

Implementation of a Comprehensive Patient Blood Management Program for Hospitalized Patients at a Large United States Medical Center

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Abstract

Objective: To assess changes in inpatient transfusion utilization and patient outcomes with implementation of a comprehensive patient blood management (PBM) program at a large US medical center.

Patients and Methods: This is an observational study of graduated PBM implementation for hospitalized adults (age ≥ 18 years) from January 1, 2010, through December 31, 2017, at two integrated hospital campuses at a major academic US medical center. Allogeneic transfusion utilization and clinical outcomes were assessed over time through segmented regression with multivariable adjustment comparing observed outcomes against projected outcomes in the absence of PBM activities.

Results: In total, 400,998 admissions were included. Total allogeneic transfusions per 1000 admissions decreased from 607 to 405 over the study time frame, corresponding to an absolute risk reduction for transfusion of 6.0% (95% confidence interval [CI]: 3.6%, 8.3%; $P < .001$) and a 22% (95% CI: 6%, 37%; $P = .006$) decrease in the rate of transfusions over projected. The risk of transfusion decreased for all blood components except cryoprecipitate. Transfusion reductions were experienced for all major surgery types except liver transplantation, which remained stable over time. Hospital length of stay (multiplicative increase in geometric mean 0.85 [95% CI: 0.81, 0.89]; $P < .001$) and incident in-hospital adverse events (absolute risk reduction: 1.5% [95% CI: 0.1%, 3.0%]; $P = .04$) were lower than projected at the end of the study time frame.

Conclusion: Patient blood management implementation for hospitalized patients in a large academic center was associated with substantial reductions in transfusion utilization and improved clinical outcomes. Broad-scale implementation of PBM in US hospitals is feasible without signal for patient harm.

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In an effort to reduce low-value medical practices, improve patient outcomes, and reduce costs of care, a growing number of hospitals have invested in patient blood management (PBM) programs as one potential solution.¹⁻³ In a general sense, PBM can be described as the design, timely implementation, and longitudinal evaluation of a multifaceted set of educational and clinical practice tools to improve the blood

health of patients. A key component of PBM is the optimization of transfusion practice, including efforts to ensure that transfusion behavior is conducted in accordance with the latest scientific evidence, thereby reducing or eliminating unnecessary allogeneic transfusions, which have consistently been associated with poor patient outcomes.⁴ This is increasingly important in times of blood shortages, such as those



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experienced during the coronavirus disease 2019 (COVID-19) pandemic.^{2,5} Indeed, the United States is currently experiencing unprecedented shortages in blood inventories secondary to insufficient donations to meet the demand of growing hospital activity,^{6,7} further highlighting the importance of efforts to safely reduce transfusion utilization.

Previous investigations in select patient groups⁸⁻¹³ and broader health care systems^{14,15} have shown that hospital-based PBM interventions are reliably associated with reductions in transfusion utilization. Assessments of PBM-associated changes in clinical outcome are more limited in scope, and it remains critical to ensure that patients are not being harmed by PBM activities, including more restrictive transfusion behaviors. Further, data regarding changes in both transfusion utilization and clinical outcomes after comprehensive PBM implementation in large US health care systems are limited. Additionally, previous models of PBM implementation have generally neglected to compare observed post-intervention outcomes against projected outcomes in the absence of PBM activities. Such analyses are likely to provide a more complete assessment of PBM-associated changes in outcomes than simple before-after comparisons.

In this investigation, we describe changes in transfusion utilization and clinical outcomes for hospitalized adults during staged PBM implementation at a large academic US medical center.

METHODS

This is a historical observational cohort study conducted under approval of the Mayo Clinic (Rochester, MN, USA) Institutional Review Board. The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.¹⁶

