	0.87	0.187–6.134	.870
Rehabilitation/aftercare	0.38	0.081–2.660	.250
Tracheostomy with long-term ventilation	3.80	1.199–23.09	.062
Transplant	2.43	0.773–14.69	.210

ENT, xxx; PMCA, Pediatric Medical Complexity Algorithm; Ref, reference. —, xxx.

interventions, and Major Diagnostic Category, each additional platelet transfusion was independently associated with increased risk of thrombus, nosocomial infection, and mortality in our cohort.

Given the risks associated with transfusion, patient blood management programs have been developed to encourage compliance with transfusion recommendations. They function similar to antibiotic stewardship committees to ensure the appropriate use of resources. Whereas antimicrobial stewardship

programs have documented significant impact,²⁵ pediatric patient blood management programs have faced many challenges, including the lack of implementation of evidence-based pediatric guidelines, and to date, are not considered standard of care at every hospital.²⁶ Despite increasing awareness of risks associated with platelet transfusion and the efforts of pediatric patient blood management programs,^{4,9–13} we did not find any decrease in the prevalence of platelet transfusion over the

10 years of the study. This finding may be a reflection of increasingly complex patients, because the number of patients requiring mechanical ventilation, ECMO, or an OR procedure during hospitalization increased over the decade. However, it does highlight the need for continued education and implementation of local restrictive platelet transfusion guidelines where warranted.

Guidelines to direct platelet transfusion in the pediatric population are somewhat limited. The Transfusion-Anemia eXpertise Initiative—Control/Avoidance of Bleeding recently published recommendations to direct platelet transfusion for a variety of subsets of critically ill children, including those after cardiac surgery, supported by ECMO, and/or with oncologic diagnoses.²⁷ However, the guidance is limited by the lack of strong evidence for or against restrictive thresholds. Therefore, research priorities were also identified that focus studies that assess the efficacy versus harm of platelet transfusion thresholds, as well as translational studies to elucidate the mechanisms of possible harm.²⁸ In addition to guideline development, the Development & Evaluation of Audit and Feedback Interventions to Increase evidence-based Transfusion practice program in the United Kingdom is seeking to understand the most effective means to implement transfusion guidelines into practice.²⁹ Their findings may influence the approaches encouraged by patient blood management programs.

This study has several strengths. It offers a broad understanding of the rates at which we currently prescribe platelet transfusions, the types of patients receiving platelet transfusions, and the associated complications of platelet transfusions in a large sample of hospitalized pediatric patients. It confirms previously reported findings from smaller, more focused databases. The findings may be used to power interventional trials and focus on particular pediatric patient populations.

However, some limitations of the study remain. The PHIS database is an administrative database, which limits the information available regarding each transfusion. We

TABLE 5 Multivariable Logistic Regression Model Describing the Independent Association Between Repeated Platelet Transfusions and the Development of Mortality

Mortality Characteristic	OR	95% CI	P
Number of platelet transfusions	1.07	1.064–1.069	<.001
Age, y	0.99	0.990–1.003	.660
PMCA category			
Nonchronic	Ref	—	—
Noncomplex chronic	0.316	0.289–0.346	<.001
Complex chronic	0.280	0.260–0.302	<.001
ECMO, yes/no	3.37	3.200–3.551	<.001
Mechanical ventilation, yes/no	29.49	27.47–31.67	<.001
Surgical intervention, yes/no	0.32	0.308–0.334	<.001
Diagnostic category, “diseases and disorders of”			
Burns	1.033	0.391–2.669	.950
Blood, blood-forming organs, and immunologic	0.389	0.212–0.770	.004
Circulatory system	0.141	0.077–0.277	<.001
Digestive system	1.242	0.676–2.459	.510
Female reproductive system	0.611	0.132–2.070	.470
Hepatobiliary system and pancreas	1.665	0.901–3.312	.120
Kidney and urinary tract	0.684	0.360–1.390	.270
Musculoskeletal and connective tissue	0.541	0.289–1.087	.068
Nervous system	1.672	0.915–3.293	.110
Respiratory system	1.297	0.709–2.557	.430
Skin, subcutaneous tissue, and breast	1.530	0.763–3.237	.250
ENT/craniofacial	0.406	0.209–0.841	.011
Endocrine, nutritional, and metabolic	1.276	0.685–2.554	.470
HIV	1.579	0.290–6.978	.560
Infectious and parasitic diseases	1.182	0.649–2.324	.600
Lymphatic, hematopoietic, and other malignancies	0.791	0.433–1.557	.470
Mental disease and disorders	1.191	0.234–4.702	.810
Multiple significant trauma	2.176	1.183–4.311	.018
Newborns and perinatal conditions	0.906	0.498–1.778	.760
Other	0.877	0.482–1.724	.690
Poisonings, toxins, and other injuries	2.456	1.306–4.954	.008
Rehabilitation/aftercare	1.598	0.851–3.218	.170
Tracheostomy with long-term ventilation	0.990	0.542–1.947	.970
Transplant	0.333	0.182–0.656	<.001

