



Published in final edited form as:

Transfusion. 2025 May ; 65(5): 937–949. doi:10.1111/trf.18229.

Hospitalizations with blood transfusions and transfusion-related adverse events in US acute care hospitals, 2016–2020

Sophia V. Kazakova¹, Opal L. Reddy², Isabel Griffin¹, Lauri A. Hicks¹, Ian Kracalik¹, Sridhar V. Basavaraju¹

¹Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

²Department of Pathology, Keck School of Medicine of USC, California, Los Angeles, USA

Abstract

Background: National data on transfusion-related adverse events (TAEs) in the United States are limited. Administrative and payment-related data may augment hemovigilance systems to assess transfusion safety.

Study Design and Methods: A nationwide administrative database was analyzed to characterize transfusion-related hospitalizations and TAEs by trends, patient/hospital characteristics, and outcomes. Transfusions and TAEs were identified using medical codes and charges. Generalized estimating equations (GEE) modeled transfusion trends, while logistic regression assessed transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI) risk factors.

Results: During 2016–2020, 8.4% of hospitalizations involved transfusions, with red blood cell (RBC) transfusion being most common (5.2%). In 2020, compared to 2016, hospitalizations with RBC transfusion decreased by 2% (Rate Ratio (RR) 0.98; 95% CI: 0.97–0.99), while plasma transfusion hospitalizations increased by 13% (RR 1.13; 95% CI: 1.08–1.19). TAEs occurred in 0.35% of hospitalizations (3.5/1000 transfusion hospitalizations). Among the TAEs included in the study, TACO, febrile nonhemolytic reactions, and TRALI were most common. In 27% of cases, the specific TAE was unidentified. TAEs were associated with higher inpatient mortality and longer lengths of stay. Variability in TAE rates was observed by patient and hospital characteristics. Risk factors for TACO included age >64, female sex, teaching hospitals, rural location, and Northeast region. TRALI risk was higher in teaching hospitals and those with >200 beds.

Conclusion: Administrative data provide insights into transfusion practices and associated morbidity and mortality but have limitations. Linking administrative, electronic health record, and blood bank data may enhance TAE identification.

This article is a U.S. Government work and is in the public domain in the USA.

Correspondence: Sophia V. Kazakova, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30329, USA. srk7@cdc.gov.

CONFLICT OF INTEREST STATEMENT

The authors have disclosed no conflicts of interest.

Keywords

acute care hospitals; blood transfusions; hemovigilance; hospitalizations; patient safety; transfusion-related adverse events

1 | INTRODUCTION

Blood transfusions are a common procedure in US acute care hospitals.¹ Although widely considered safe, transfusions can cause adverse reactions ranging from mild to life-threatening and, in some cases, fatality. Ensuring the safety of transfusion procedures and adequacy of the blood supply requires monitoring blood utilization and transfusion-related adverse events (TAEs). In the United States, the National Healthcare Safety Network (NHSN) Hemovigilance Module, operated by the Centers for Disease Control and Prevention (CDC), and the National Blood Collection and Utilization Survey (NBCUS), operated by the CDC and the Department of Health and Human Services Office of the Assistant Secretary of Health, collect national data on blood utilization and TAEs.^{2,3} Although these systems provide critical insights into blood transfusion safety at a national level, they offer limited information on hospitalizations involving transfusion and TAEs, including patient and hospital characteristics and the impact of adverse events on patient outcomes such as length of stay and all-cause mortality. Additionally, the voluntary nature of the NHSN Hemovigilance system has resulted in low hospital engagement, with only 360 hospitals enrolled, primarily from Massachusetts, where participation is mandatory. This limited participation may result in incomplete representation of TAEs nationwide. The increasing availability of large electronic healthcare databases presents an opportunity to address these limitations and evaluate their potential to complement current hemovigilance efforts. By leveraging these resources, we can better understand the risks associated with blood transfusions, supporting efforts to improve transfusion practices and outcomes.

This study utilized PINC AI™, a real-world healthcare database representing acute care hospitals nationwide, to identify and characterize hospitalizations involving blood transfusions by blood product type, as well as by patient and hospital characteristics. As a secondary objective, we identified TAEs using clinical diagnostic codes and described the frequency of these events across census divisions and according to patient and hospital characteristics. Lastly, we investigated factors associated with the two leading causes of transfusion-associated fatality: transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI).⁴

2 | MATERIALS AND METHODS

Hospital discharge and inpatient billing records from over 900 hospitals participating in the PINC AI™⁵ healthcare database (Premier hospitals) from 2016 to 2020 were evaluated. The PINC AI™ database comprises administrative, clinical, and financial data submissions from participating US hospitals representing diverse geographical and practice settings. Hospitalizations with blood transfusion were identified using the International Classification of Diseases, 10th Revision, Procedure Coding System (ICD-10-PCS)⁶ and Current Procedural Terminology (CPT) (Supplementary Tables S1 and S2). To ensure

complete identification of blood transfusion procedures, we also reviewed hospital billing records for charge descriptions that clearly identified a transfusion procedure.

For each reporting year, the proportion of hospitalizations with transfusion was calculated by dividing the total number of hospitalizations with transfusion by the total number of hospitalizations among all transfusing hospitals. A transfusing hospital was defined as a hospital with at least one transfusion during the reporting year.

Annual trends in the proportions of hospitalizations with transfusion were examined using three multivariable generalized estimating equation (GEE) models⁷ for each blood product: red blood cells (RBC), plasma, or platelets. The models accounted for autocorrelation in transfusion proportions within each facility and specified a negative binomial distribution of outcome, natural log of monthly discharges as an offset for the proportions, and exchangeable working correlation structure. The models were adjusted for seasonality, categorical annual trend, and facility characteristics (urban vs. rural location, bed size [five categories], teaching status, and census region).

For hospitalizations involving a transfusion, we identified the occurrence of TAEs using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes that specifically indicate an adverse event related to transfusion (Supplementary Table S3).⁸ These ICD-10-CM codes were categorized into 10 groupings: transfusion associated circulatory overload (TACO), febrile nonhemolytic transfusion reaction (FNHTR), transfusion-related acute lung injury (TRALI), hemolytic, transfusion-related anaphylaxis (Anaphylactic), posttransfusion purpura (PTP), transfusion-transmitted infection (TTI), air embolism following transfusion, ABO incompatibility, and adverse event unspecified (Unspecified). As overlap among diagnostic codes existed between acute and delayed hemolytic reactions, both were grouped into a single category. The Unspecified category included ICD-10-CM diagnostic codes that did not specify the type of reaction and were included to fully describe the burden of adverse events related to transfusion.

The proportion of hospitalizations with a TAE was calculated by dividing the total number of hospitalizations with adverse events by the total number of hospitalizations with transfusion. The TAE rates per 1000 hospitalizations with transfusion were also calculated and described by patient and hospital characteristics. The hospitalizations involving transfusion and TAE as well as TAE rates were described by outcomes such as inpatient all-cause mortality and length of stay.