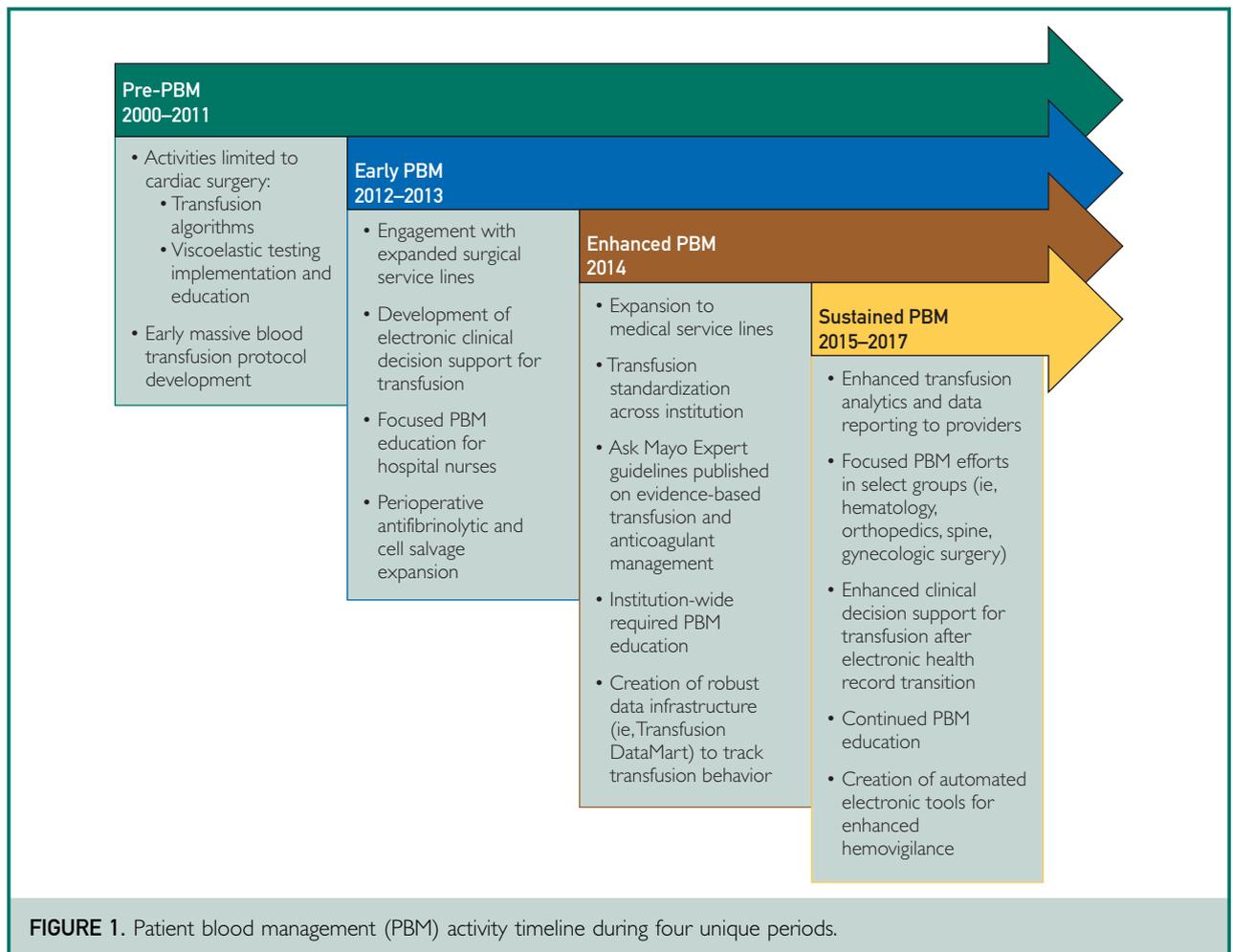
Study Population

This study included all inpatient admissions (hospital duration ≥ 24 hours) for adults (age ≥ 18 years) at Mayo Clinic in Rochester, Minnesota, from January 2010 through December 2017, including admissions at

two integrated but free-standing hospital campuses: Rochester Methodist Campus (794 licensed beds) and Saint Marys Campus (1265 licensed beds). The following exclusions were applied before data analysis: 1) patients who previously denied medical record authorization for observational research, and 2) patients receiving massive transfusion (ie, ≥ 10 units in any 24-hour period).

Description of the PBM Intervention

Patient blood management efforts at the study institution initiated in cardiac surgery in the early-to-mid 2000s, with these efforts focused on defining and implementing transfusion algorithms for the reduction of allogeneic transfusions in cardiac surgery.¹⁷ In 2012, broader engagement of clinical practices at the Mayo Clinic Rochester campus was initiated, including expansion to additional surgical services, with a complete timeline of PBM activities provided in Figure 1. These early PBM efforts were substantially enhanced in 2014 and have been sustained since. Several key activities initiated in 2014 include: 1) the Transfusion Standardization project, which defined evidence-based transfusion guidelines (Supplemental Table 1, available online at <http://www.mayoclinicproceedings.org>) to ensure that all practice areas across the Mayo Clinic enterprise were using consistent and appropriate thresholds for transfusion; these guidelines were incorporated into the Ask Mayo Expert clinical practice tool (an internal Web-based platform that provides guidance for clinical decisions) and electronic clinical decision support for blood transfusion orders; 2) the creation of a robust transfusion data infrastructure to monitor transfusion behavior (ie, the Transfusion DataMart, described below); and 3) required PBM education for all medical professionals, completed as a series of online modules describing the goal of PBM activities and encouraging appropriate transfusion utilization (ie, evidence-based thresholds for transfusion, single unit default orders¹⁸) and hemovigilance. In this investigation, the intervention is presented



in four unique periods based on the intensity of PBM activities: pre-PBM (2010–2011), early PBM (2012–2013), enhanced PBM (2014), and sustained PBM (2015–2017).

