

Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals

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BACKGROUND: Patient blood management (PBM) programs are associated with improved patient outcomes, reduced transfusions and costs. In 2008, the Western Australia Department of Health initiated a comprehensive health-system-wide PBM program. This study assesses program outcomes.

STUDY DESIGN AND METHODS: This was a retrospective study of 605,046 patients admitted to four major adult tertiary-care hospitals between July 2008 and June 2014. Outcome measures were red blood cell (RBC), fresh-frozen plasma (FFP), and platelet units transfused; single-unit RBC transfusions; pretransfusion hemoglobin levels; elective surgery patients anemic at admission; product and activity-based costs of transfusion; in-hospital mortality; length of stay; 28-day all-cause emergency readmissions; and hospital-acquired complications.

RESULTS: Comparing final year with baseline, units of RBCs, FFP, and platelets transfused per admission decreased 41% ($p < 0.001$), representing a saving of AU\$18,507,092 (US\$18,078,258) and between AU\$80 million and AU\$100 million (US\$78 million and US\$97 million) estimated activity-based savings. Mean pretransfusion hemoglobin levels decreased 7.9 g/dL to 7.3 g/dL ($p < 0.001$), and anemic elective surgery admissions decreased 20.8% to 14.4% ($p = 0.001$). Single-unit RBC transfusions increased from 33.3% to 63.7% ($p < 0.001$). There were risk-adjusted reductions in hospital mortality (odds ratio [OR], 0.72; 95% confidence interval [CI], 0.67-0.77; $p < 0.001$), length of stay (incidence rate ratio, 0.85; 95% CI, 0.84-0.87; $p < 0.001$), hospital-acquired infections (OR, 0.79; 95% CI, 0.73-0.86; $p < 0.001$), and acute myocardial infarction-stroke (OR, 0.69; 95% CI, 0.58-0.82; $p < 0.001$). All-cause emergency readmissions increased (OR, 1.06; 95% CI, 1.02-1.10; $p = 0.001$).

CONCLUSION: Implementation of a unique, jurisdiction-wide PBM program was associated with improved patient outcomes, reduced blood product utilization, and product-related cost savings.

The term patient blood management (PBM) was coined in 2005 to help bring about a realignment of transfusion practice from product focus to patient focus.^{1,2} PBM is an evidence-based bundle of care that optimizes medical and surgical patient outcomes by clinically managing and preserving a

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patient's blood.²⁻⁵ In 2010, the World Health Assembly recommended PBM to its member states by resolution; as a result, PBM is high on international health agendas.⁶⁻⁸ PBM is most effective when it is part of a multidisciplinary program.^{6,9,10} The Australian national *Patient Blood Management Guidelines* contain an evidence-based recommendation that health care services should establish a multidisciplinary, multimodal PBM program; and The Australian Commission on Safety and Quality in Health Care has recently listed the National Patient Blood Management Collaborative as a top national priority and also has included PBM in hospital accreditation.¹¹⁻¹³

A programmatic approach to PBM has been associated with improved patient and economic outcomes and reductions in transfusion.¹⁴⁻²¹ However, those programs focused on specific surgical procedures, implemented selected PBM strategies, or were confined to individual institutions. Several challenges to wider implementation of PBM have been identified, namely, clinicians' resistance to change; a broader systems approach; needed resources; engagement of senior leadership across the health system; changes across the whole patient pathway, including primary care; translating evidence-based guidelines into clinical practice; and linking patient, laboratory, and transfusion databases to report on outcomes.^{6,22-25}

After the successful implementation in 1990 of a blood-conservation program in one of the state's private hospitals,^{1,26} in 2008, the Western Australia Department of Health initiated a 5-year project to implement a comprehensive, sustainable health-system-wide PBM program.^{6,27} This was fundamentally a quality, safety, and effectiveness initiative with resource and economic implications. Implementing a PBM program across an entire health system required a redesign of clinical processes and culture change at all levels of the health care organization.^{25,28} Implementation was based on a predefined program design incorporating successful hospital-based models and change management principles. Its primary aim was "improving medical and surgical patient outcomes while achieving significant cost savings" by applying PBM principles.^{6,27}

Western Australia is an Australian state with a population of approximately 2.6 million, with 74% living in the capital, Perth. There are five major public tertiary-care hospitals, four adult and one pediatric, which consume almost 60% of the blood products issued to the state. In the financial year 2008-2009, the Western Australia red blood cell (RBC) issuance rate was 31.8 per 1000 population, one of the lowest reported rates in the developed world (issuance rates for Germany, Denmark, and United Kingdom were 57.3, 60.0, and 36.3 per 1000, respectively, and the transfusion rate in the United States was 48.8 per 1000).^{6,29} However, from financial years 2002-2003 to 2008-2009, total RBC unit issues to the Western Australia state rose 12% and were projected to continue rising over the next 4 years, largely due to the rapidly growing and aging population.⁶ Data showed that 88% of all RBC transfusions were one to three units, suggesting that considerable numbers of transfusions could be preempted with PBM,³⁰ thus avoiding the unintended negative consequences^{31,32} and inherent risks of transfusion^{22,33} along with the associated costs.³⁴ With commencement of the program, the upward issuance trend was arrested and decreased each year thereafter despite average annual increases of 3% in population and 6% in hospital discharges. In the financial year 2015-2016, the RBC issuance rate per 1000 population decreased to a low of 19.4 (Fig. 1).

This retrospective, observational study assessed what impact the jurisdiction-wide PBM program had on key outcome measures in all emergency and elective acute-care adult inpatients admitted to the four major adult metropolitan tertiary hospitals where the majority of emergency care and high-complexity procedures and interventions are performed, including the major trauma, burns, and obstetrics referral services for Western Australia (see Appendix S1, available as supporting information in the online version of this paper).