To examine factors associated with the development of TACO and TRALI among all hospitalizations involving transfusion, we fitted two individual-level logistic regression models, one for the outcome of TRALI and one for the outcome of TACO. Each model included all hospitalizations involving transfusion, the outcome of the TRALI or TACO (Yes/No), and the following parameters: year of discharge (categorical, with 2016 as a referent year); patient age (five categories), sex (male, female), and race (White, Black, Asian, Other, Unknown); and facility characteristics (urban vs. rural location, bed size [five categories], teaching status, and census region [four categories]). In addition, we described the transfusion hospitalizations' primary diagnoses and procedures, using Healthcare Cost

and Utilization Project (HCUP) Clinical Classification Software (CCS) categories,^{9,10} which were part of the PINC AI™ database (For results refer to Supplementary Table S4).

This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy (See e.g., 45 CFR part 46; 21 CFR part 56; 42 USC §241 (d), 5 USC §552a, 44 USC §3501 et seq.). All data were analyzed using SAS version 9.4 software (SAS Institute, Cary, NC).

3 | RESULTS

During the study period, blood transfusion procedures occurred in 8.4% of all hospitalizations in the Premier hospitals. Among these, RBC transfusions were the most common (5.2%), followed by plasma, platelet, and whole blood transfusions (0.95%, 0.78%, and 0.02%, respectively) (Table 1). The overall proportion of hospitalizations with a blood transfusion procedure was stable during 2016–2019 (around 8.2%), but then increased to 9.5% in 2020. In the multivariable analysis of temporal trends by specific blood products, we observed a small but statistically significant increase (1%) in the proportion of hospitalizations with RBC transfusions in 2018 and 2019 compared to 2016 (Figure 1). However, in 2020, this proportion decreased by 2% compared to 2016 (rate ratio [RR] 0.98, $p < .001$). In contrast, the proportion of hospitalizations involving plasma transfusion decreased by 6% in 2019 but subsequently increased by 13% in 2020, relative to 2016. No consistent trend was observed for hospitalizations with platelet transfusion. For full model results see Supplementary Table S5.

A transfusion-related adverse event was identified in 12,145 (0.35%) of all hospitalizations involving transfusion. Among these events, TACO, FNHTR, and TRALI were the most documented, with rates of 1.16, 0.71, and 0.65 per 1000 transfusion hospitalizations, respectively (Table 2). Posttransfusion purpura and transfusion transmitted infections were rare, occurring at rates of 0.04 and 0.02 per 1000 transfusion hospitalizations, respectively. In 3275 (27%) hospitalizations with a TAE, the specific event could not be identified (Table 1).

The transfusion-related adverse event rates varied by patient age, event type, and race/ethnicity (Table 2). The highest TAE rate occurred in patients aged 18–54 years (3.93 per 1000 transfusion hospitalizations), followed closely by pediatric patients (3.73). This elevated rate in pediatric patients was primarily driven by a higher incidence of FNHTR, hemolytic reactions, anaphylactic reactions, and unspecified reactions. Conversely, TACO was more prevalent among older patients, with rates of 1.22 and 1.61 per 1000 transfusion hospitalizations in those aged 65–74 and ≥ 75 years, respectively. TRALI exhibited a different pattern, being most common among middle-aged adults, with rates of 0.78, 0.73, and 0.70 per 1000 transfusion hospitalizations in the 18–54, 55–64, and 65–74 age groups, respectively. The youngest (0–17 years) and oldest (> 75 years) age groups had the lowest TRALI rates. Sex disparities were observed, with higher rates of TACO and FNHTR in females (1.24 and 0.73, respectively) compared to males (1.07 and 0.68). Racial/ethnic differences were evident, with White and Asian patients experiencing the highest TACO rates (1.23 and 1.31, respectively), while Black patients had the highest rates of FNHTR and

hemolytic reactions (0.78 and 0.19, respectively). Hispanic patients had the highest rates of FNHTR and TRALI (0.89 and 0.75, respectively).

Emergency and urgent admissions had the highest rates of TACO (1.30 and 1.22, respectively) and FNHTR (0.76 and 0.74, respectively). Transfusion hospitalizations at trauma centers showed the highest rate of TRALI (0.98). Among insurance groups, Medicare patients had the highest TACO rate (1.37), while Medicaid patients had the highest FNHTR rate (1.00). Patients classified as charity or uninsured had the highest overall rate of TAEs (4.10). This elevated rate was primarily driven by a higher incidence of unspecified TAEs (1.41) in this group.

Adverse event rates also varied by hospital characteristics. The largest hospitals (500+ beds) had the highest overall adverse event rate (3.95 per 1000 transfusion hospitalizations), as well as the highest rates for specific events, including TACO, FNHTR, TRALI, and hemolytic reactions. In contrast, the smallest hospitals (<100 beds) had the lowest overall event rate (2.93); however, their FNHTR rate was the second highest, following the largest hospitals. Rural hospitals had a higher rate of TACO compared to urban hospitals (1.39 vs. 1.13). Conversely, urban hospitals had higher rates of FNHTR and TRALI (0.72 and 0.66, respectively) than rural hospitals (0.58 and 0.57). Teaching hospitals had the highest overall adverse event rate (4.03 vs. 2.93), as well as higher rates across all types of TAEs compared to nonteaching hospitals. Lastly, regional variability was observed, with hospitals in New England recording the highest overall adverse event rate (4.73) and the highest TACO rate (2.10).

Hospitalizations with TAE were associated with longer lengths of stay (12.4 days) compared to all hospitalizations with transfusion (9.6 days) (Table 2). The longest LOS was observed in hospitalizations with PTP, TRALI, and TTI at 17.8, 16.5, and 16.2 days, respectively. Inpatient mortality was also higher in hospitalizations with a TAE (15.5%) compared to the mortality rate (11.4%) in all hospitalizations with transfusion. The highest mortality was observed in hospitalizations with TRALI (32.3%).

In the individual-level multivariable logistic regression analysis of factors associated with TACO (Figure 2), the odds of TACO increased by 16% in 2018 and 30% in 2019 compared to 2016 (odds ratios [ORs]: 1.16, $p = .027$; and 1.30, $p < .001$, respectively). A steady increase in the odds of TACO was observed across age groups, with ORs ranging from 0.45 for the youngest group (ages 0–17) to 1.62 in those aged 75 and older, relative to the 55–64 age group. Additionally, Black patients had 14% lower odds of developing TACO compared to White patients (OR 0.86; $p < .001$). Higher odds of TACO were significantly associated with teaching hospitals, location in the Northeast census region, and rural setting, with ORs of 1.29, 1.38, and 1.35, respectively.

In a similar analysis of TRALI (Figure 3), both the youngest (0–17) and the oldest (≥ 75) age groups had significantly lower odds of developing TRALI compared to those aged 55–64 (ORs: 0.55 and 0.66, respectively). Asian and Black patients also had significantly lower odds of TRALI compared to White patients, with ORs of 0.59 and 0.79, respectively. Teaching hospitals and those with more than 200 beds were associated with higher odds of

TRALI. Lastly, hospitals located in the Midwest, Northeast, or South census regions had lower odds of TRALI compared to hospitals in the West.