During the study period, the Mayo Clinic PBM program has been led by a physician medical director (no protected full-time equivalent [FTE]), one to two dedicated registered nurse program coordinators (each 1.0 FTE), and a data engineer/programmer (0.2 FTE). This group meets formally every week and directs all day-to-day activities of PBM at the study institution. Additionally, the medical director of the PBM program also leads the institutional blood management committee. This multidisciplinary committee contains broader membership of relevant institutional stakeholders (eg, physician, nurse, administrative,

and technical staff from various surgical and medical specialties, Emergency Medicine, Critical Care, Pediatrics, Obstetrics, Pharmacy, and Transfusion Medicine). The committee meets every other month and is responsible for overseeing transfusion utilization and safety across the practice, while ensuring alignment of PBM activities with broader institutional objectives. Engagement with other key personnel, including those from Information Systems, Education, and Operations Management, happens on an as-needed basis.

Transfusion Data Analytics

The Transfusion DataMart was created by the PBM program to facilitate the collection and validation of data relating to transfusion therapies. This institutional resource

integrates data streams from the electronic health record systems and transfusion medicine services to gather highly granular information on all transfusion episodes, with comprehensive data available from 2005 through the present. This includes details related to the transfusion episode (eg, ordering and supervising medical professional, product and donor characteristics, location and timing of product ordering, issuing, and administration, and pretransfusion and post-transfusion laboratory values) as well as information related to recipient outcomes (eg, transfusion reactions and physiologic responses to the transfusion episode). Additional clinical outcomes of interest (ie, morbid events, intensive care unit [ICU] admissions, hospital duration, and mortality) are obtained through other validated internal data systems, including the Advanced Cohort Explorer and the Acute Care DataMart.¹⁹ Each of these data systems undergoes continuous data validation.

Outcomes

Outcomes were divided into transfusion utilization and patient clinical outcomes, with each outcome defined before data collection. The primary transfusion outcome of interest was the rate of admissions with any allogeneic transfusion, with secondary outcomes including the rates of admissions with any individual component therapy (ie, red blood cells [RBCs], plasma, platelets, and cryoprecipitate) and the total number of allogeneic units transfused. These outcomes were ascertained through the Transfusion DataMart. Clinical outcomes of interest included the hospital length of stay, hospital mortality, composite incident adverse events during hospitalization (ie, myocardial infarction, venous thromboembolic disease including deep venous thrombosis and pulmonary embolism, stroke, acute respiratory failure, and transfusion reactions), and the individual adverse event components. Incident adverse events were identified through the Transfusion DataMart (ie, transfusion reactions, such as febrile, allergic, and hemolytic transfusion reactions, transfusion-related acute lung injury, and transfusion-associated

circulatory overload) and by Advanced Cohort Explorer—facilitated queries of the medical record for new clinical diagnoses not present on admission. Additionally, we assessed changes in transfusion utilization across several prespecified surgery types with historically high rates of transfusion, including: major gynecologic oncology surgery (ie, open abdominal-pelvic tumor debulking), total hip and total knee arthroplasty, major spine surgery exclusive of minimally invasive approaches, orthotopic liver transplantation, and isolated coronary artery bypass grafting of any number of vessels exclusive of operations with combined valve or other procedures.

Statistical Approach

Demographic and clinical features are presented for each of the four discrete study periods with data summarized as n (%) for categorical variables and median (interquartile range [IQR]) for continuous variables. Changes in transfusion and clinical outcomes over the study period are assessed using segmented generalized linear regression models²⁰ adjusted for variables selected a priori, including patient age, sex, Charlson comorbidity index scores, medical versus surgical admissions, and admission location (ie, general care, ICU, progressive care unit). The segmented regression models changes associated with early PBM, enhanced PBM, and sustained PBM. Admission date in years since January 1, 2010, was the unit of time. Categorical outcomes were modeled using the linear probability model, and model estimates are presented as risk differences (ie, absolute risk reduction [ARR] for negative risk differences when estimated outcomes are lower than projected outcomes) with 95% CI. Rate of transfusions per admission was modeled using the linear count model, and model estimates are presented as rate differences. Hospital length of stay was modeled on the log scale with the identity link function and estimates presented are for the multiplicative increase in the geometric mean. All models account for multiple observations per subject (multiple admissions during the

study period) using robust variance estimates (ie, generalized estimating equations). We compared estimated 2017 rates of outcomes from our model to those projected from our model under the assumption of no PBM (setting the PBM-related coefficients to zero).