MATERIALS AND METHODS

Program design

Details of program structure, rationale, and implementation are discussed elsewhere.^{6,27} The program incorporated principles of the Kotter model^{35,36} for successful change management, including: motivation for change, executive and clinical leadership, multidisciplinary clinical team engagement, clinical strategies, education and communication initiatives for clinicians and patients, feedback on practice change and embedding the changes with policies and procedures (see Appendix S1, Summary Table).⁶ A literature review identified a triad of independent but modifiable risk factors for adverse patient outcomes: namely, anemia, blood loss, and blood transfusion.⁶ Mitigation of these risk factors by the application of the three-pillar concept of PBM could

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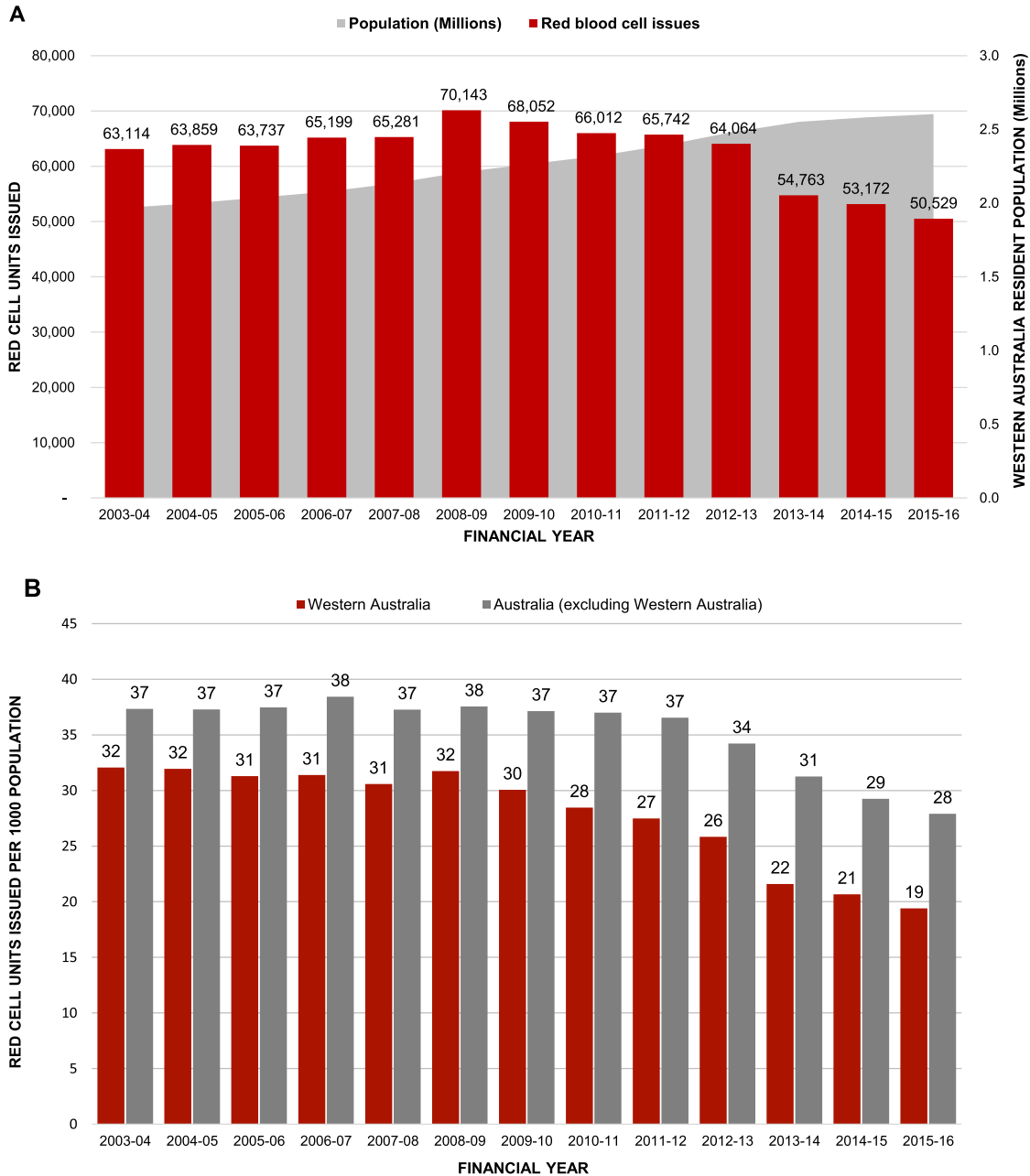


Fig. 1. (A) Data on RBC issues and resident population for the State of Western Australia from 2002-2003 to 2013-2014. RBC issuance data published and unpublished National Blood Authority (Australia) data printed with permission. Issuance of RBCs was progressively increasing in Western Australia. With the introduction of the Patient Blood Management Program in 2008-2009, this upward trend was arrested, and issuance has decreased each year despite an annual population increase. (B) RBCs issued per 1000 population in Western Australia compared with the Australian national average. Published and unpublished National Blood Authority (Australia) data printed with permission. [Color figure can be viewed at wileyonlinelibrary.com]

achieve improved patient outcomes with the corollary of reducing RBC, fresh-frozen plasma (FFP), and platelet transfusions and costs.^{3,6,27,34,37} Clinical implementation was built around a three-pillar, nine-field matrix with principles applied equally to surgical and nonsurgical patients (Fig. 2).^{6,27} The strategies employed included the following:

Pillar 1. Optimize RBC mass

Systems were re-engineered to facilitate timely preintervention patient assessment and optimization of hemoglobin and iron stores, and the use of intravenous iron and other hematinics for postoperative and in-hospital anemia as well as anemia and iron deficiency in pregnancy and primary care.^{26,38}