ENT, xxx; PMCA, Pediatric Medical Complexity Algorithm; Ref, reference. —, xxx.

cannot identify the transfusion threshold used for a given transfusion, the indication for transfusion, the type of platelets (including storage solution, storage age and ABO compatibility), the platelet dose administered, or the

location in which the transfusion was administered. This lack of data limits our ability to identify particular platelet-specific factors that may be contributing to their associated morbidity. Additionally, information pertaining to patients’ underlying diagnosis is limited; we cannot determine the number of children with specific coagulopathies, which hinders our ability to analyze our populations’ baseline predisposition to thrombus. Because of the nature of the deidentified data, it could only be validated for those patients at our own institution and not across the entire data set. Although our validation process was thorough, we did not pull charts of those at our own institution who did not receive platelet transfusions according to the PHIS database, and therefore the sensitivity of the prevalence values was not tested. The database represents admissions at pediatric tertiary care centers and therefore may not be generalizable across all centers caring for children in the United States. Given the observational nature of the data, we cannot speak directly to the relationship and causality among different variables, which limits our understanding of how platelet transfusions may lead or pathologically contribute to their associated complications. Prospective interventional studies would be needed to prove causation.

This study provides an updated understanding of the epidemiology of platelet transfusions among pediatric inpatients over the past decade. The consistent prevalence of platelet transfusion from 2010 to 2019, despite increasing literature highlighting the adverse outcomes potentially associated with transfusion, emphasizes the need to explore the potential mechanisms underlying these associations.

COMPANION PAPER: A companion to this article can be found online at www.hosppeds.org/cgi/doi/10.1542/hpeds.2022-007034.

Ms Lang and Dr Nellis conceptualized and designed the study, and drafted the initial manuscript; Ms An completed the statistical analysis; Ms Finn and Mr Prishtina collected the data from the entire cohort; Dr Desimone collected data from the validation cohort; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

