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Promoting High-Value Practice by Reducing Unnecessary Transfusions With a Patient Blood Management Program

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Although blood transfusion is a lifesaving therapy for some patients, transfusion has been named 1 of the top 5 overused procedures in US hospitals. As unnecessary transfusions only increase risk and cost without providing benefit, improving transfusion practice is an effective way of promoting high-value care. Most high-quality clinical trials supporting a restrictive transfusion strategy have been published in the past 5 to 10 years, so the value of a successful patient blood management program has only recently been recognized. We review the most recent transfusion practice guidelines and the evidence supporting these guidelines. We also discuss several medical societies' Choosing Wisely campaigns to reduce or eliminate overuse of transfusions. A blueprint is presented for developing a patient blood management program, which includes discussion of specific methods for optimizing transfusion practice.

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Blood transfusion is the most common procedure performed during inpatient hospitalizations[1] and has been named 1 of the top 5 overused procedures by the Joint Commission.[2] Approximately 85 million red blood cell (RBC) units are transfused annually worldwide, and 12 million RBC units are transfused annually in the United States.[3,4] Between the cost of blood itself (approximately $2.5 billion) and the associated overhead costs of transfusion, the annual financial burden is approximately $10 billion.[5] These costs do not include those associated with managing transfusion-associated infectious and noninfectious adverse reactions.[6,7] Given the opportunity to reduce risks and costs, there are now 5 specialties with Choosing Wisely aims to reduce overuse of transfusions.[8-12]

The current RBC transfusion guidelines developed by the AABB (formerly the American Association of Blood Banks) recommend a restrictive transfusion strategy, with hemoglobin (Hb) thresholds of less than 7 g/dL (to convert to grams per liter, multiply by 10.0) in hospitalized stable patients and less than 8 g/dL in patients with coexisting cardiovascular disease and those undergoing cardiac or orthopedic surgery.[4] These Hb transfusion thresholds have been evaluated by randomized clinical trials (RCTs) in many settings, which include critically ill patients in adult and pediatric intensive care units,[13,14] those with gastrointestinal bleeding,[15] those with septic shock,[16] those who have undergone cardiac surgery,[17,18] those with traumatic brain injury,[19] and orthopedic surgical patients with high risk for cardiovascular complications.[20] Across clinical spectrums, these restrictive transfusion strategies have consistently proven to result in the same or improved outcomes when compared with liberal transfusion strategies (Hb threshold, <9 to 10 g/dL) (**Table**).[13-20]

Despite well-established evidence-based guidelines, significant variation in clinical practice continues to exist.[21,22] Efforts to reduce overuse of transfusions through patient blood management programs have been successful.[23-25] With a goal to promote value-based quality improvement, we review the safety and quality outcomes data for blood transfusions and provide an implementation blueprint for setting up a patient blood management program. We are members of the High Value Practice Academic Alliance, a group of clinicians working to advance high-value health care through collaborative quality improvement, research, and education.

Evidence-Based Guidelines

The current AABB recommendations for RBC transfusion[4] are based on a literature review of RCTs from the 1950s to 2016 assessing Hb thresholds for RBC transfusions. This review encompasses 31 studies, which included 12 587 participants, and all compared restrictive (Hb threshold, <7 to 8 g/dL) vs liberal (Hb threshold, <9 to 10 g/dL) transfusion strategies. Seven of the 8 largest and most widely cited trials, however, were published within the past decade,[14-20] and 4 of these were published in the past 4 years.[15,16,18,19] The following 3 recommendations summarize evidence-based RBC transfusion practices, and are derived from the AABB clinical practice guidelines[4] and Choosing Wisely aims.[11]

First Recommendation

Red blood cell transfusion is not indicated in hemodynamically stable adult hospitalized patients with a Hb level of 7 g/dL or more. This population includes critically ill patients.

Second Recommendation

Red blood cell transfusion is not indicated in patients undergoing orthopedic or cardiac surgery or in patients with underlying cardiovascular disease with a Hb level of 8 g/dL or more.