4 | DISCUSSION

Blood transfusions are a cornerstone of modern healthcare, with 11% of all hospital stays in the United States in 2010 involving this life-saving procedure.¹¹ Although blood transfusions are generally considered safe, they are not without risk. Continuous national surveillance of transfusion practices and transfusion-related adverse events is essential to improving patient care and identifying trends that may place patient safety at risk. Existing hemovigilance systems in the United States collect valuable information on transfusion practices and adverse events through surveys and both voluntary and mandatory reporting mechanisms. However, these systems currently provide limited granular detail specific to patient and healthcare facility characteristics. To address this gap, our study leveraged a large, nationwide administrative healthcare database to analyze hospitalizations involving blood transfusions. Our primary motivation for this study was to evaluate the feasibility of using administrative data to complement traditional hemovigilance systems to uncover new insights into transfusion safety and utilization.

Overall, our findings support the feasibility of using administrative data to evaluate blood transfusion practices and safety in the United States, though certain limitations remain. By analyzing medical procedure codes and hospital charges, we identified 3.5 million hospitalizations involving transfusion out of a total of 40.9 million hospitalizations across 999 transfusing facilities. This extensive dataset enabled us to uncover critical trends and identify rare TAEs. We found that red blood cell transfusion, the most common type, was involved in 5.2% of hospitalizations during 2016–2020, aligning with the 4% reported for 2015–2018 in the National Inpatient Sample, the largest all-payer inpatient database.¹² Additionally, when compared with the published estimate of hospitalizations with transfusion in 2010 (11%), our estimate from 2016 to 2020 (8.4%) reflects a 24% decline. This reduction aligns with the widespread adoption of patient blood management programs, advancements in surgical techniques, and improved management of clinical conditions that previously required transfusion.^{13,14}

Our characterization of hospitalizations involving transfusions revealed that transfusions were more frequent among older adults, males, Black, and non-Hispanic patients. They were also more common in emergent, urgent, or trauma center admissions, patients with Medicare coverage, and in larger (≥ 500 beds) or teaching hospitals. Furthermore, we observed a 16% increase in the overall proportion of hospitalizations involving transfusion in 2020 compared to 2019, driven largely by a 13% rise in plasma transfusions. This increase aligns with the heightened use of COVID-19 convalescent plasma during the early pandemic period.^{15,16} Interestingly, when we excluded patients with a COVID-19 diagnosis, plasma transfusion trends showed a decline, emphasizing the unique impact of the pandemic on transfusion practices (Supplementary Figures S1 and S2). Despite the surge in plasma transfusions, our individual-level risk factor analysis for TACO and TRALI showed no elevated risks for these severe adverse events in 2020 compared to 2016 (Figures 2 and 3). These findings

suggest that while transfusion practices and overall healthcare utilization shifted during the pandemic, the underlying risk factors for severe adverse events remained stable.

Our analysis of TAE incidence relied on ICD-10 diagnostic codes and showed that TAEs remained relatively rare, being observed in 0.35% of all hospitalizations involving transfusions. Previous studies using alternative methods, such as clinical reports and symptom-based assessments, have reported TAE incidence rates ranging from 0.2% to 3%.^{17–20} These variations reflect differences in detection methods, populations studied, and the types of adverse events included. For instance, a prospective six-hospital study, which relied on clinical reports and other data, estimated the incidence of transfusion reactions at 0.67%.²⁰ This aligns with our finding of 0.35%, especially since our analysis excluded mild allergic reactions, which represent the majority of TAEs.^{20,21} When considering all TAEs, pediatric patients in our study demonstrated a higher overall rate (3.73 per 1000 hospitalizations with transfusion), compared to older adults (3.5 and 3.3 per 1000 in 65–74 and >75 age groups, respectively). Pediatric patients also had the highest rate of hemolytic and anaphylactic reactions and a high rate of FNHTR, consistent with previously reported analyses.^{20,22} These findings highlight the necessity of vigilant monitoring and targeted preventive strategies to mitigate the risks of these reactions in the pediatric population.

Our evaluation of the incidence of TRALI showed that it was coded in 0.07% of all hospitalizations involving transfusion, similar to previous studies.^{23,24} However, the incidence of TACO was 0.12%, which is significantly lower than the 1%–10% reported previously.^{23,25–27} Data from the NHSN HM and other international systems also demonstrate that TACO is more common than TRALI.^{28–30} The likely under-recognition of TACO in ICD-10 codes can be attributed to several factors, one of which is the overlap of TACO symptoms (e.g., shortness of breath, cough, pulmonary edema) with those of other medical conditions, such as heart failure, acute respiratory distress syndrome, or fluid overload from non-transfusion causes. TACO may be underrecognized as a distinct transfusion-related complication, leading to underdocumentation or miscoding. Given TACO's role as a leading cause of transfusion-associated morbidity and mortality, accurate identification and reporting are essential for patient safety and national policy guidance.

Several other important findings emerged regarding hospital and patient characteristics and outcomes. Specifically, we observed higher rates of TAEs in larger hospitals and those with academic affiliations compared to smaller and nonacademic facilities. Several factors may explain this variability: (1) greater awareness of transfusion reactions and the presence of dedicated transfusion medicine specialists in teaching hospitals, (2) targeted training on diagnosing, managing, and reporting adverse reactions in facilities with formal hemovigilance programs, and (3) the more complex patient populations in academic centers, who may be at higher risk for TAEs. Our finding of the highest overall TAE rate among uninsured/charity patients, primarily driven by a high rate of unspecified events, warrants further investigation. This elevated rate may suggest deficiencies in documentation and coding quality in facilities serving underserved populations, or greater disease complexity and severity among uninsured patients.

In terms of patient outcomes, we found that patients with TAEs had a longer average LOS (12.4 days) compared to those without (9.6 days), consistent with previous research.^{31,32} Prolonged stays increase resource utilization and the risk of healthcare-associated complications, such as infections.³³ Additionally, inpatient mortality was significantly higher among patients with TAE (15.5%) than those without (11.4%), with the highest mortality observed in TRALI cases (32.3%). To fully understand the impact of TAEs on patient outcomes, it is essential to include data on the timing of transfusion procedures and TAEs. While large administrative data offer significant potential for analyzing the impact of adverse events across facilities and regions, their utility will be limited without detailed information on timing.