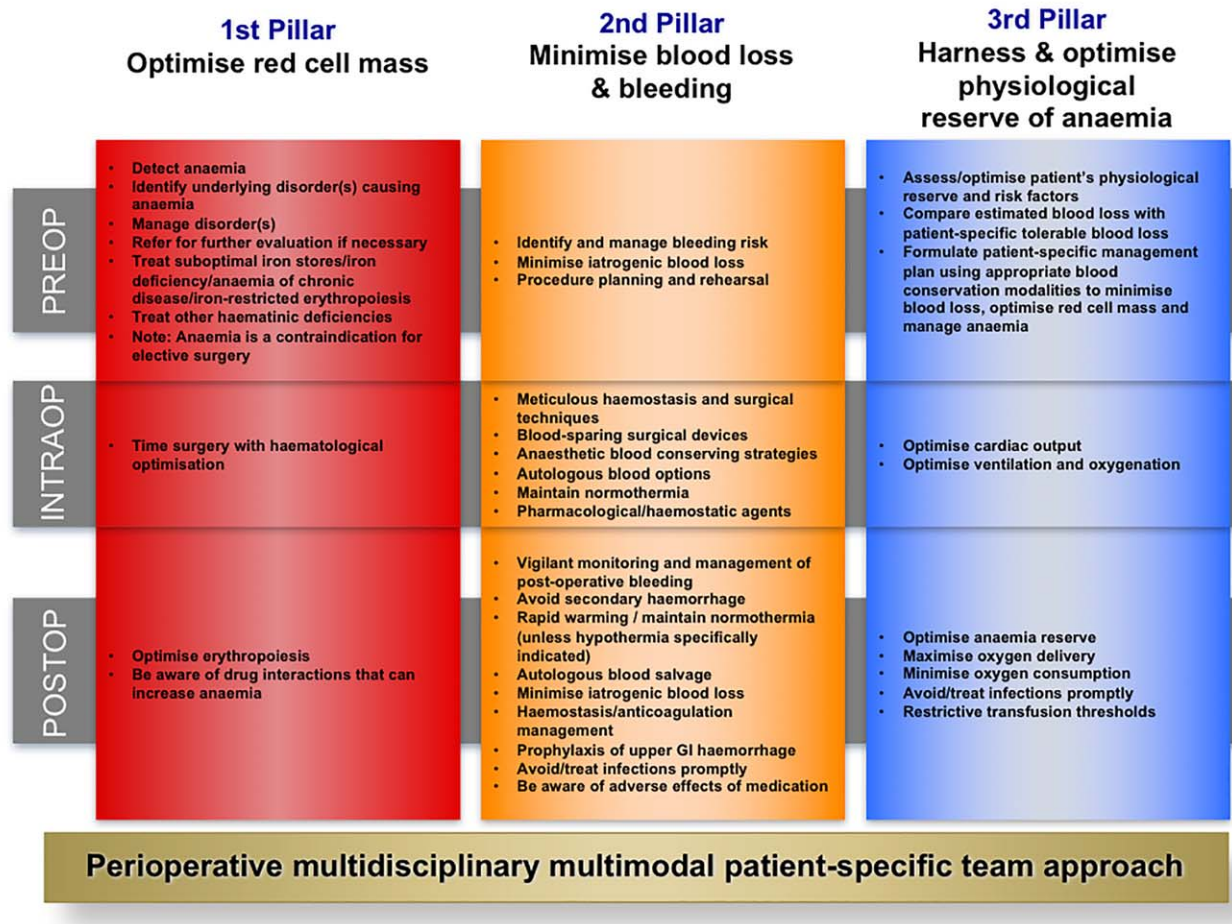


Fig. 2. The three-pillar, nine-field matrix of patient blood management. This matrix was designed for the Western Australia Patient Blood Management Program to assist in the clinical implementation of multiple patient blood management (PBM) strategies. These strategies are considered in the perioperative period in a patient and procedure-specific context. (Reformatted from Hofmann A, Friedman D, Farmer S. Western Australia Patient Blood Management Project 2008-2012: Analysis, Strategy, Implementation and Financial Projections. Perth, Western Australia: Medicine and Economics; 2007:1-215.²⁷) The principles of this matrix were also applied to nonsurgical patients before, during, and after treatment. [Color figure can be viewed at wileyonlinelibrary.com]

Pillar 2. Minimize blood loss

Educational and clinical initiatives were undertaken to reduce blood loss, including preintervention bleeding risk assessment and management, surgical hemostasis workshops and symposia, use of blood-preserving anesthetic techniques, hemostatic agents, autologous blood salvage, viscoelastic coagulation testing with targeted therapy in critical bleeding and coagulopathy, and minimize laboratory blood sampling volumes.^{26,38}

Pillar 3. Optimize the patient-specific tolerance of anemia

No specific transfusion threshold values were established for the program. Transfusion decisions were encouraged to take into account patient-specific clinical and physiological factors and accept evidence-based, more restrictive but individualized thresholds.³⁸ A single-unit RBC

transfusion policy was adopted in symptomatic, nonactively bleeding anemic patients.^{26,38}

Implementation of the program was planned in stages, with PBM staff to be appointed in Year 1 at the five tertiary-care hospitals and further state leadership and hospital and health service staff to be appointed in Years 2 and 3.²⁷ However, the global financial crisis resulted in delays and cancellations of staff employment and modifications to implementation and program structure.^{1,6} PBM staff were appointed only in the four adult tertiary-care hospitals, and 2013-2014 was the first full year in which the program operated with these positions filled.

Patient involvement

Patients were not involved in the design of this study or in the development of outcome measures. However, patient education initiatives were incorporated into program

implementation, including educational information on the website, a patient fact sheet, a hospital open day, and patient informed consent/refusal (see Appendix S1).

Data sources

The data included in this study were sourced from the Western Australia PBM data system. This automated reporting system does not use a probabilistic linkage. Details of the linking are published elsewhere.³⁹ The system links data from five core hospital information systems: laboratory (ULTRA LIS), transfusion (ULTRA TM), patient administration (TOPAS and WebPAS), theatre (surgical) management (TMS), and emergency department (EDIS), creating a detailed view of patient characteristics and outcomes associated with anemia and transfusion practices. The study included all emergency and elective multiday stay inpatients aged 16 years and older who were admitted to the four adult tertiary-care hospitals in Western Australia between July 2008 and June 2014, including major trauma, burns, obstetrics, hematology and oncology, gastroenterology, and all major surgery, including cardiac and major organ transplantation surgery. Because of changes in hospital configuration in early 2015, it was not possible to make comparisons with the baseline year beyond June 2014.

The study was reviewed by the Department of Health Western Australia Human Research Ethics Committee and complied with the national guidelines for research.

Outcome measures

Five primary key program-performance indicators and four primary hospital-wide patient outcome measures were selected before our analysis. Performance indicators were: mean RBC, FFP, and platelet units transfused per inpatient discharge; mean pretransfusion hemoglobin; proportion of single-unit RBC transfusions; proportion of elective surgical patients admitted anemic (hemoglobin level <13.0 g/dL for men and <12.0 g/dL for women); and cost of blood product acquisition. Operating room transfusions and patients identified as bleeding were excluded from the single-unit and pretransfusion hemoglobin measures. Costs were based on the yearly prices charged by the National Blood Authority (Australia) under the National Blood Agreement and were calculated by product type (see Appendix S1). Conversion to US dollars was based on the average yearly exchange rate.

The patient outcome measures selected were in-hospital mortality, hospital length of stay, 28-day all-cause emergency readmissions, and hospital-acquired complications; namely, infection and composite acute myocardial infarction (AMI)-stroke (a composite chosen because of the low incidence of each). Hospital-acquired complications were identified using data coded according to the *International Statistical Classification of Diseases and Related*

Problems, Tenth Revision, Australian Modification (ICD-10). These codes include a condition-onset flag to distinguish between hospital-acquired diagnoses and comorbidities present on admission in routinely coded administrative data. We defined emergency readmissions as any inpatient who was readmitted within 28 days of discharge. A predefined secondary measure selected was an estimation of gross savings based on published calculations of activity-based cost of transfusion.