Table. Summary of Recent Large Randomized Clinical Trials Comparing Restrictive With Liberal Transfusion Strategies[a]

Source	Patient Population	Restrictive Strategy (Hb Threshold to Target Range)[b]	Liberal Strategy (Hb Threshold to Target Range)[b]	Reduction in Blood Use, %	Clinical Outcomes			
					Event	Restrictive (Incidence), %	Liberal (Incidence), %	*P* Value
Hébert et al,[13] 1999	Critically ill adults (N = 838)	7.0-8.5 g/dL	10.0-10.7 g/dL	54	30-d mortality (all)	18.7	23.3	.11
					30-d mortality (age <55)	5.7	13.0	.02
					30-d mortality (APACHE II score ≤20)	8.7	16.1	.03
					In-hospital mortality	22.2	28.1	.05
Lacroix et al,[14] 2007	Critically ill pediatric patients (N = 637)	7.0-9.4 g/dL	9.5-11.2 g/dL	47	In-hospital multiple organ dysfunction syndrome	12	12	NS
Hajjar et al,[17] 2010	Cardiac surgery in adults (N = 502)	8.0-9.1 g/dL	10.0-10.5 g/dL	58	30-d composite all-cause mortality and severe morbidity	11	10	.85
Carson et al,[20] 2011	Femur fracture in elderly adults (N = 2016)	8.0-9.5 g/dL	10.0-11.0 g/dL	65	Composite endpoint	34.7	35.2	NS
					60-d mortality	28.1	27.6	NS
					60-d inability to walk	6.6	7.6	NS
Villanueva et al,[15] 2013	Gastrointestinal bleeding in adults (N = 921)	7.0-9.2 g/dL	9.0-10.1 g/dL	59	45-d all-cause mortality	5	9	.02
Robertson et al,[19] 2014	Traumatic brain injury (N = 200)	7.0-9.7 g/dL	10.0-11.4 g/dL	49	Favorable Glasgow Outcome Scale	42.5	33.0	.28
					Thrombotic events	8.1	21.8	.009
Holst et al,[16] 2014	Septic shock in adults (N = 998)	7.0-7.5 g/dL	9.0-9.5 g/dL	50	90-d all-cause mortality	43.0	45.0	.44
Murphy et al,[18] 2015	Cardiac surgery in adults (N = 2007)	7.5-9.0 g/dL	9.0-10.0 g/dL	40	Serious infections or ischemic event at 90 d	35.1	33.0	.30

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; Hb, hemoglobin; NS, not significant.

[a] All studies used single-unit red blood cell transfusion strategies, except Robertson et al (unspecified strategy) and Lacroix et al (pediatric transfusions).

[b] Threshold: the Hb threshold for starting red blood cell transfusion; target: the mean daily Hb concentration in the study population.

Third Recommendation

Single-unit RBC transfusions followed by reassessment should be the standard of care for patients who are hemodynamically stable and not actively bleeding.

Evidence

A total of 23 of the 31 RCTs that compared liberal vs restrictive transfusion strategies in hemodynamically stable hospitalized patients had 30-day mortality as the primary outcome.[4] These RCTs demonstrated no difference in outcome, with 3 fewer deaths per 1000 patients in the restrictive transfusion group (relative risk, 0.97; 95% CI, 0.81-1.16; *P* = .77). In addition, restrictive transfusion thresholds were noninferior with respect to multiple secondary outcomes, including myocardial infarction, cerebral vascular events, venous thromboembolism, and pneumonia. There was no evidence to suggest that restrictive transfusion strategies harmed patients. As most studies in surgical patients and those with cardiovascular disease used a transfusion threshold of 8 g/dL,[17,18,20] there is no evidence comparing transfusion thresholds of 7 g/dL vs 8 g/dL in these populations, so this threshold remains an area for future investigation.