Changes in outcomes were also estimated according to admission type (medical vs surgical) and transfusion (yes vs no, only for clinical outcomes) in interaction analyses. Subgroup estimates are reported using a linear contrast with the interaction terms. A comparison *P* value reflects the difference between medical versus surgical in the assessment of the association between PBM and event. A two-sided alpha of .05 was used to determine statistical significance. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

A total of 400,998 hospital admissions were included (Supplemental Figure 1, available online at <http://www.mayoclinicproceedings.org>) with median (IQR) patient age of 62 (46-74) years and equal gender distribution.

This included 98,784 pre-PBM, 99,859 early PBM, 50,059 enhanced PBM, and 152,296 sustained PBM patients. Demographic, clinical, and hospitalization characteristics for the study cohort were generally similar throughout the study period (Table 1). Medical admissions (n=227,692; 56.8%) were more common than surgical admissions.

The proportion of admissions with any transfusion and the distribution of transfused units over time (normalized per 1000 admissions) are displayed graphically for the entire cohort and for medical and surgical admissions (Figure 2). A total of 30,052 units were transfused in 2010 which decreased to 20,926 units in 2017, corresponding to 607 transfusions per 1000 admissions in 2010 and 405 per 1000 admissions in 2017. These changes were mediated by both complete transfusion avoidance (ie, more patients with no transfusion exposure) and by progressive reductions in the number of allogeneic units administered to transfusion recipients (Supplemental Table 2, available online at <http://www.mayoclinicproceedings.org>). In adjusted analyses, the risk of any transfusion was lower than projected by 6% (ARR: 6.0%

TABLE 1. Patient Demographics and Admission Characteristics by Patient Blood Management Implementation Period^{a,b}

	Pre-PBM (n=98,784)	Early PBM (n=99,859)	Enhanced PBM (n=50,059)	Sustained PBM (n=152,296)
Age, years	61 (46-73)	61 (46-73)	61 (46-74)	62 (47-74)
Sex				
Female	50,012 (50.6)	50,054 (50.1)	24,769 (49.5)	74,918 (49.2)
Male	48,772 (49.4)	49,805 (49.9)	25,290 (50.5)	77,378 (50.8)
Charlson score	4 (2-7)	4 (2-7)	4 (2-7)	4 (2-7)
Initial admission location				
General care	78,165 (79.1)	78,871 (79.0)	39,293 (78.5)	116,030 (76.2)
ICU	14,557 (14.7)	14,678 (14.7)	7,522 (15.0)	22,939 (15.1)
Progressive care unit	6,062 (6.1)	6,310 (6.3)	3,244 (6.5)	13,327 (8.8)
Surgical encounter ^c	43,738 (44.3)	43,357 (43.4)	21,260 (42.5)	64,951 (42.6)
ICU stay during hospitalization	20,338 (20.6)	20,595 (20.6)	10,189 (20.4)	30,896 (20.3)

^aPBM, patient blood management; ICU, intensive care unit.

^bData are summarized as n (%) for categorical variables and median (interquartile range) for continuous variables. Multiple admissions per patient are summarized.

^cDefined as any encounter during which the patient underwent a surgical procedure, exclusive of other interventional procedures (eg, endoscopy, interventional radiology). Encounters not defined as surgical were considered medical encounters.

[95% CI: 3.6%-8.3%]; $P < .001$) (Table 2, Figure 3). Decreases were observed in RBCs (ARR: 5.6% [95% CI: 3.3%-7.9]; $P < .001$), plasma (ARR: 1.2% [95% CI: 0.2%-2.2%]; $P = .02$), and platelets (ARR: 1.3% [95% CI 0.1%-2.5%]; $P = .04$). Cryoprecipitate administration increased over time, although increases were not significantly different than projected (ARR: 0.2% [95% CI: -0.1% to 0.5%]; $P = .19$). The rate of allogeneic transfusions decreased by 22% more than projected (rate difference: -0.22 [95% CI: -0.37 to -0.06]; $P = .006$). Similar changes in transfusions were observed in both medical and surgical admissions, although platelet transfusion reductions were greater in medical (ARR: 2.4% [95% CI: 0.7%-4.2%]) than surgical admissions (ARR: 0.2% [95% CI: -1.6 to 1.3]; $P = .02$) (Supplemental Table 3, available online at <http://www.mayoclinicproceedings.org>).