Because the purpose of the study was to measure the potential impact of the PBM program over time, the key exposure of interest was the discharging Australian financial year (July 1 to June 30), with July 1, 2008 to June 30, 2009 as the baseline comparator.

Statistical analysis

A multivariate analysis was performed and adjusted for the following potential confounders: hospital, patient age, sex, admission type (elective or emergency), Diagnosis-Related Group (DRG) category (medical, surgical, or other), indigenous status, and patient comorbidities. These confounders were chosen to control for the possible effects of any changes in patient case-mix on patient outcomes over the study period. Continuous variables were not grouped into categories. Patient comorbidities were given a score based on the Charlson Comorbidity Index (CCI). The ICD-10 version of the CCI, as described by Quan and colleagues was applied, with hospital-acquired diagnoses excluded.⁴⁰

Poisson regression analysis was used to evaluate the rate of blood units transfused per discharge over time and to calculate the rate ratios. Linear regression was used to test the relationship between the year of discharge and the mean pretransfusion hemoglobin level. Logistic regression was used to test changes in the proportion of single-unit RBC transfusions, elective surgical patients admitted anemic, in-hospital mortality, hospital-acquired complications, and emergency readmissions. A zero-truncated, negative binomial regression was used to model the data for analysis of the impact on hospital length of stay. A robust variance adjustment was applied in the regression models to account for correlation between multiple admissions for the same patient.

RESULTS

Overall, 605,046 inpatient admissions were included in the 6-year study. The mean patient age was 55.4 years (standard deviation, 21.7 years), and 51.4% of patients (n = 311,214) were women. Of these admissions 7.8% of patients (n = 47,382) received at least one unit of RBCs, FFP, or platelets, for a total of 152,636 RBC units, 46,030 FFP units, and 28,089 platelet units transfused (Table 1).

TABLE 1. Units of blood transfused by hospital department

Specialty*	RBCs		FFP		Platelets		Combined	
	Units	% of total	Units	% of total	Units	% of total	Units	% of total
Hematology	25,544	16.7	2,248	4.9	13,101	46.6	40,893	18.0
Tracheostomy†	18,335	12.0	11,783	25.6	3,029	10.8	33,147	14.6
Gastroenterology	18,934	12.4	4,449	9.7	1,640	5.8	25,023	11.0
Gastrointestinal surgery	12,097	7.9	4,457	9.7	980	3.5	17,534	7.7
Orthopedics	15,112	9.9	1,170	2.5	402	1.4	16,684	7.4
Cardiothoracic	8,908	5.8	4,786	10.4	2,246	8.0	15,940	7.0
Trauma	6,665	4.4	2,583	5.6	504	1.8	9,752	4.3
Vascular surgery	6,310	4.1	1,428	3.1	311	1.1	8,049	3.5
Urology	4,984	3.3	1,279	2.8	239	0.9	6,502	2.9
Miscellaneous surgery	4,341	2.8	1,247	2.7	836	3.0	6,424	2.8
Cardiology	4,589	3.0	735	1.6	375	1.3	5,699	2.5
Immunology	3,022	2.0	636	1.4	1,534	5.5	5,192	2.3
Respiratory medicine	3,457	2.3	489	1.1	551	2.0	4,497	2.0
Rheumatology	425	0.3	3,424	7.4	73	0.3	3,922	1.7
Gynecology	3,022	2.0	616	1.3	144	0.5	3,782	1.7
Obstetrics	2,582	1.7	474	1.0	157	0.6	3,213	1.4
Nephrology	1,340	0.9	1,377	3.0	159	0.6	2,876	1.3
Medical oncology	2,379	1.6	254	0.6	213	0.8	2,846	1.3
Neurosurgery	1,632	1.1	758	1.6	430	1.5	2,820	1.2
General medicine	1,976	1.3	377	0.8	222	0.8	2,575	1.1
Other	6,982	4.6	1,460	3.2	943	3.4	9,385	4.1
Total	152,636	100.0	46,030	100.0	28,089	100.0	226,755	100.0

* Shown are the top 20 specialties (based on diagnosis-related group) by total number of RBCs, FFP units, and platelet units transfused between July 2008 and June 2014.

† This specialty group refers to patients who had a tracheostomy and/or ventilation for ≥ 96 hours.

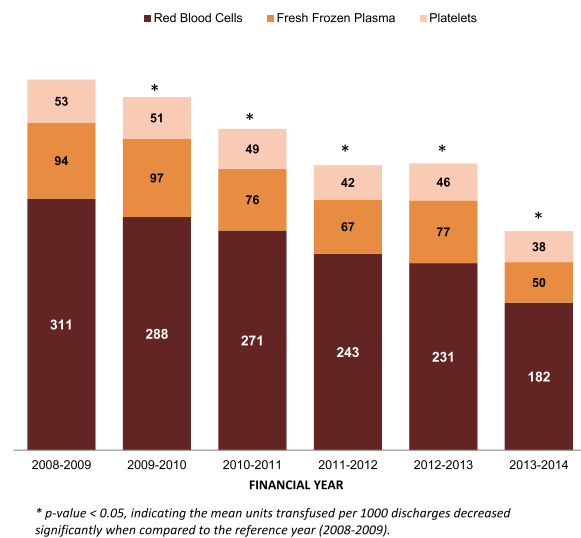


Fig. 3. Mean units of blood transfused per 1000 discharges. Shown are the mean units of RBCs, FFP, and platelets transfused per 1000 discharges. An asterisk denote a *p* value < 0.05, indicating that the mean units transfused per 1000 discharges decreased significantly compared with the reference year 2008-2009. [Color figure can be viewed at wileyonlinelibrary.com]

Mean units transfused per 1000 discharges

Mean units transfused are presented by year in Fig. 3. RBC, FFP, and platelet units transfused per 1000 discharges decreased 41% compared with the baseline

year (rate ratio [RR], 0.59; 95% confidence interval [CI], 0.58-0.60; *p* < 0.001). This decrease included reductions of 41% in RBC units (RR, 0.59; 95% CI 0.58-0.60; *p* < 0.001), 47% in FFP units (RR, 0.53; 95% CI, 0.51-0.55; *p* < 0.001), and 27% in units of platelets transfused (RR, 0.73; 95% CI, 0.70-0.76; *p* < 0.001).

Pretransfusion hemoglobin, single-unit RBC transfusions, and patients admitted anemic

The mean RBC pretransfusion hemoglobin level decreased from a baseline mean level of 7.9 g/dL to 7.3 g/dL (*p* < 0.001) in Year 6. The proportion of single-unit RBC transfusions increased from 33.33% to 63.69% (*p* < 0.001). The proportion of elective surgical patients admitted anemic decreased from 20.81% to 14.42% (*p* = 0.001).