The Table outlines the 8 recent large trials[13-20] that have evaluated restrictive vs liberal RBC transfusion strategies, including their Hb transfusion thresholds and clinical outcomes. Six of the 7 trials in adults specified that single-unit RBC transfusions followed by reassessment was the standard protocol. Seven of the 8 trials showed no difference in the primary clinical outcome,[13,14,16-20] and 1 trial showed increased mortality[15] with a liberal transfusion strategy. The TRICC trial (Transfusion Requirements in Critical Care)[13] was the first large randomized trial comparing a restrictive vs liberal transfusion strategy, defined as Hb thresholds of 7 vs 10 g/dL in critically ill patients. In this trial, 30-day mortality was not significantly different between groups (18.7% vs 23.3%; *P* = .11), although inpatient mortality during hospitalization was borderline significant, favoring a restrictive strategy (22.2% vs 28.1%; *P* = .05). Two subgroups in the TRICC trial (those under age 55 years and those with Acute Physiology and Chronic Health Evaluation scores ≤20) showed increased mortality with liberal transfusion thresholds. A study of patients with traumatic brain injury demonstrated an increased incidence of venous thromboembolism (the secondary outcome) in the group with a liberal transfusion threshold.[19] A recent Cochrane systematic review concluded that 30-day mortality was similar between patients with a restrictive transfusion strategy and those with a liberal transfusion strategy.[26] The risks of cardiac and cerebrovascular ischemic events, thromboembolism, and infections were also similar, and the restrictive strategy resulted in a 43% reduction in the proportion of patients who received a transfusion. In summary, with most trials showing no benefit, and a few showing harm with liberal transfusion thresholds, transfusing more RBC units than is necessary simply adds risks and costs without adding benefit.

There is insufficient evidence to make recommendations regarding RBC transfusion thresholds in patients with acute coronary syndrome, severe thrombocytopenia, and chronic transfusion-dependent anemia, including sickle cell and other hemoglobinopathies.[26] Therefore, the above recommendations do

not apply to patients with these conditions. There is also insufficient evidence to support clear transfusion thresholds for plasma to treat coagulopathy,[27] and for platelets, outside the setting of chemotherapy in oncology.[28] Blood management programs should use caution in establishing transfusion threshold guidelines based on laboratory values for these blood components.

Safety and Quality Efforts: Patient Blood Management Programs

Embracing evidence-based transfusion guidelines reduces risks and costs while improving outcomes, thus increasing the value of care provided. The RCTs evaluating restrictive transfusion practices also showed a successful reduction of 40% to 65% in the units of blood transfused (Table).[13-20] Leahy et al[24] described a health system–wide comprehensive patient blood management program, resulting in a 41% decrease in blood use, with a concomitant decrease in risk-adjusted mortality (odds ratio, 0.72; 95% CI, 0.67-0.77; $P < .001$), as well as decreased length of stay, hospital-acquired infections, and cardiac or cerebral ischemic events. Roubinian and colleagues[29] reported a 26% decrease in RBC use with no change in 30-day mortality. This outcome was accomplished by education, clinical decision support in the electronic medical record (EMR), and a multidisciplinary approach to blood conservation measures.

Saag et al[30] described a combined approach of EMR-based decision support and targeted education to reduce the number of blood transfusions based on liberal thresholds (Hb level, ≥7 g/dL) at their institution. The EMR-based tool involved the embedding of mandatory selection of clinical indication—with all options except for major or emergency surgery or "other" being a Hb level in accordance with evidence-based guidelines—in every transfusion order. The targeted education piece provided specialty-specific, evidence-based information, including guidelines, to the 4 services in the hospital with the highest level of blood transfusions. Using this approach, the authors were able to decrease blood transfusions based on liberal thresholds from 13.4 to 10.0 units per 100 patient discharges ($P = .002$). This decrease was sustained for the entire 9 months of follow-up. Clinically, this decrease resulted in a projected 1380 fewer unnecessary units of blood transfused over a 12-month period, for a cost saving of $720 360. Equally important, there was no significant difference in either length of stay or the observed to expected mortality rate.

Frank et al[31] have reported successful blood management efforts that include education, clinical decision support, guideline compliance audits, and reports, as well as other blood conservation measures designed to reduce blood loss and transfusion requirements in the perioperative setting (**Box**).[4,13-20,23,27,28,32-46] Members of this group also reported a successful "Why Give 2 When 1 Will Do?" Choosing Wisely campaign to reduce orders of multiunit RBC transfusions.[35] This campaign included a screensaver image (**Figure 1**)[11] displayed on workstations throughout the health care system that was visible to all clinicians and even some patients. Lessons learned include the importance of education as an adjunct to decision support,[32] the utility of data dashboards to assess compliance with guidelines,[34] and the value of single-unit RBC transfusions in reducing blood use.[47] Initial reports include a 14% reduction in surgical RBC use; however, blood management was challenging in trauma, transplant, and complex cardiac cases that often require massive transfusion.[32] Subsequent work reduced RBC use by 20%, with a concomitant decrease in use of plasma and platelets.[31] The result of these efforts was an annual savings for blood acquisition costs of $2.1 million, representing a 400% return on investment for funding to support a multi-institutional health system–wide patient blood management program.[31] These results were achieved incrementally over a 4-year time period.