Hospital length of stay and composite in-hospital adverse events were lower than projected at the end of the study period (multiplicative increase in geometric mean: 0.85 [IQR: 0.81-0.89]; $P < .001$; and ARR: 1.5% [IQR: 0.1%-3.0%]; $P = .04$; respectively) (Table 2). Hospital mortality and individual in-hospital adverse events were not significantly different from projected. Observed versus estimated changes in clinical outcomes are displayed graphically (Supplemental Figure 2, available online at <http://www.mayoclinicproceedings.org>). Similar differences from projected clinical outcomes were observed in admissions with and without transfusions, with the exception of hospital length of stay which was decreased in admissions without transfusion and was not significantly different from expected in admissions with transfusion (interaction $P = .003$) (Supplemental Table 4, available online at <http://www.mayoclinicproceedings.org>).

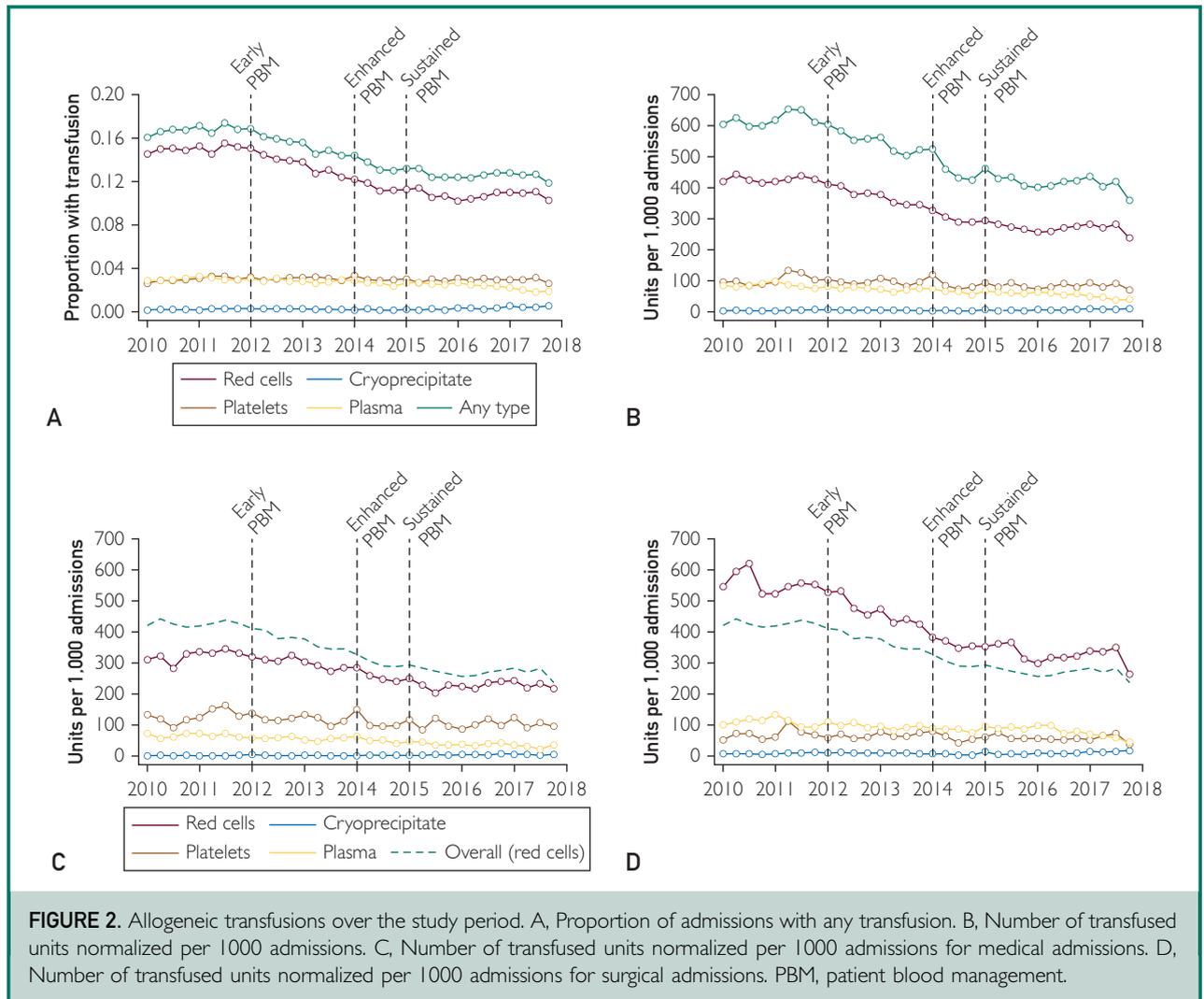
Regarding major surgical procedures, there were progressive reductions in the annual rates of transfusion for major gynecologic, total hip and knee arthroplasty, major spine, and coronary artery bypass surgery (Table 3). Transfusions for liver transplantation remained largely stable over time. For

all other surgical admissions, the annual rate of transfusion per 1000 admissions decreased from 762 to 480 over the study period.