Product-acquisition cost savings

Historic data and forward projections at program design predicted that, without practice change, product utilization would continue to increase. Adopting a conservative approach, if the annual rate of transfusion remained at baseline year levels, then an additional 50,115 units of blood would have been transfused over the study period, comprising 35,423 RBC units, 10,721 of FFP units, and 3970 platelets units. Based on product-acquisition cost, the calculated savings from this reduction is \$18,507,092 in Australian dollars (AU\$) and \$18,078,258 in US dollars (\$US).

TABLE 2. Key hospital-wide patient outcomes

Outcome variable*	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
In-hospital mortality						
Unadjusted rate, %	2.03	2.10	1.85	1.76	1.77	1.65
Adjusted OR (95% CI)†	Ref	1.01 (0.94-1.08)	0.95 (0.89-1.02)	0.89 (0.83-0.95)	0.81 (0.76-0.87)	0.72 (0.67-0.77)
Hospital length of stay						
Unadjusted mean, days	5.91	5.95	5.72	5.51	5.46	5.26
Adjusted rate ratio (95% CI)†	Ref	1.05 (1.03-1.07)	1.01 (0.99-1.03)	0.96 (0.94-0.98)	0.92 (0.90-0.94)	0.85 (0.84-0.87)
28-Day readmissions						
Unadjusted rate, %	11.42	11.82	12.74	13.57	13.27	12.42
Adjusted OR (95% CI)†	Ref	1.03 (0.99-1.07)	1.14 (1.10-1.18)	1.21 (1.17-1.26)	1.16 (1.12-1.20)	1.06 (1.02-1.10)
Hospital-acquired infection‡						
Unadjusted rate, %	—	2.34	2.04	1.78	1.80	1.95
Adjusted OR (95% CI)†	—	Ref	0.92 (0.85-0.99)	0.80 (0.74-0.87)	0.77 (0.71-0.83)	0.79 (0.73-0.86)
Acute myocardial infarction-stroke‡						
Unadjusted rate, %	—	0.50	0.48	0.40	0.42	0.36
Adjusted OR (95% CI)†	—	Ref	1.02 (0.86-1.20)	0.84 (0.71-1.00)	0.85 (0.71-1.00)	0.69 (0.58-0.82)

* Shown are the unadjusted and adjusted patient outcomes by financial year over the period of the patient blood management program.
 † Ratios and 95% confidence intervals are adjusted for hospital, age, sex, Diagnosis-Related Group (DRG) category, admission type, indigenous status, and comorbidities.
 ‡ Data were available for two of the four hospitals.
 CI = confidence interval; OR = odds ratio; Ref = reference category.

Estimation of activity-based cost of transfusion savings

Activity-based costs of RBC transfusion reportedly are threefold to fivefold higher than-acquisition costs,^{41,42} and it has been determined that the cost of FFP is more than nine times the cost of product acquisition.⁴³ Activity-based costs of platelets are currently unknown. Using these published calculations, the gross savings in this 6-year study are estimated at between AU\$80M and AU\$100M (between US\$78M and US\$97M).

Hospital-wide patient outcomes

Unadjusted and adjusted patient outcomes are presented by year in Table 2. Unadjusted in-hospital mortality decreased from 2.0% in 2008-2009 to 1.7% in 2013-2014 ($p < 0.001$). After adjusting for potential confounders, this represented a 28% reduction ($p < 0.001$).

The mean length of stay decreased significantly over the study period (5.9 days vs 5.3 days; $p < 0.001$). After adjusting for confounders, the mean length of stay was reduced by 15% ($p < 0.001$).

The proportion of all-cause, 28-day emergency readmissions increased from 11.4% to 12.4%. After adjustment, this represented a 6% increase ($p = 0.001$).

Hospital-acquired complications were analyzed for two of the study hospitals, because data were incomplete for the others. Data also were missing from the baseline year, because reporting began in the year 2009-2010. The unadjusted incidence of hospital-acquired infections in the two hospitals decreased from 2.3% in 2009-2010 to 2.0% in 2013-2014, representing a 21% reduction after adjusting for confounders ($p < 0.001$). The incidence of AMI-stroke decreased from

0.5% to 0.4%, representing a 31% reduction after adjusting for confounders ($p < 0.001$).

DISCUSSION

The implementation of a health-system-wide PBM program was associated in four adult public tertiary hospitals within that health system with significant reductions in hospital mortality, length of stay, RBC, FFP, and platelet transfusions, considerable product-acquisition and estimated activity-based transfusion cost savings, and an increase in all-cause emergency readmissions. There were significant reductions in infection and AMI-stroke at the two institutions that coded hospital-acquired complications.

Reduced blood product utilization in this study was associated with product-acquisition cost savings of AU\$18.5M (US\$18.1M). However, gross savings include activity-based costs of transfusion,⁴¹⁻⁴⁴ which are estimated in this 6-year study at between AU\$80M and AU\$100M (US\$78M and US\$97M). These costs, both acquisition and activity-based, are jointly borne by the state and federal governments.⁶ A one-time investment of AU\$4.5M was made to cover the health-system-wide, 5-year change management and implementation process. This included funds for external PBM experts to plan, coordinate, and guide the project; a state PBM Medical Director (0.1 full-time equivalent); a state PBM Clinical Nurse Coordinator (0.5 full-time equivalent); Department of Health project officers (providing administrative and data support, including creating a sustainable PBM data and reporting system); and honoraria and travel support for national and international key opinion leaders in PBM to clinically support the implementation process. This budget covered

various other items, including attendance at conferences, educational sessions, and study tours.