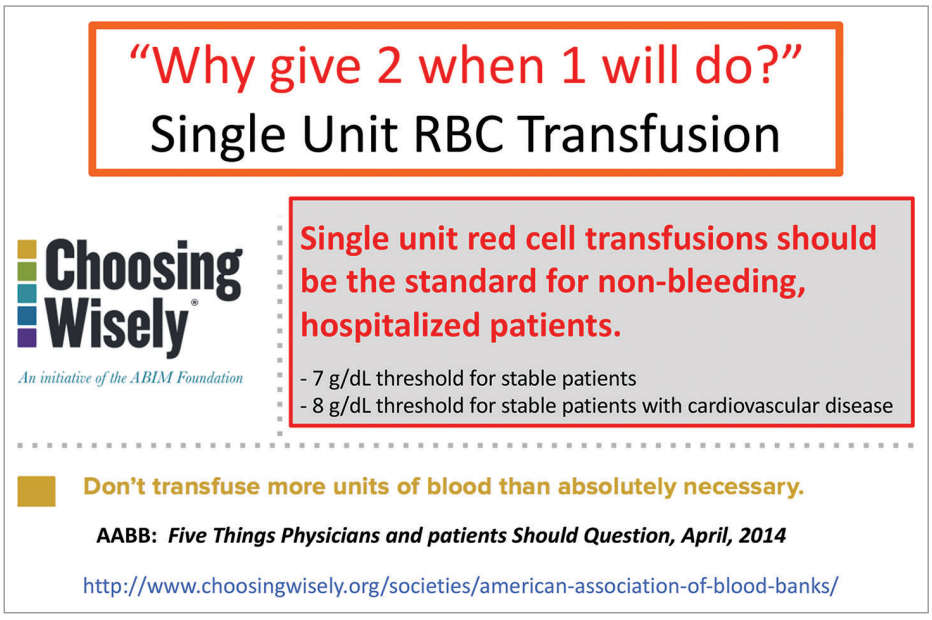
Box. Steps for Implementing a Patient Blood Management Program

1. Obtain support from health system leadership with a business plan
2. Assemble multidisciplinary team of clinicians and stakeholders
3. Education (with emphasis on the randomized clinical trials supporting restrictive transfusion)[13-20]
4. Harmonize transfusion guidelines for hospital or health system
5. Clinical decision support for computerized clinician order entry (with best practice advisories)[32,33]
6. Data acquisition and analytics
7. Create guideline compliance dashboards[34]
8. Transfusion guideline compliance audits with feedback (reports) to clinicians[23]
9. Methods for improving blood use
   - Evidence-based transfusion thresholds[4,27,28]
   - "Why give 2 when 1 will do" Choosing Wisely campaign for red blood cell transfusions[35]
   - Preoperative anemia management for elective surgery (eg, oral or intravenous iron, or erythropoietin)[36]
   - Antifibrinolytics to reduce blood loss (eg, aminocaproic acid or tranexamic acid)[37]
   - Intraoperative autologous transfusion (cell salvage)[38]
   - Anesthetic management (eg, autologous normovolemic hemodilution, controlled hypotension, and normothermia)[39-42]
   - Surgical methods (eg, newer cautery methods, topical hemostatics, and sealants)[43,44]
   - Reduce phlebotomy blood loss (eg, use microtainers and reduce unnecessary laboratory tests)[45]
   - Point of care testing (eg, thromboelastography)[46]

Implementation Blueprint for a Patient Blood Management Program

Given the compelling evidence supporting RBC transfusion practices with a restrictive threshold, the High Value Practice Academic Alliance recognizes the importance of promoting evidence-based transfusion for patient care quality and safety. Widespread improvements in transfusion practice can yield substantial reductions in health care expenditure and increase the blood supply for patients with life-threatening hemorrhage, while improving outcomes for patients who benefit from such a restrictive practice. We recommend using the following as a model for building support and promoting evidence-based transfusion practice in individual medical centers or across health systems. This blueprint outlines the steps to implement a successful patient blood management program, according to the standards endorsed by both the AABB and The Joint Commission, 2 societies that have recently joined efforts to offer hospital certification for patient blood management programs.[48] The in-