Another limitation of administrative data is its reliance on ICD-10 codes in capturing TAEs. Previous research highlighted the misalignment between adverse events recorded in electronic health records and those reported and confirmed by blood bank investigation.^{34,35} These inconsistencies may be due to hospitals' variations in adverse event documentation practices. Inpatient coders typically rely on clinical provider notes from admission, daily progress, and discharge summaries when assigning ICD-10 codes. However, provider notes may not consistently document transfusion reaction diagnoses in the medical record even if these reactions are reported to and investigated by transfusion services. Generally, mild adverse reactions, such as simple allergic or febrile nonhemolytic events, which resolve quickly and often appear clinically insignificant, may be under-recorded in provider diagnoses. Even when documented and reported to hemovigilance systems, these events may not be routinely reviewed during the hospitalization coding process. Consequently, healthcare databases may be skewed toward documenting more severe reactions. To address this, efforts should focus on improving clinician awareness, standardizing documentation practices, integrating transfusion service data, and leveraging electronic health record technology to flag potential TAEs based on clinical parameters, laboratory findings, or transfusion-related entries.

In our study, 27% of hospitalizations with TAEs were coded as "Unspecified transfusion reaction," potentially contributing to both underestimation and overestimation of specific reactions. Additionally, the structure of administrative data poses limitations. Unlike hemovigilance systems that express reaction rates relative to total units transfused, our dataset lacked information on number of products transfused per hospitalization, preventing trend analysis by transfusion volume. Furthermore, the lack of chronological data linking adverse events to transfusion procedures limited our ability to attribute these events to specific types of transfused products. Lastly, our analysis of inpatient service charges enabled identification of an additional 31% of hospitalizations with transfusion that were not captured by ICD-10 and CPT procedure codes alone (Supplementary Table S6). We validated our method of identifying transfusion procedures using charges and billing records by comparing TAE rates between hospitalizations identified through codes and those identified through charge review, finding similar rates across both methods. However, due to the lack of detailed blood product information in charge descriptions, our estimates of hospitalizations by blood product type are likely lower than the actual numbers.

In conclusion, this study highlights the value of utilizing large administrative and billing records to supplement hemovigilance systems, thereby enhancing our understanding of transfusion safety in the United States. These data provide detailed patient- and facility-level information, making them particularly useful for identifying and characterizing transfusion practices and their impact on patient outcomes. However, reliance on ICD-10 codes limits the ability to reliably and accurately identify transfusion-related adverse events. Improving data completeness and accuracy will require linking administrative datasets with blood bank records and clinical documentation from electronic health records. Lastly, the observed variation in rate estimates for reactions such as TACO underscores the ongoing need for hospitals to engage in formal hemovigilance to accurately capture the risks of transfusion and better inform patients and providers. CDC continues to collaborate with partners, including the Association for the Advancement of Blood and Biotherapies, to streamline and improve hemovigilance reporting in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We thank Dr. James Baggs for his valuable review and insightful contribution to the statistical analysis methods employed in this study.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. This work was supported through salary funds of the authors. The authors have no conflicts or other relevant financial support to report.

Abbreviations:

CCS	clinical classification software
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus Disease 2019
CPT	Current Procedural Terminology
FNHTR	febrile non-hemolytic transfusion reaction
GEE	generalized estimating equation
HCUP	healthcare cost and utilization project
ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification
ICD-10-PCS	International Classification of Diseases, 10th Revision, Procedure Coding System
LOS	length of stay
NBCUS	National Blood Collection and Utilization Survey

NHSN	National Healthcare Safety Network
PTP	post-transfusion purpura
RBC	red blood cells
TACO	transfusion-associated circulatory overload
TAE	transfusion-related adverse event
TRALI	transfusion-related acute lung injury
TTI	transfusion-transmitted infection

REFERENCES

- Goel R, Chappidi MR, Patel EU, Ness PM, Cushing MM, Frank SM, et al. Trends in red blood cell, plasma, and platelet transfusions in the United States, 1993–2014. *JAMA*. 2018; 319(8):825–7. [PubMed: 29486023]
- Kracalik I, Sapiano MRP, Wild RC, Chavez Ortiz J, Stewart P, Berger JJ, et al. Supplemental findings of the 2021 National Blood Collection and utilization survey. *Transfusion*. 2023;63-(Suppl 4):S19–42. [PubMed: 37702255]
- Kracalik I, Mowla S, Basavaraju SV, Sapiano MRP. Transfusion-related adverse reactions: data from the National Healthcare Safety Network Hemovigilance Module - United States, 2013–2018. *Transfusion*. 2021;61(5):1424–34. [PubMed: 33880771]
- Fatalities Reported to FDA Following Blood Collection and Transfusion. 2021 Accessed August 23, 2024.
- PINC AI Healthcare Database: Data that Informs and Performs. https://offers.premierinc.com/rs/381-NBB-525/images/PINC_AI_Healthcare_Data_White_Paper.pdf
- Centers for Medicare & Medicaid Services. ICD-10 Procedure Coding System (ICD-10-PCS), 2024 (10th ed.). U.S. Department of Health and Human Services. 2024 Accessed August 23, 2024.
- Inc. SI. SAS/STAT® 14.3 User's Guide: The GENMOD Procedure. 2020.
- Centers for Disease Control and Prevention. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) 2019. National Center for Health Statistics. 2019 Accessed August 23, 2024.
- Clinical Classifications Software Refined (CCSR) for ICD-10-CM diagnoses. Accessed September 12, 2024.
- Clinical Classifications Software Refined (CCSR) for ICD-10-PCS Procedures. Accessed September 12, 2024.
- Pfuntner ATHA, Wier LM, Truven Health Analytics, Stocks C, AHRQ. Most Frequent Procedures Performed in U.S. Hospitals, 2010. HCUP Statistical Brief #149. 2013 Agency for Healthcare Research and Quality Rockville, MD.
- Goel R, Zhu X, Patel EU, Crowe EP, Ness PM, Katz LM, et al. Blood transfusion trends in the United States: national inpatient sample, 2015 to 2018. *Blood Adv*. 2021;5(20):4179–84. [PubMed: 34551093]
- Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, et al. Red blood cell transfusion: a clinical practice guideline from the AABB*. *Ann Intern Med*. 2012;157(1):49–58. [PubMed: 22751760]
- Carson JL, Guyatt G, Heddle NM, Grossman BJ, Cohn CS, Fung MK, et al. Clinical practice guidelines from the AABB: red blood cell transfusion thresholds and storage. *JAMA*. 2016; 316(19):2025–35. [PubMed: 27732721]
- Kazakova SV, Baggs J, Parra G, Yusuf H, Romano SD, Ko JY, et al. Declines in the utilization of hospital-based care during COVID-19 pandemic. *J Hosp Med*. 2022;17(12):984–9. [PubMed: 36039477]