Relation to other studies

The present study is novel, in that it reports on multicenter, hospital-wide outcomes associated with the world's first comprehensive health-system-wide PBM program. The program employed multiple, evidence-based PBM clinical strategies and used culture change methodology, systems and patient pathway re-engineering, and continuous automated data collection and feedback. Its findings are consistent with and strengthen the findings of others who have examined the impact of either individual PBM strategies or PBM programs in selected patient groups.^{14-17,20,45} Goodnough and colleagues reported reductions in mortality and length of stay associated with their single-hospital-wide intervention to implement more restrictive RBC transfusion practices, with millions of dollars in cost savings.¹⁷ Their findings correlate with a systematic review and meta-analysis of randomized control trials by Salpeter and colleagues demonstrating that trials with more restrictive transfusion thresholds significantly reduced cardiac events, infection, rebleeding, and mortality compared with trials that used less restrictive thresholds.⁴⁶ Large numbers of risk-adjusted observational studies have demonstrated an independent dose-dependent association between RBC transfusion and increased morbidity, including infection, AMI-stroke, and hospital length of stay, and mortality.^{38,47-58} There is limited evidence for the efficacy of FFP transfusions in most clinical situations, likely contributing to overuse and adverse patient outcomes.^{38,59} Platelet transfusions may be associated with adverse events, there is low-quality evidence to guide practice, and they are often inappropriately used.^{23,38,60}

Although we observed an already relatively restrictive mean RBC transfusion threshold become more restrictive, the Western Australia program was not primarily an appropriate or restrictive transfusion initiative.³⁰ It adopted a comprehensive application of the three pillars of PBM.^{26,30} These pillars aim to modify the triad of risk factors for adverse patient outcomes and preempt what could otherwise result in an "appropriate" transfusion.³⁰ When an RBC transfusion is indicated, a single-unit policy may reduce the exposure dose.

Increases in anemia and blood loss are independently associated with poorer outcomes and increase the likelihood of transfusion.^{15,61,62} PBM programs in surgical patients have shown an association between improved anemia management and reduced blood loss, and improved outcomes. Kotze and colleagues observed significantly reduced preoperative anemia incidence and blood loss in their orthopedic surgery program with an associated reduction in transfusions.¹⁵ Gross and colleagues noted

significantly reduced blood loss and increased mean discharge hemoglobin levels despite a more restrictive transfusion threshold in cardiac surgery.¹⁶ Program implementation was associated with significant reductions in RBC, FFP, and platelet transfusion as well as product costs. Both programs were associated with improved patient outcomes.

It is not possible to determine the effect of any one strategy used within the Western Australia PBM program; likely a combination of strategies contributed to the modification of risk factors. The multifaceted multimodal multidisciplinary team approach adopted has been shown to be effective in change management and clinical improvement.⁶³ Up-to-date, evidence-based education and practice feedback played key roles (Appendix S1). Evaluation forms completed at more than 60 departmental PBM road shows revealed that 82% of responders said there was information that was new to them, 69% said they would change their clinical practice based on evidence presented, and 13% said they would not change their practice; the main reason provided for the latter response was that the information reinforced their already conservative practice. The provision of benchmarking data to hospitals, departments, and individual clinicians also gave strong motivation for practice improvement.^{6,39,64}

The current study differs from others in finding an increase in all-cause emergency readmissions.^{15-17,21} Loftus and colleagues reported a significant reduction in 30-day readmissions in a multicenter study of patients undergoing total hip and knee arthroplasty.²¹ Gross and colleagues observed a nonsignificant reduction in 30-day readmission in a single-center study of patients undergoing cardiac surgery.¹⁶ In a single center study of primary hip and knee arthroplasties, Kotze and colleagues identified a significant reduction in 90-day readmissions.¹⁵ Goodnough and colleagues, in a single-center study of a hospital-wide initiative, found that 30-day readmission rates remained stable.¹⁷ Although this measure is commonly used in clinical research, it has limitations in interpretation. Future subgroup analyses may provide insights into which clinical contexts have higher or lower readmission rates. However, because this outcome measures *all-cause* emergency readmissions, we are unable to determine the number of patients who were readmitted for reasons unrelated to their previous admission. Given this limitation, we recommend caution, as have others, in interpreting this result as an indicator of quality of care.⁶⁵

Strengths and weaknesses of this study

Because this was an observational study in which a linked data system was used, it has both strengths and limitations. A strength is that exposures, outcomes, and covariates were sourced from validated hospital data systems, which undergo regular quality audits. It also included a large,

multicenter population of all acute-care, adult inpatients. A limitation is that there was no control group, because we sought to measure change over time, and comparisons were based on a baseline year. We were also unable to compare outcomes with other Australian jurisdictions, because we had no access to equivalent patient outcomes data. Comparisons with other Australian jurisdictions would have been problematic because during the same period other states had implemented various PBM initiatives, Australia released its national PBM guidelines, and PBM was included in national hospital accreditation.

An observational study in itself cannot establish a causal link between program implementation and outcomes of interest. Nor can outcomes be attributed completely to the PBM program, as other hospital initiatives may have played a role. However, the greatest reduction in blood utilization was in the only year in which all study hospitals had their PBM Medical Director and PBM Nurse—positions that have been identified as key to a successful PBM program.⁶

Improvements in patient outcomes, including length of stay, mortality, and hospital-acquired complications, were significant even after adjusting for potential confounders, reducing the likelihood that they were due to changes in patient mix. We adopted a similar approach to that used by Goodnough and colleagues, who reported concurrent hospital-wide outcomes associated with a single-hospital-wide intervention.¹⁷

Implications for clinicians and policymakers

Blood transfusion is one of the most frequently performed therapeutic procedures; it crosses many medical disciplines, has been identified as one of the top five overused therapies, and is associated with negative patient outcomes and increased costs.^{17,31,37,66,67} Therefore, the impact of PBM programs may be substantial considering the global health sector's challenge to improve patient outcomes with increasingly restricted funding.

Unanswered questions and future research

Cost-saving calculations in this study were based on blood product utilization but did not include the impact of the program on other modalities, for example, iron therapy in anemia management, and cryoprecipitate (or fibrinogen concentrate) and antifibrinolytics such as tranexamic acid in coagulopathy. A comprehensive, cost-effectiveness analysis would include these modalities and the savings associated with reduced complications and hospital length of stay.³⁷ This assessment was beyond the scope of this study and will be the subject of future analysis.

One way to confirm the findings of this and other studies on the impact of PBM would be to conduct a cluster, randomized controlled trial to assess complex, process-of-care interventions. However, such an assessment may not be possible for ethical reasons alone;

currently, it would appear to be almost impossible in developed countries with wide uptake of PBM. For example, many authoritative international bodies—including the AABB, the Joint Commission, and the Advisory Committee on Blood Safety and Availability in the United States; European Union Patient Blood Management, the National Health Service Blood and Transplant, Department of Health, and National Blood Transfusion Committee in the United Kingdom; the Ontario Nurse Transfusion Coordinators (ONTraC) Program in Canada; and the Australian Commission on Safety and Quality in Health Care and the National Blood Authority in Australia—have various PBM initiatives and are promoting it as a standard of care to improve outcomes.^{4-6,8,68-70} However, replicating the current findings across another jurisdiction would provide additional evidence for the overall benefits of such a program.