DISCUSSION

In this investigation of graduated PBM implementation in a large tertiary care hospital system, the intervention was associated with substantial reductions in transfusion utilization over time, including a 22% multiplicative decrease in total allogeneic units transfused and a 6% ARR for transfusion beyond projections after multivariable adjustment. These decreases were experienced for all major blood components, except for cryoprecipitate, and across both medical and surgical admissions. Additionally, PBM implementation was associated with an estimated 15% reduction in hospital length of stay beyond projected and a reduction in composite in-hospital adverse events.

This study adds to the growing body of evidence regarding the value of PBM programs in reducing unnecessary transfusion behaviors.⁸⁻¹⁵ Indeed, transfusion reductions are a key metric for all PBM programs, with the greatest reductions observed in RBC utilization. These reductions were likely driven by several factors: 1) widespread education efforts, including required educational modules, to disseminate the most up-to-date evidence-based transfusion guidelines; 2) computerized physician order entry and clinical decision support implementation to provide “just-in-time” assistance for transfusion decisions incorporating real-time clinical and laboratory information, as described previously^{1,15,18}; 3) the use of transfusion analytics with direct feedback to the ordering provider regarding his/her transfusion practice in relation to peers; 4) direct engagement with surgical and medical service lines regarding the optimization of transfusion behavior; and 5) other factors not directly related to internal PBM activities, such as broader recognition and acceptance of the importance of blood conservation through resources such as the



American Board of Internal Medicine's Choosing Wisely campaign.²¹

Whereas RBC, plasma, and platelet utilization were all significantly lower than projected, the greatest absolute reductions were observed in RBC and plasma components with less pronounced changes in platelet utilization. Although the reason for this is unclear, platelet transfusions are typically given for the prevention and/or treatment of bleeding episodes in high-risk patients (eg, perioperatively and for the critically ill) and evidence to support or refute more restrictive platelet transfusion practices in these patient groups lacks the same weight of evidence as that in the robust RBC literature. Importantly, medical admissions did

experience greater reductions in platelet utilization when compared with surgical patients, and our group has previously reported substantial reductions in use with focused PBM activities in select patient groups, such as those undergoing hematopoietic stem cell transplantation.⁸ Additionally, the cardiac surgery team is one of our largest users of platelet components, and algorithms to optimize platelet utilization in this group were already in place preceding broader PBM efforts.¹⁷ Unlike other blood components, cryoprecipitate utilization actually increased over the study period, although not beyond projections. This is likely related to increased emphasis on the importance of hypofibrinogenemia

TABLE 2. Estimated Differences in Transfusion and Clinical Outcomes Correlated With Patient Blood Management Implementation^a

Outcome	Difference	
	Estimate (95% CI)	P
Transfusion outcomes		
Any allogeneic transfusion	-6.0 (-8.3 to -3.6)	<.001
Number of transfusions ^b	-0.22 (-0.37 to -0.06)	.006
Red blood cells	-5.6 (-7.9 to -3.3)	<.001
Plasma	-1.2 (-2.2 to -0.2)	.02
Platelets	-1.3 (-2.5 to -0.1)	.04
Cryoprecipitate	-0.2 (-0.5 to 0.1)	.19
Hospital outcomes/events		
Hospital length of stay ^c	0.85 (0.81 to 0.89)	<.001
Hospital mortality	-0.2 (-0.9 to 0.4)	.47
Any in-hospital adverse event ^d	-1.5 (-3.0 to -0.1)	.04
Acute respiratory failure	-0.4 (-1.4 to 0.6)	.40
Myocardial infarction	-0.5 (-1.2 to 0.2)	.18
Venous thromboembolism	-0.6 (-1.5 to 0.4)	.24
Stroke	-0.2 (-0.5 to 0.2)	.32
Transfusion reaction	-0.1 (-0.4 to 0.1)	.18

^aResults are from segmented regression analyses adjusted for Charlson comorbidity index, medical vs surgical admission, age, sex, and admission source. Estimates correspond to risk differences and are presented as absolute percentages except for hospital length of stay, which corresponds to multiplicative increase in the geometric mean, and number of transfusions which corresponds to the estimated rate difference. To assess the association between patient blood management (PBM) and outcomes we compared estimated 2017 rates of outcomes from our model to those extrapolated from our model under the assumption of no PBM (setting the PBM-related coefficients to zero).