16. Senefeld JW, Gorman EK, Johnson PW, Moir ME, Klassen SA, Carter RE, et al. Rates among hospitalized patients with COVID-19 treated with convalescent plasma: a systematic review and meta-analysis. *Mayo Clin Proc Innov Qual Outcomes*. 2023;7(5):499–513. [PubMed: 37859995]
17. Goel R, Tobian AAR, Shaz BH. Noninfectious transfusion-associated adverse events and their mitigation strategies. *Blood*. 2019;133(17):1831–9. [PubMed: 30808635]
18. Roubinian NH, Hendrickson JE, Triulzi DJ, Gottschall JL, Chowdhury D, Kor DJ, et al. Incidence and clinical characteristics of transfusion-associated circulatory overload using an active surveillance algorithm. *Vox Sang*. 2017;112(1):56–63. [PubMed: 28001313]
19. Semple JW, Rebetz J, Kapur R. Transfusion-associated circulatory overload and transfusion-related acute lung injury. *Blood*. 2019;133(17):1840–53. [PubMed: 30808638]
20. Vossoughi S, Chacreton D, Jimenez A, Stone E, Luban N, Josephson CD, et al. On behalf of the REDS-IV-P: Maternal, In-utero, Neonatal, Kids (MINeKids) Committee. Febrile and allergic transfusion reaction rates are higher in children than in adults. Presented at: 2024 AABB Annual Meeting; Houston, Texas.
21. Hirayama F Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. *Br J Haematol*. 2013;160(4):434–44. [PubMed: 23215650]
22. Vossoughi S, Perez G, Whitaker BI, Fung MK, Stotler B. Analysis of pediatric adverse reactions to transfusions. *Transfusion*. 2018;58(1):60–9. [PubMed: 28948619]
23. Roubinian N TACO and TRALI: biology, risk factors, and prevention strategies. *Hematology Am Soc Hematol Educ Program*. 2018;2018(1):585–94. [PubMed: 30570487]
24. Toy P, Gajic O, Bacchetti P, Looney MR, Gropper MA, Hubmayr R, et al. Transfusion-related acute lung injury: incidence and risk factors. *Blood*. 2012;119(7):1757–67. [PubMed: 22117051]
25. Li G, Rachmale S, Kojicic M, Shahjehan K, Malinchoc M, Kor DJ, et al. Incidence and transfusion risk factors for transfusion-associated circulatory overload among medical intensive care unit patients. *Transfusion*. 2011;51(2):338–43. [PubMed: 20723173]
26. Edens C, Haass KA, Cumming M, Osinski A, O’Hearn L, Passanisi K, et al. Evaluation of the National Healthcare Safety Network Hemovigilance Module for transfusion-related adverse reactions in the United States. *Transfusion*. 2019;59(2):524–33. [PubMed: 30427540]
27. Clifford L, Jia Q, Yadav H, Subramanian A, Wilson GA, Murphy SP, et al. Characterizing the epidemiology of perioperative transfusion-associated circulatory overload. *Anesthesiology*. 2015;122(1):21–8. [PubMed: 25611653]
28. Harvey AR, Basavaraju SV, Chung KW, Kuehnert MJ. Transfusion-related adverse reactions reported to the National Healthcare Safety Network Hemovigilance Module, United States, 2010 to 2012. *Transfusion*. 2015;55(4):709–18. [PubMed: 25371300]
29. Rana R, Fernandez-Perez ER, Khan SA, Rana S, Winters JL, Lesnick TG, et al. Transfusion-related acute lung injury and pulmonary edema in critically ill patients: a retrospective study. *Transfusion*. 2006;46(9):1478–83. 10.1111/j.1537-2995.2006.00930.x [PubMed: 16965572]
30. van den Akker TA, Grimes ZM, Friedman MT. Transfusion-associated circulatory overload and transfusion-related acute lung injury. *Am J Clin Pathol*. 2021;156(4):529–39. [PubMed: 33822854]
31. West KA, Barrett ML, Moore BJ, Miller JL, Steiner CA. Trends in Hospitalizations With a Red Blood Cell Transfusion, 2000–2013. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Healthcare Research and Quality; 2006.
32. Morton J, Anastassopoulos KP, Patel ST, Lerner JH, Ryan KJ, Goss TF, et al. Frequency and outcomes of blood products transfusion across procedures and clinical conditions warranting inpatient care: an analysis of the 2004 healthcare cost and utilization project nationwide inpatient sample database. *Am J Med Qual*. 2010;25(4):289–96. [PubMed: 20530223]
33. Jeon CY, Neidell M, Jia H, Sinisi M, Larson E. On the role of length of stay in healthcare-associated bloodstream infection. *Infect Control Hosp Epidemiol*. 2012;33(12):1213–8. [PubMed: 23143358]
34. Jhaveri P, Bozkurt S, Moyal A, Belov A, Anderson S, Shan H, et al. Analyzing real world data of blood transfusion adverse events: opportunities and challenges. *Transfusion*. 2022;62(5): 1019–26. [PubMed: 35437749]

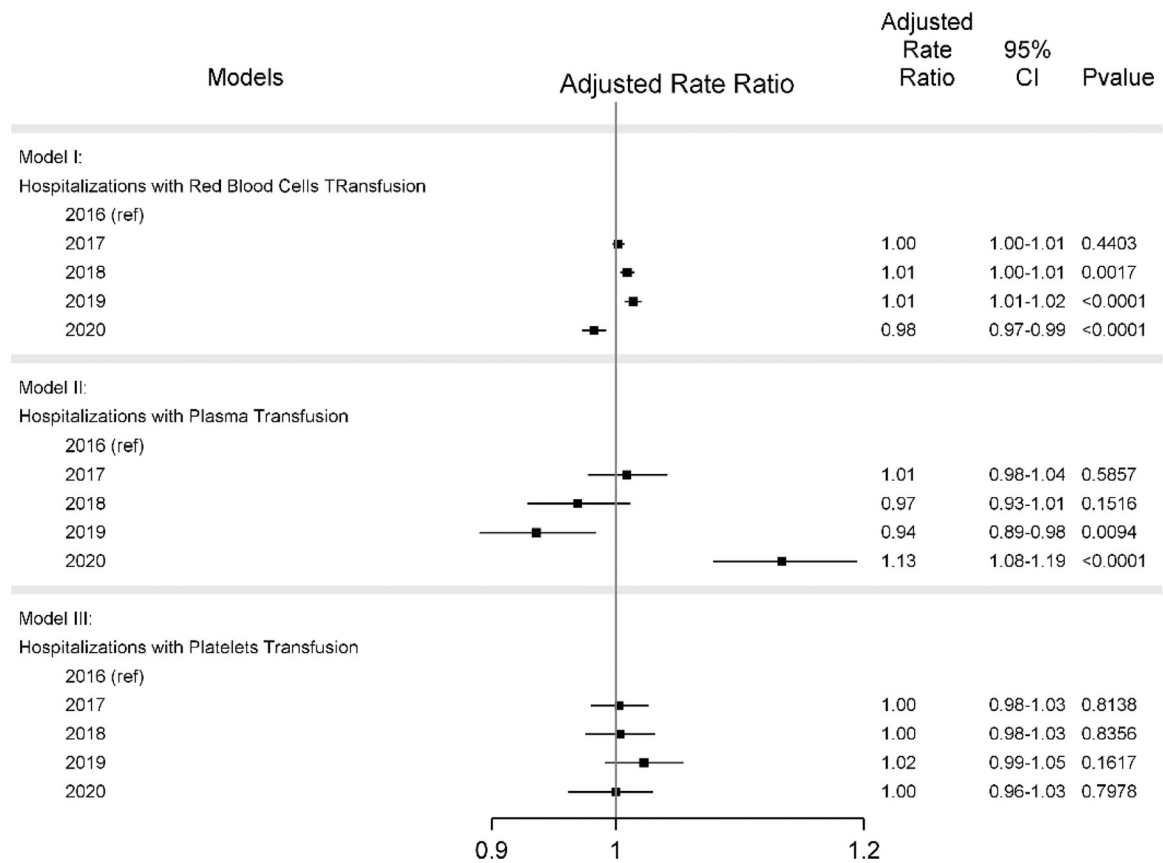
35. Dubeck D Blood transfusion events—lessons learned from a complex process. Pa Patient Saf Advis. 2016;13(3):100–7.