REFERENCES

1. Sapiiano MRP, Savinkina AA, Ellingson KD, et al. Supplemental findings from the National Blood Collection and Utilization Surveys, 2013 and 2015. *Transfusion*. 2017;57(Suppl 2):1599–1624
2. Goel R, Josephson CD, Patel EU, et al. Individual- and hospital-level correlates of red blood cell, platelet, and plasma transfusions among hospitalized children and neonates: a nationally representative study in the United States. *Transfusion*. 2020;60(8):1700–1712
3. Nellis ME, Goel R, Hendrickson JE, et al. NHLBI Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric. Transfusion practices in a large cohort of hospitalized children. *Transfusion*. 2021;61(7):2042–2053
4. Nellis ME, Karam O, Mauer E, et al. Pediatric Acute Lung Injury and Sepsis Investigators Network; Pediatric Critical Care Blood Research Network; P3T Investigators. Platelet transfusion practices in critically ill children. *Crit Care Med*. 2018;46(8):1309–1317
5. Nellis ME, Saini A, Spinella PC, et al. Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network; Pediatric Critical Care Blood Research Network; PlasmaTV Investigators; P3T Investigators. Pediatric plasma and platelet transfusions on extracorporeal membrane oxygenation: a subgroup analysis of 2 large international point-prevalence studies and the role of local guidelines. *Pediatr Crit Care Med*. 2020;21(3):267–275
6. Parker RI. Transfusion in critically ill children: indications, risks, and challenges. *Crit Care Med*. 2014;42(3):675–690
7. Lieberman L, Liu Y, Barty R, Heddle NM. Platelet transfusion practice and platelet refractoriness for a cohort of pediatric oncology patients: a single-center study. *Pediatr Blood Cancer*. 2020;67(12):e28734
8. Patel RM, Hendrickson JE, Nellis ME, et al. National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric. Variation in neonatal transfusion practice. *J Pediatr*. 2021;235:92–99.e4
9. Cashen K, Dalton H, Reeder RW, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Platelet transfusion practice and related outcomes in pediatric extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2020;21(2):178–185
10. Garraud O, Cognasse F, Tissot JD, et al. Improving platelet transfusion safety: biomedical and technical considerations. *Blood Transfus*. 2016;14(2):109–122
11. Kahn S, Chegondi M, Nellis ME, Karam O. Overview of plasma and platelet transfusions in critically ill children. *Front Pediatr*. 2020;8:601659
12. Akk k CA, Seghatchian J. Pediatric red cell and platelet transfusions. *Transfus Apheresis Sci*. 2018;57(3):358–362
13. Du Pont-Thibodeau G, Tucci M, Robitaille N, Ducruet T, Lacroix J. Platelet transfusions in pediatric intensive care. *Pediatr Crit Care Med*. 2016;17(9):e420–e429
14. Burstein DS, Griffiths H, Zhang X, et al. Resource utilization in children with paracorporeal continuous-flow ventricular assist devices. *J Heart Lung Transplant*. 2021;40(6):478–487
15. Benneyworth BD, Bennett WE, Carroll AE. Cross-sectional comparison of critically ill pediatric patients across hospitals with various levels of pediatric care. *BMC Res Notes*. 2015;8:693
16. Goel R, Nellis ME, Karam O, et al. NHLBI Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric. Transfusion practices for pediatric oncology and hematopoietic stem cell transplantation patients: data from the National Heart Lung and Blood Institute Recipient Epidemiology and Donor Evaluation Study-III (REDS-III). *Transfusion*. 2021;61(9):2589–2600
17. Nellis ME, Goel R, Karam O, et al. Pediatric Acute Lung Injury and Sepsis Investigators Network; Pediatric Critical Care Blood Research Network; Point Prevalence Study of Platelet Transfusions in Critically Ill Children Investigators. International study of the epidemiology of platelet transfusions in critically ill children with an underlying oncologic diagnosis. *Pediatr Crit Care Med*. 2019;20(7):e342–e351
18. Hanson SJ, Karam O, Birch R, et al. National Heart, Lung, and Blood Institute Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric. Transfusion practices in pediatric cardiac surgery requiring cardiopulmonary bypass: a secondary analysis of a clinical database. *Pediatr Crit Care Med*. 2021;22(11):978–987
19. Closson R, Mauer E, Stock A, et al. The use of hemostatic blood products in children following cardiopulmonary bypass and associated outcomes. *Crit Care Explor*. 2020;2(8):e0172
20. Pollak U, Ruderman T, Borik-Chiger S, Mishaly D, Serraf A, Vardi A. Transfusion-related acute hepatic injury following postoperative platelets administration in pediatric patients undergoing the Fontan procedure. *Congenit Heart Dis*. 2019;14(6):968–977
21. Cremer M, Sallmon H, Kling PJ, B hrer C, Dame C. Thrombocytopenia and platelet transfusion in the neonate. *Semin Fetal Neonatal Med*. 2016;21(1):10–18
22. Kasap T, Tak   S, Erdo an Irak B, et al. Neonatal thrombocytopenia and the role of the platelet mass index in platelet transfusion in the neonatal intensive care unit. *Balkan Med J*. 2020;37(3):150–156
23. Curley A, Stanworth SJ, Willoughby K, et al. PlaNet2 MATISSE Collaborators. Randomized trial of platelet-transfusion thresholds in neonates. *N Engl J Med*. 2019;380(3):242–251
24. Solutions for Patient Safety. Our results. Available at: <https://www.solutionsforpatientsafety.org/our-results/>. Accessed February 27, 2022
25. Goff Z, Abbotsford J, Yeoh DK, et al. The impact of a multifaceted tertiary pediatric hospital's antimicrobial stewardship service. *Pediatr Infect Dis J*. 2022;41(12):959–966

26. Goel R, Cushing MM, Tobian AA. Pediatric patient blood management programs: not just transfusing little adults. *Transfus Med Rev.* 2016;30(4):235–241
27. Nellis ME, Karam O, Valentine SL, et al. Pediatric Critical Care Transfusion and Anemia Expertise Initiative—Control/Avoidance of Bleeding, in collaboration with the Pediatric Critical Care Blood Research Network and the Pediatric Acute Lung Injury and Sepsis Investigators Network. Executive summary of recommendations and expert consensus for plasma and platelet transfusion practice in critically ill children: from the Transfusion and Anemia Expertise Initiative-Control/Avoidance of Bleeding (TAXI-CAB). *Pediatr Crit Care Med.* 2022;23(1):34–51
28. Nellis ME, Remy KE, Lacroix J, et al. Research priorities for plasma and platelet transfusion strategies in critically ill children: from the Transfusion and Anemia Expertise Initiative-Control/Avoidance of Bleeding. *Pediatr Crit Care Med.* 2022;23(13 Supple 1 1S):e63–e73
29. Foy R, Lorencatto F, Walwyn R, et al. Enhanced feedback interventions to promote evidence-based blood transfusion guidance and reduce unnecessary use of blood components: the AFFINITIE research programme including two cluster factorial RCTs. *NIHR Journals Library.* 2022:35377572