^bEstimates are for the difference in rate of transfusions.

^cEstimates are for the multiplicative increase in geometric mean hospital length of stay.

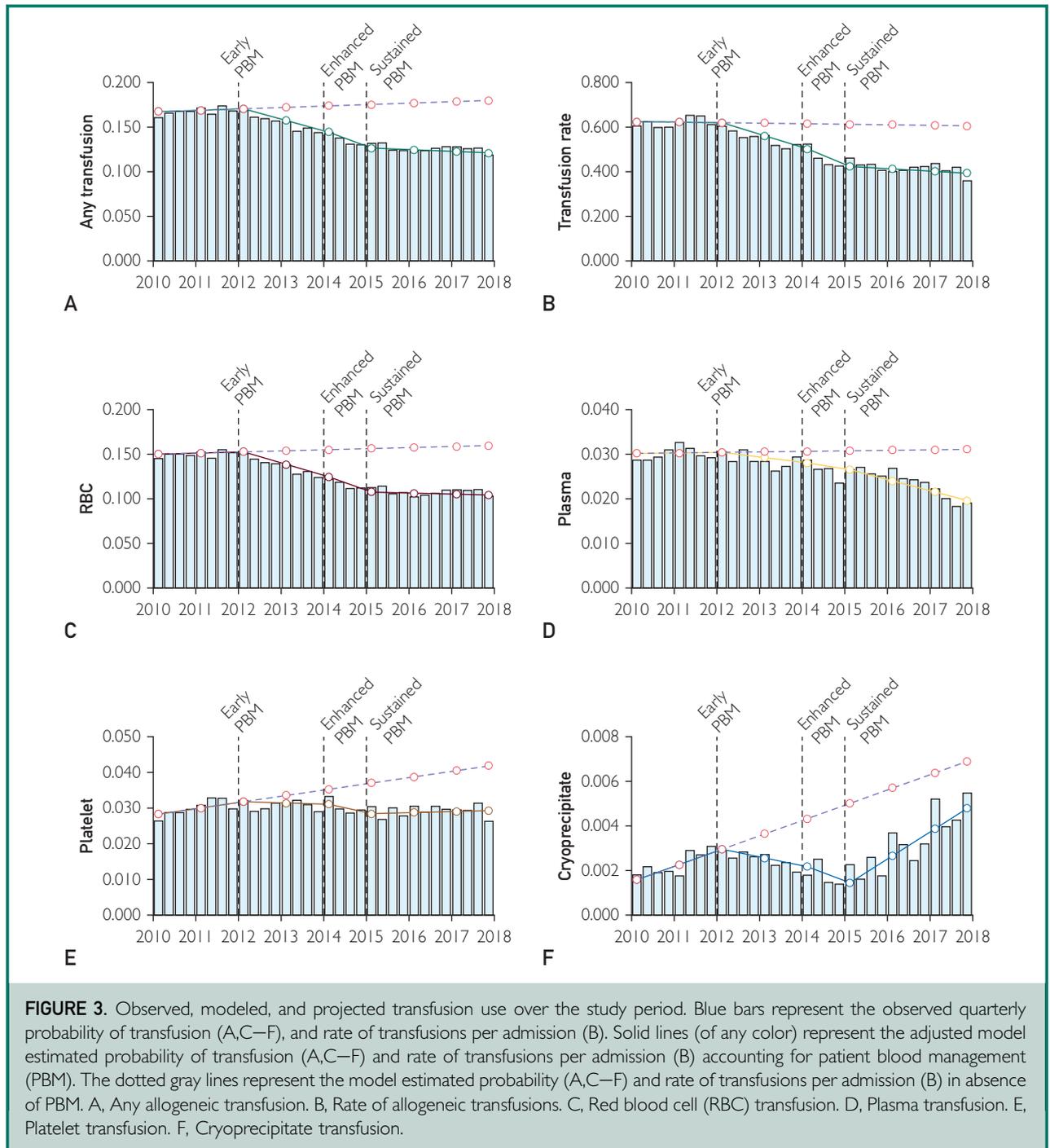
^dIncludes myocardial infarction, stroke, venous thromboembolism, transfusion reaction, and acute respiratory failure.

and dysfibrinogenemia in hemorrhaging patients.