Author Manuscript

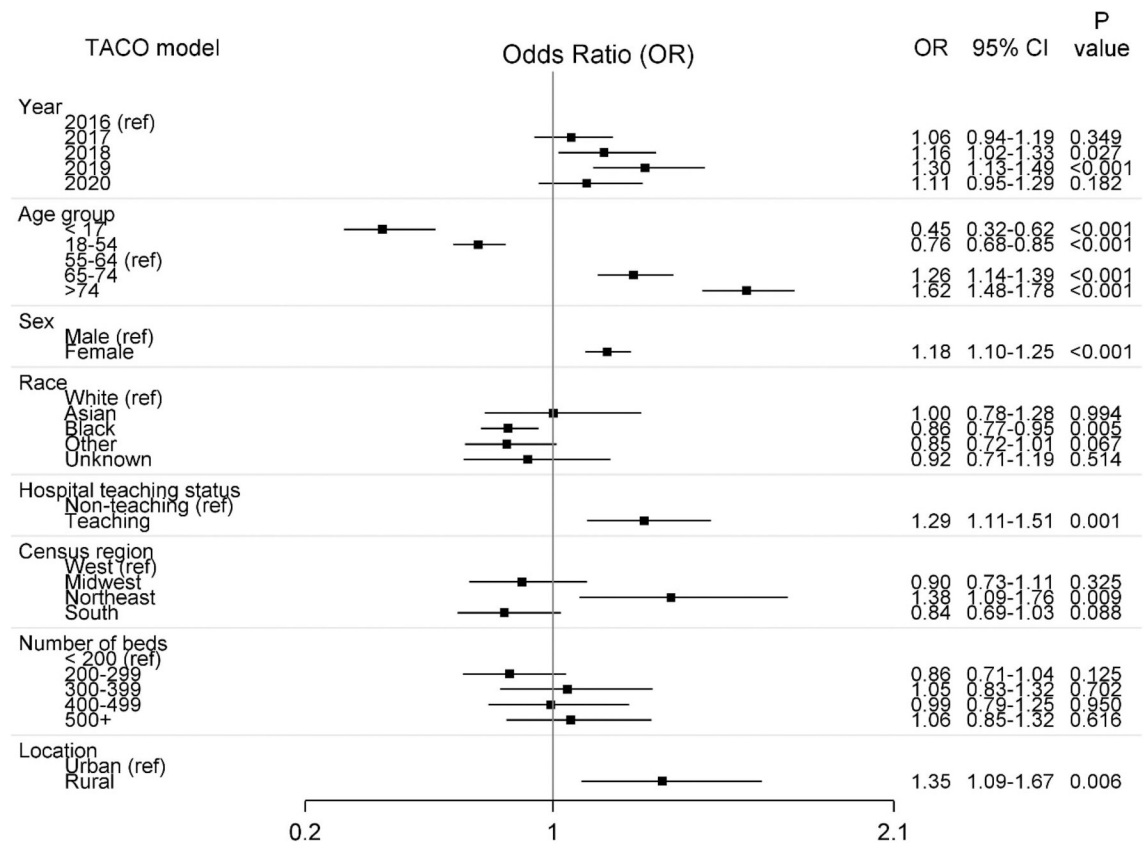
Author Manuscript

Author Manuscript

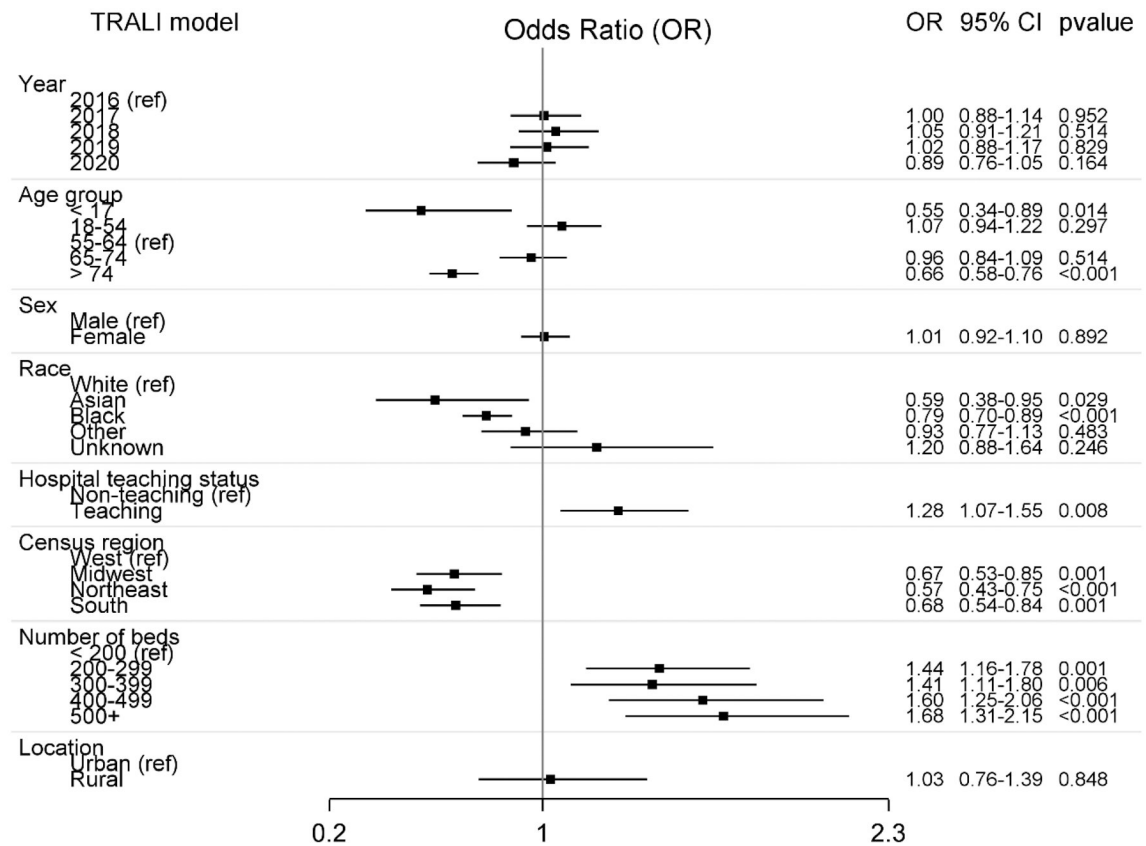
Author Manuscript

**FIGURE 1.**

Adjusted^a annual trends in the proportions of hospitalizations with red blood cell (Model I), plasma (Model II), and platelet (Model III) transfusions in premier hospitals, 2016–2020. CI, confidence interval. ^aEach model adjusted for facility characteristics (number of beds [five categories], teaching status, rural versus urban location, and census region) and autocorrelation of facility-level rates within hospitals through the GEE modeling approach. For the full model results, see Supplement Table S5.