CONCLUSIONS

In a health system with one of the world's lowest RBC issuance rates per 1000 population and an already relatively restrictive mean RBC transfusion threshold, a comprehensive, jurisdiction-wide PBM program in the study hospitals was associated with significant hospital-wide reductions in morbidity, mortality, length of stay, blood product use, and costs. The decreasing blood product issuance rates highlight the finding that, since conclusion of the 5-year project, the culture generated by the PBM program in Western Australia has been sustained. These findings may have considerable implications for health systems across the globe, including high-income and low-income countries.

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CONFLICT OF INTEREST


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REFERENCES

- Farmer S, Towler S, Hofmann A. The Australian PBM concept—a success story. In: Gombotz H, Zacharowski K, Spahn D, editors. Patient blood management. Stuttgart (Germany): Thieme; 2016:207-17.
- Isbister J. The three-pillar matrix of patient blood management. *ISBT Sci Series* 2015;10:286-94.
- Isbister JP. The three-pillar matrix of patient blood management—an overview. *Best Pract Res Clin Anaesthesiol* 2013;27:69-84.
- Australian Commission on Safety and Quality in Health Care. What is Patient Blood Management? Sydney, Australia: Australian Commission on Safety and Quality in Health Care [cited 2015 Feb 13]. Available from: <http://www.safetyandquality.gov.au/national-priorities/pbm-collaborative/what-is-patient-blood-management/>.
- National Blood Authority. Patient Blood Management. Canberra, Australia: National Blood Authority (Australia) [cited 2016 Mar 22]. Available from: <http://www.blood.gov.au/patient-blood-management-pbm>.
- Farmer SL, Towler SC, Leahy MF, Hofmann A. Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA). *Best Pract Res Clin Anaesthesiol* 2013;27:43-58.
- Spahn DR, Shander A, Hofmann A. The chiasm: transfusion practice versus patient blood management. *Best Pract Res Clin Anaesthesiol* 2013;27:37-42.
- Waters JH, Ness PM. Patient blood management: a growing challenge and opportunity. *Transfusion* 2011;51:902-3.
- Thomson A, Farmer S, Hofmann A, et al. Patient blood management—a new paradigm for transfusion medicine? *ISBT Sci Series* 2009;4:423-35.
- Goodnough LT, Shander A. Blood management. *Arch Pathol Lab Med* 2007;131:695-701.
- National Blood Authority. Patient Blood Management Guidelines: Module 2-Perioperative. Canberra, Australia: National Blood Authority (Australia); 2012 [cited 2016 Dec 02]. Available from: <http://www.nba.gov.au/pbm-guidelines>.
- Australian Commission on Safety and Quality in Health Care. National Priorities. Sydney, Australia: Australian Commission on Safety and Quality in Health Care [cited 2016 Nov 24]. Available from: <https://www.safetyandquality.gov.au/national-priorities/>.
- Australian Commission on Safety and Quality in Health Care. National Standards and Accreditation. Sydney, Australia: Australian Commission on Safety and Quality in Health Care [cited 2016 Nov 24]. Available from: <https://www.safetyandquality.gov.au/our-work/national-standards-and-accreditation/>.
- Moskowitz DM, McCullough JN, Shander A, et al. The impact of blood conservation on outcomes in cardiac surgery: is it safe and effective? *Ann Thorac Surg* 2010;90:451-8.
- Kotze A, Carter LA, Scally AJ. Effect of a patient blood management programme on preoperative anaemia, transfusion rate, and outcome after primary hip or knee arthroplasty: a quality improvement cycle. *Br J Anaesth* 2012;108:943-52.
- Gross I, Seifert B, Hofmann A, Spahn DR. Patient blood management in cardiac surgery results in fewer transfusions and better outcome. *Transfusion* 2015;55:1075-81.
- Goodnough LT, Maggio P, Hadhazy E, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. *Transfusion* 2014;54:2753-9.
- Freedman J, Luke K, Escobar M, Vernch L, Chiavetta JA. Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). *Transfusion* 2008;48:237-50.
- Meybohm P, Herrmann E, Steinbicker AU, et al. Patient blood management is associated with a substantial reduction of red blood cell utilization and safe for patient's outcome: a prospective, multicenter cohort study with a noninferiority design. *Ann Surg* 2016;264:203-11.
- LaPar DJ, Crosby IK, Ailawadi G, et al. Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery. *J Thorac Cardiovasc Surg* 2013;145:796-803. discussion 803-4.
- Loftus TJ, Spratling L, Stone BA, Xiao L, Jacofsky DJ. A patient blood management program in prosthetic joint arthroplasty decreases blood use and improves outcomes. *J Arthroplasty* 2016;31:11-4.
- Goodnough LT. Blood management: transfusion medicine comes of age. *Lancet* 2013;381:1791-2.
- Goodnough LT, Levy JH, Murphy ME. Concepts of blood transfusion in adults. *Lancet* 2013;381:1845-54.
- Spahn DR, Goodnough LT. Alternatives to blood transfusion. *Lancet* 2013;381:1855-65.
- Williamson LM, Devine DV. Challenges in the management of the blood supply. *Lancet* 2013;381:1866-75.
- Leahy MF, Roberts H, Mukhtar SA, et al. A pragmatic approach to embedding patient blood management in a tertiary hospital. *Transfusion* 2014;54:1133-45.
- Hofmann A, Friedman D, Farmer S. Western Australia Patient Blood Management Project 2008-2012: Analysis, Strategy, Implementation and Financial Projections. Perth, Western Australia: Medicine and Economics; 2007:1-215. [cited 2016 Nov 11]. Available from https://www.researchgate.net/publication/281308410_Western_Australia_Patient_Blood_Management_Project_2008-2012_Analysis_Strategy_Implementation_and_Financial_Projections.
- Mortimer PP. Making blood safer. *BMJ* 2002;325:400-1.
- US Department of Health and Human Services. The 2011 National Blood Collection and Utilization Survey Report. US Department of Health and Human Services; 2012 [cited 2016