This study also adds important information regarding the associations between PBM implementation and patient outcomes. Notably, hospital length of stay decreased by 15% beyond projections and composite in-hospital adverse events were modestly reduced. These clinical outcomes were generally consistent across transfused and nontransfused admissions, which may, in part, be related to reductions in total transfusion volumes in the transfused group and a greater proportion of admissions with complete transfusion avoidance. Alternatively, changes in clinical outcomes may have occurred independent of changes in transfusion practice, and these findings should not be interpreted as being causally linked to PBM activities given the observational study design. As an example, hospital length of

stay is a complex metric that may be driven by numerous factors, including changes in clinical practice, bed availability, medical reimbursement, patient illness, and socioeconomic status, among others. Nevertheless, the results are encouraging as they provide evidence that comprehensive PBM implementation and transfusion reductions are not associated with overt clinical harm. Further, observed improvements in clinical outcomes are consistent with previous work from a large Australian health care system.¹⁴ Taken together, PBM activities represent not only a tool to optimize transfusion utilization but perhaps also an opportunity to improve the health of our patients.

Previous investigations have noted substantial cost savings with PBM implementation secondary to reductions in transfusion utilization.^{14,15} Although not directly assessed in this investigation, it is likely



that similar transfusion-related cost savings occurred. Activity-based analyses incorporating both direct (eg, costs related to the acquisition, storage, processing, and transfusion of the blood unit) and indirect costs (eg, costs related to discarded blood

products, treatment of transfusion-related adverse events, and other overhead costs) estimate that actual blood transfusion costs exceed acquisition costs by a factor of 3 to 5.²² As an example, the mean activity-based cost for a single unit of RBCs has

TABLE 3. Allogeneic Transfusions Per 1000 Admissions for Major Surgeries Over the Study Period^{a,b}

Year	Gynecologic oncology	Total hip/knee	Major spine	Liver transplant	CABG	All others
2010	1093	270	1175	3893	1997	762
2011	1034	229	1342	3281	2094	757
2012	1192	178	1073	3586	1925	688
2013	1078	138	944	3407	2184	631
2014	984	77	840	2875	1579	533
2015	687	80	671	4148	1679	532
2016	600	52	401	2879	1631	495
2017	573	42	599	3500	1362	480

^aCABG, coronary artery bypass grafting (any number of vessels, exclusive of combined cardiac procedures).

^bGynecologic oncology indicates open abdominal-pelvic tumor debulking. Hip/knee indicates total hip and knee arthroplasty. Spine indicates spine surgery excluding minimally invasive techniques. Liver transplant indicates orthotopic liver transplantation.

been estimated at \$761 US dollars (USD, 2008),²² whereas activity-based costs of plasma and platelet units are likely to be modestly lower and higher, respectively.^{23,24} Extrapolation of \$761 per unit to a greater than 9000 unit reduction in transfused blood units (year 2017 versus 2010) would result in approximately \$7 million in annual transfusion-associated cost savings. Improvements in clinical outcomes, including shorter hospital lengths of stay, would likely further generate institutional cost savings through reductions in costs of care. Previous work has shown that PBM-associated savings secondary to transfusion reductions greatly outweigh the costs of PBM implementation.¹⁵

There are limitations to this analysis. First, it is observational; relationships between PBM activities and outcomes should not be interpreted as causal. Second, the possibility for residual confounding exists despite prespecified covariate adjustment. Third, this analysis was limited to those PBM activities applicable to our inpatient practice. Although PBM activities were robust, one limitation was the absence of formal preoperative anemia management activities, which were not active during the study period. It is possible that changes in transfusion utilization and clinical outcomes for surgical admissions would be enhanced with preoperative anemia management. Fourth, there is a possibility that study results reflect survival and immortal time biases during the inpatient

period. Clinical events may influence transfusion decisions with transfusions given in response to a clinical event or transfusions withheld because of a recent event. Our analyses are unable to account for the granular timing of clinical events in relation to transfusions. Finally, the results are representative of a single academic medical center in the Midwestern United States and may not be applicable to all environments.

CONCLUSION

In conclusion, PBM implementation at a large academic medical center was associated with substantial transfusion reductions and improvements in clinical outcomes in hospitalized adults. Outcomes were similarly experienced across surgical and medical hospital admissions. These data suggest that the graduated implementation of PBM activities is feasible and is associated with substantial conservation of blood resources without negative impact on patient outcomes.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mayoclinicproceedings.org>. Supplemental material attached to journal articles

has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: ARR, absolute risk reduction; CI, confidence interval; IQR, interquartile range; PBM, patient blood management; RBC, red blood cell

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