**FIGURE 2.**

Logistic regression analysis of factors associated with transfusion associated circulatory overload (TACO) among hospitalized patients with blood transfusion, 2016–2020.

**FIGURE 3.**

Logistic regression analysis of factors associated with transfusion-related acute lung injury (TRALI) among hospitalized patients with blood transfusion, 2016–2020.

TABLE 1
Hospitalizations with blood transfusion and transfusion-related adverse events occurring among US acute care hospitals participating in the PINC AI™ Healthcare Database, 2016–2020.

	2016	2017	2018	2019	2020	Total
No. of facilities ^a	811	850	814	847	789	999
No. of hospitalizations ^b	8,353,641	8,753,275	8,365,360	8,387,478	7,118,336	40,978,090
No. (%) ^c of hospitalizations with blood product transfusion	681,580 (8.16)	718,731 (8.21)	693,724 (8.29)	684,136 (8.16)	672,527 (9.45)	3,450,698 (8.42)
Red Blood Cells	426,793 (5.11)	438,029 (5.00)	425,184 (5.08)	433,585 (5.17)	406,783 (5.71)	2,130,374 (5.20)
Plasma	80,881 (0.97)	79,700 (0.91)	74,477 (0.89)	71,619 (0.85)	84,318 (1.18)	390,955 (0.95)
Platelets	64,386 (0.77)	66,601 (0.76)	64,159 (0.77)	65,183 (0.78)	60,327 (0.85)	320,656 (0.78)
Whole Blood	2132 (0.03)	1825 (0.02)	1708 (0.02)	1653 (0.02)	1545 (0.02)	8863 (0.02)
Blood product unknown	200,783 (2.40)	228,766 (2.61)	220,705 (2.64)	205,351 (2.45)	209,054 (2.94)	1,064,659 (2.60)
No. (%) of transfusion hospitalizations with transfusion-related adverse event	2192 (0.32)	2396 (0.33)	2446 (0.35)	2689 (0.39)	2422 (0.36)	12,145 (0.35)
TACO	694 (0.10)	785 (0.11)	839 (0.12)	920 (0.13)	761 (0.11)	3999 (0.12)
FNHTR	393 (0.06)	457 (0.06)	500 (0.07)	559 (0.08)	526 (0.08)	2435 (0.07)
TRALI	448 (0.07)	472 (0.07)	470 (0.07)	451 (0.07)	396 (0.06)	2237 (0.06)
Hemolytic	66 (0.01)	76 (0.01)	65 (0.01)	80 (0.01)	80 (0.01)	367 (0.01)
Anaphylactic	53 (0.01)	49 (0.01)	62 (0.01)	44 (0.01)	40 (0.01)	248 (0.01)
Posttransfusion Purpura	27 (0.00)	23 (0.00)	26 (0.00)	32 (0.00)	20 (0.00)	128 (0.00)
Transfusion Transmitted Infection	9 (0.00)	10 (0.00)	12 (0.00)	13 (0.00)	11 (0.00)	55 (0.00)
Air embolism	6 (0.00)	4 (0.00)	1 (0.00)	11 (0.00)	2 (0.00)	24 (0.00)
ABO incompatibility	3 (0.00)	4 (0.00)	3 (0.00)	3 (0.00)	2 (0.00)	15 (0.00)
Unspecified	588 (0.09)	623 (0.09)	599 (0.09)	726 (0.11)	739 (0.11)	3275 (0.09)

Abbreviations: TACO, transfusion-associated circulatory overload; FNHTR, febrile nonhemolytic transfusion reaction; TRALI, transfusion-related acute lung injury.

^a Facilities included in the study are those that had at least one blood transfusion during the reported year.

^b All hospitalizations in the included facilities.

^c Percentage calculated as: number of hospitalizations with specific blood product transfusion/total number of hospitalizations with transfusion * 100.

TABLE 2
 Characteristics of hospitalizations with blood transfusion and rates of transfusion-related adverse events (per 1000 hospitalizations with transfusion) in US acute care hospitals ($N = 999$), 2016–2020.

	All hospitalizations (%) ($N = 40,978,090$)	Hospitalizations with transfusion (%) ($N = 3,450,698$)	Hospitalizations with transfusion adverse event (%) ($N = 12,145$)	Any adverse event ($N = 12,145$)	TACO ($N = 3999$)	FNHTR ($N = 2435$)	TRALI ($N = 2237$)	Hemolytic ($N = 367$)	Anaphylactic ($N = 248$)	PIP ($N = 128$)	TTI ($N = 55$)	Unspecified ($N = 3275$)
Transfusion-related Adverse event rate per 1000 hospitalizations with transfusion												
Hospitalization outcome												
Mean length of stay, days (SD)	4.5 (6.7)	9.6 (13.5)	12.4 (15.5)	12.4 (15.5)	11.7 (13.4)	10.5 (13.4)	16.5 (17.2)	13.3 (17.5)	10.3 (10.9)	17.8 (40.2)	16.2 (16.9)	11.9 (16.1)
Died during hospitalization or discharged to hospice	3.9%	11.4%	15.5%	15.5%	16.1%	7.9%	32.3%	10.6%	10.5%	12.5%	10.9%	11.7%
Patient characteristics												
Overall				3.52	1.16	0.71	0.65	0.11	0.07	0.04	0.02	0.95
Age group (years)												
0–17	13.8%	2.8%	3.0%	3.73	0.45	0.97	0.43	0.18	0.19	0.03	0.01	1.62
18–54	32.4%	23.9%	26.6%	3.93	0.73	1.00	0.78	0.16	0.11	0.05	0.02	1.25
55–64	15.0%	18.3%	17.2%	3.30	0.96	0.65	0.73	0.11	0.06	0.04	0.02	0.92
65–74	17.0%	23.7%	23.6%	3.50	1.22	0.69	0.70	0.10	0.06	0.04	0.01	0.87
75+	22.0%	31.4%	29.7%	3.33	1.61	0.50	0.48	0.06	0.05	0.02	0.02	0.74
Sex												
Female	56.8%	53.3%	55.1%	3.64	1.24	0.73	0.64	0.13	0.07	0.04	0.01	0.98
Male	43.2%	46.7%	44.9%	3.38	1.07	0.68	0.65	0.08	0.08	0.04	0.02	0.91
Unknown	0.0%	0.0%	0.0%	0	0	0	0	0	0	0	0	0.00
Race												
White	70.8%	69.2%	69.5%	3.54	1.23	0.67	0.66	0.09	0.07	0.03	0.02	0.93
Black	14.4%	17.6%	16.8%	3.36	0.94	0.78	0.57	0.19	0.07	0.04	0.01	0.95
Asian	2.4%	2.7%	2.7%	3.59	1.31	0.70	0.48	0.03	0.09	0.03	0.01	1.06
Other	9.1%	8.1%	8.4%	3.64	1.00	0.82	0.68	0.09	0.09	0.07	0.01	1.06
Unknown	3.3%	2.5%	2.6%	3.75	1.12	0.78	0.86	0.07	0.07	0.07	0.01	0.97