- Dec 02]. Available from <https://www.aabb.org/research/hemovigilance/bloodsurvey/Documents/11-nbcus-report.pdf>.
30. Hofmann A, Farmer S, Shander A. Five drivers shifting the paradigm from product-focused transfusion practice to patient blood management. *Oncologist* 2011;16Suppl 3: 3-11.
 31. Isbister JP, Shander A, Spahn DR, Erhard J, Farmer SL, Hofmann A. Adverse blood transfusion outcomes: establishing causation. *Transfus Med Rev* 2011;25:89-101.
 32. Rawn J. The silent risks of blood transfusion. *Curr Opin Anaesthesiol* 2008;21:664-8.
 33. Vamvakas EC, Blajchman MA. Blood still kills: six strategies to further reduce allogeneic blood transfusion-related mortality. *Transfus Med Rev* 2010;24:77-124.
 34. Shander A, Hofmann A, Gombotz H, Theusinger OM, Spahn DR. Estimating the cost of blood: past, present, and future directions. *Best Pract Res Clin Anaesthesiol* 2007;21:271-89.
 35. Kotter J, Cohen D. *The heart of change*. Boston (MA): Harvard Business School Press; 2002.
 36. Kotter JP, Schlesinger LA. Choosing strategies for change. *Harv Bus Rev* 1979;57:106-14.
 37. Trentino KM, Farmer SL, Swain SG, et al. Increased hospital costs associated with red blood cell transfusion. *Transfusion* 2015;55:1082-9.
 38. National Blood Authority (Australia). *Patient Blood Management Guidelines*. National Blood Authority (Australia), 2008. [cited 2016 July 14]. Available from <http://www.blood.gov.au/pbm-guidelines>.
 39. Mukhtar S, Leahy ME, Koay K, et al. Effectiveness of a patient blood management data system in monitoring blood use in Western Australia. *Anaesth Intensive Care* 2013;41:207-15.
 40. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130-9.
 41. Shander A, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. *Transfusion* 2010;50:753-65.
 42. Abraham I, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. *Transfusion* 2012;52: 1983-8.
 43. Shander A, Ozawa S, Hofmann A. Activity-based costs of plasma transfusions in medical and surgical inpatients at a US hospital. *Vox Sang* 2016;111:55-61.
 44. The cost of blood: multidisciplinary consensus conference for a standard methodology. *Transfus Med Rev* 2005;19:66-78.
 45. Farmer SL, Trentino K, Hofmann A, et al. A programmatic approach to patient blood management – reducing transfusions and improving patient outcomes. *Open Anesthesiol J* 2015;9:6-16.
 46. Salpeter SR, Buckley JS, Chatterjee S. Impact of more restrictive blood transfusion strategies on clinical outcomes: a meta-analysis and systematic review. *Am J Med* 2014;127: 124-31.e3.
 47. Farmer S, Isbister J, Hofmann A. Transfusion and outcomes. In: Gombotz H, Zacharowski K, Spahn D, editors. *Patient blood management*. 2nd ed. Stuttgart, Germany: Thieme; 2016:19-28.
 48. Whitlock EL, Kim H, Auerbach AD. Harms associated with single unit perioperative transfusion: retrospective population based analysis. *BMJ* 2015;350:h3037.
 49. Patel SV, Kidane B, Klingel M, Parry N. Risks associated with red blood cell transfusion in the trauma population, a meta-analysis. *Injury* 2014;45:1522-33.
 50. Paone G, Likosky DS, Brewer R, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. *Ann Thorac Surg* 2014;97:87-93. discussion 93-4.
 51. Paone G, Brewer R, Theurer PE, et al. Preoperative predicted risk does not fully explain the association between red blood cell transfusion and mortality in coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2012;143:178-85.
 52. Ferraris VA, Davenport DL, Saha SP, Austin PC, Zwischenberger JB. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. *Arch Surg* 2012; 147:49-55.
 53. Mikkola R, Gunn J, Heikkinen J, et al. Use of blood products and risk of stroke after coronary artery bypass surgery. *Blood Transfus* 2012;10:490-501.
 54. Al-Refai WB, Parsons HM, Markin A, Abrams J, Habermann EB. Blood transfusion and cancer surgery outcomes: a continued reason for concern. *Surgery* 2012; 152:344-54.
 55. Khorana AA, Francis CW, Blumberg N, Culakova E, Refaai MA, Lyman GH. Blood transfusions, thrombosis, and mortality in hospitalized patients with cancer. *Arch Intern Med* 2008;168:2377-81.
 56. Horvath KA, Acker MA, Chang H, et al. Blood transfusion and infection after cardiac surgery. *Ann Thorac Surg* 2013;95: 2194-201.
 57. Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JG. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg* 2009;208:931-7, 937.e1-2; discussion 938-9.
 58. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Critic Care Med* 2008;36:2667-74.
 59. Tinmouth A. Assessing the rationale and effectiveness of frozen plasma transfusions: an evidence-based review. *Hematol Oncol Clin North Am* 2016;30:561-72.
 60. Estcourt LJ, Stanworth SJ, Doree C, Hopewell S, Trivella M, Murphy MF. Comparison of different platelet count thresholds to guide administration of prophylactic platelet transfusion for preventing bleeding in people with haematological disorders after myelosuppressive chemotherapy or stem cell transplantation. *Cochrane Database Syst Rev* 2015; CD010983.

61. Shander A, Javidroozi M, Ozawa S, et al. What is really dangerous: anaemia or transfusion? *Br J Anaesth* 2011;107Suppl 1:i41-59.
62. Shander A. Financial and clinical outcomes associated with surgical bleeding complications. *Surgery* 2007;142:S20-5.
63. Haas DA, Helmers RA, Rucci M, Brady M, Kaplan RS. The Mayo Clinic Model for running a value-improvement program [Internet]. *Harvard Business Rev* 22 October 2015 [cited 2016 Dec 02]. Available from: <http://www.hbs.edu/faculty/Pages/item.aspx?num=50183>.
64. Trentino KM, Swain SG, Geelhoed GC, Daly FF, Leahy MF. Interactive patient blood management dashboards used in Western Australia. *Transfusion* 2016;56:3140-41.
65. Benbassat J, Taragin M. Hospital readmissions as a measure of quality of health care: advantages and limitations. *Arch Intern Med* 2000;160:1074-81.
66. Rohde JM, Dimcheff DE, Blumberg N, et al. Health care-associated infection after red blood cell transfusion: a systematic review and meta-analysis. *JAMA* 2014;311:1317-26.
67. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med* 2013;368:11-21.
68. AABB. Patient Blood Management. Bethesda (MD): AABB. [cited 2016 Nov 24]. Available from: <http://www.aabb.org/pbm/Pages/default.aspx>.
69. National Health Service. Patient Blood Management. NHS Blood and Transplant [cited 2016 Nov 24]. Available from: <http://hospital.blood.co.uk/patient-services/patient-blood-management/>.
70. European Union. European Guide on Good Practices for Patient Blood Management (PBM). Brussels, Belgium: European Union; 2016 [cited 2016 Nov 24]. Available from: <http://www.europe-pbm.eu>. 

SUPPORTING INFORMATION

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Supplementary Appendix