Figure 1. Image Used for "Why Give 2 When 1 Will Do?" Campaign to Emphasize the Importance of Single-Unit Red Blood Cell (RBC) Transfusions in Hemodynamically Stable Patients Who Are Not Bleeding



The image was displayed as a screensaver on workstations across the health system. This recommendation is backed by Choosing Wisely guidelines.[11] ABIM indicates American Board of Internal Medicine.

dividual steps in setting up a patient blood management program are outlined in the Box.[4,13-20,23,27,28,32-46]

Step 1: Organization and Support

Building a task force to implement this initiative with multidisciplinary representation from departments, including medicine, pediatrics, transfusion medicine (blood bank), various surgical services with high use of blood products, anesthesiology, critical care medicine, nursing, pharmacy, quality and safety representatives, and information technology (data analytics), is likely to increase buy-in and compliance.[31] Involvement of these stakeholders in creating the specific guidelines and protocols for the hospital and designing the decision support and educational program is also recommended. Ideally, the institution will provide funding to support the primary team leading the efforts, so that nonclinical time can be devoted to these efforts. This funding can be justified based on a calculated return on investment resulting from reduced blood acquisition costs,[31] given that blood is reimbursed either poorly or not at all, in today's bundled care environment. If the institution has an institute for patient safety and quality, this is a good way to sponsor the efforts and to justify the allocated resources.

Step 2: Transfusion Guidelines

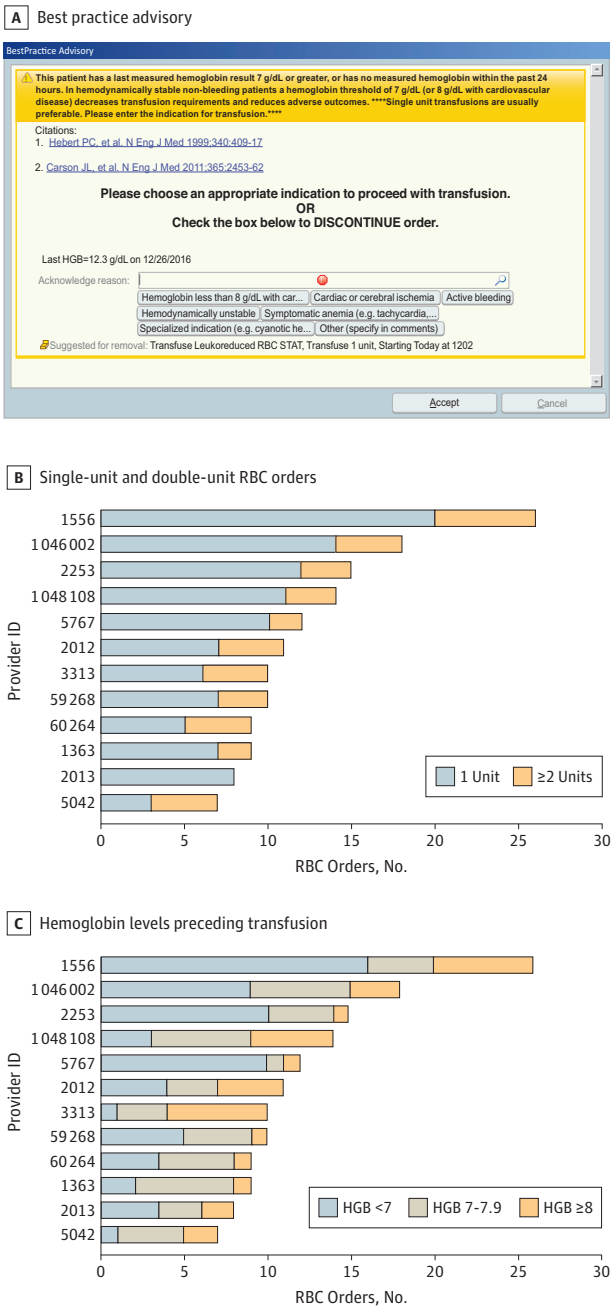
Agreed-upon transfusion guidelines are important; these guidelines can be drafted and adopted as official hospital policy. Such guidelines usually include laboratory-based thresholds for RBCs,[4] plasma,[27] and platelets,[28] along with reasons for ordering transfusions outside of typical guidelines. These reasons can be used as indications for bypassing the best practice advisory alerts in the decision support algorithm described below. Again, the relatively weak evidence supporting plasma indications, and platelet indications outside of oncology, should be recognized.