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

	All hospitalizations (%) (N = 40,978,090)	Hospitalizations with transfusion (%) (N = 3,450,698)	Hospitalizations with transfusion adverse event (%) (N = 12,145)	Any adverse event (N = 12,145)	TACO (N = 3999)	FNHTR (N = 2435)	TRALI (N = 2237)	Hemolytic (N = 367)	Anaphylactic (N = 248)	PIP (N = 128)	TTI (N = 55)	Unspecified (N = 3275)
Ethnicity												
Hispanic	9.3%	8.8%	9.9%	3.97	0.98	0.89	0.75	0.07	0.09	0.04	0.02	1.38
Non-Hispanic	71.1%	75.9%	74.3%	3.45	1.15	0.68	0.63	0.11	0.07	0.03	0.01	0.92
Unknown	19.6%	15.4%	15.8%	3.63	1.33	0.72	0.67	0.11	0.06	0.06	0.02	0.82
Admission type												
Emergency	54.3%	66.0%	69.7%	3.71	1.30	0.76	0.64	0.12	0.06	0.04	0.02	0.97
Elective	19.4%	15.5%	11.1%	2.52	0.61	0.55	0.52	0.05	0.09	0.03	0.01	0.76
Urgent	13.7%	14.9%	16.7%	3.96	1.22	0.74	0.80	0.11	0.10	0.03	0.02	1.11
Trauma Center	0.9%	1.8%	1.6%	3.06	0.77	0.40	0.98	0.18	0.08	0.02	0.00	0.77
Newborn	10.6%	0.9%	0.1%	0.47	0.13	0.00	0.13	0.07	0.00	0.03	0.03	0.10
Unknown	1.1%	1.0%	0.9%	2.99	0.71	0.34	0.68	0.06	0.00	0.03	0.00	1.31
Payor												
Medicare	43.4%	60.5%	57.8%	3.36	1.37	0.59	0.58	0.09	0.05	0.03	0.02	0.80
Medicaid	21.8%	14.6%	16.1%	3.89	0.81	1.00	0.75	0.16	0.09	0.06	0.01	1.22
Managed Care	20.7%	14.3%	15.2%	3.74	0.84	0.86	0.75	0.12	0.13	0.05	0.02	1.15
Commercial	7.2%	5.9%	5.4%	3.20	0.88	0.80	0.87	0.16	0.09	0.05	0.01	0.99
Charity or Uninsured	6.9%	4.8%	5.6%	4.10	0.80	0.71	0.66	0.10	0.10	0.03	0.02	1.41
Hospital characteristics												
Number of beds												
500+	35.1%	39.6%	44.4%	3.95	1.25	0.82	0.77	0.13	0.08	0.04	0.02	1.08
400–499	12.1%	11.8%	11.7%	3.49	1.12	0.65	0.72	0.11	0.07	0.04	0.01	0.92
300–399	17.0%	17.2%	15.7%	3.21	1.12	0.62	0.59	0.08	0.08	0.03	0.01	0.83
200–299	16.7%	15.4%	13.9%	3.18	1.01	0.60	0.60	0.09	0.06	0.03	0.01	0.93
100–199	13.8%	11.6%	10.7%	3.22	1.17	0.63	0.47	0.10	0.07	0.04	0.02	0.86
0–99	5.3%	4.4%	3.7%	2.93	1.08	0.76	0.27	0.10	0.03	0.05	0.01	0.66
Urban/rural location												
Urban	88.1%	88.2%	88.4%	3.53	1.13	0.72	0.66	0.11	0.07	0.04	0.02	0.96

	All hospitalizations (%) (N = 40,978,090)	Hospitalizations with transfusion (%) (N = 3,450,698)	Hospitalizations with transfusion adverse event (%) (N = 12,145)	Any adverse event (N = 12,145)	TACO (N = 3999)	FNHTR (N = 2435)	TRALI (N = 2237)	Hemolytic (N = 367)	Anaphylactic (N = 248)	PIP (N = 128)	TTI (N = 55)	Unspecified (N = 3275)
Rural	11.9%	11.8%	11.6%	3.44	1.39	0.58	0.57	0.11	0.07	0.03	0.02	0.84
Teaching status												
Yes	49.6%	53.7%	61.4%	4.03	1.31	0.85	0.74	0.13	0.09	0.04	0.02	1.07
No	50.4%	46.3%	38.6%	2.93	0.98	0.54	0.54	0.08	0.05	0.03	0.01	0.81
Census division												
South Atlantic (DC, DE, FL, GA, MD, NC, SC, VA, WV)	27.3%	30.5%	29.9%	3.44	1.04	0.62	0.67	0.11	0.07	0.03	0.02	1.07
Middle Atlantic (NJ, NY, PA)	14.7%	14.5%	18.9%	4.59	1.71	1.25	0.59	0.15	0.09	0.06	0.03	0.92
East North Central (IL, IN, MI, OH, WI)	16.1%	14.0%	13.6%	3.43	1.01	0.79	0.65	0.10	0.04	0.03	0.02	0.96
West South Central (AR, LA, OK, TX)	11.4%	13.8%	12.0%	3.07	1.02	0.49	0.67	0.09	0.08	0.04	0.01	0.83
Pacific (AK, CA, HI, OR, WA)	10.0%	8.8%	8.3%	3.33	1.10	0.57	0.72	0.08	0.06	0.03	0.01	0.93
East South Central (AL, KY, MS, TN)	7.3%	8.7%	5.8%	2.38	0.77	0.41	0.46	0.07	0.08	0.04	0.01	0.61
West North Central (IA, KS, MN, MO, ND, NE, SD)	5.6%	4.9%	5.0%	3.63	1.43	0.63	0.63	0.14	0.10	0.03	0.02	0.78
New England (CT, MA, ME, NH, RI, VT)	2.4%	2.4%	3.2%	4.73	2.10	1.02	0.44	0.14	0.10	0.05	0.01	1.01
Mountain (AZ, CO, ID, MT, NM, NV, UT, WY)	5.3%	2.5%	3.2%	4.50	1.04	0.61	1.13	0.06	0.07	0.03	0.00	1.82

Abbreviations: ACO, transfusion-associated circulatory overload; FNHTR, febrile nonhemolytic transfusion reaction; PTP, posttransfusion Purpura; TRALI, transfusion-related acute lung injury; TTI, transfusion-transmitted infection.