Step 3: Education and Clinical Decision Support

Two essential components are clinical decision support in the EMR and targeted education, which work synergistically.[32,33,49,50] Clinical decision support serves multiple purposes: it obligates the ordering clinician to think about the medical necessity of the transfusion and provide reasoning for the decision, and it provides a real-time reminder of evidence-based indications for RBC transfusion. If available, embedding decision support within an EMR transfusion orderset is most effective. Ideally, an interruptive pop-up alert (best practice advisory) triggered by the most recent laboratory value (eg, Hb ≥7 g/dL) using built-in logic is most effective (**Figure 2**A).[23] These alerts can include the institution's transfusion guidelines, with or without a hyperlink to the published RCTs supporting the alert message, which lends more credibility to the alert.[33] Accepted reasons for bypassing the alert can then be chosen to proceed with the transfusion (eg, active bleeding or symptomatic anemia). The electronic ordersets can be designed to encourage single-unit transfusions, unless the transfusion is being ordered as part of a massive transfusion protocol. In hemodynamically stable patients who are not hemorrhaging, the AABB Choosing Wisely guidelines recommend single-unit RBC transfusions followed by reassessment before additional transfusions are given.[11]

The role of targeted education is to educate those who might be unaware of the guidelines and the RCTs supporting restrictive transfusion, and to create buy-in for adherence to the guidelines. The education is most effective when the forum and content of the presentation is reviewed in advance with a respected clinician or leader within each department who can review the material to be presented in advance to ensure that appropriate, respected studies relevant to that field are included. Education can take place in a large forum such as grand rounds or other setting as deemed appropriate by department leadership, and should include house staff,

Figure 2. Leveraging the Electronic Medical Record to Promote Evidence-Based Transfusion Practice



A, When a red blood cell (RBC) order is placed, an interruptive best practice advisory (BPA) is triggered if the preceding hemoglobin value is ≥7 g/dL or has not been measured in the previous 24 hours. After acknowledging the BPA, the clinician can either cancel the order or proceed by choosing a reason to override the BPA and transfuse RBCs. These reasons are taken from the health system's transfusion guidelines. B, The proportion of single-unit RBC orders and double unit RBC orders in a typical monthly report for a clinical service (Department of Surgery) showing rates of compliance with transfusion guidelines for individual clinicians compared with their peers. The length of the bar represents the number of RBC units ordered for the month. C, The proportion of RBC orders with a preceding hemoglobin (HGB) level of <7, 7-7.9, and ≥8 g/dL in a typical monthly report for a clinical service (Department of Surgery) showing rates of compliance with transfusion guidelines for individual clinicians compared with their peers.

attending physicians, fellows, and other clinicians who have ordering privileges (eg, nurse practitioners and physicians' assistants). A required online tutorial can also be effective, which may include a mandatory quiz with a passing grade that can be tracked and documented.

Step 4: Data Dashboards, Audits, and Reports

Blood management programs rely heavily on data collection from the EMR, which requires significant effort from the data analytics team. Ideally, these data can be obtained through a user-friendly interactive dashboard with the capability to show data specific to the clinical service and the individual clinician level.[34] Peer-to-peer comparison of rates of compliance with guidelines is an effective method for encouraging quality improvement and reducing inappropriate transfusions. Monthly reports can include the proportion of RBC orders that include more than 1 unit (Figure 2B) and the proportion that are ordered with a preceding Hb level less than 7, 7 to 7.9, and more than 8 g/dL, in a green, yellow, and red color bar graph display (Figure 2C).

Each clinical service should select a champion or leader who will receive and review a monthly report of inpatient transfusion orders. The report to be distributed should include all inpatient RBC transfusions that month, the Hb levels prior to each transfusion, and the indication given for the transfusion. The report should include information for the entire hospital broken down by service, such that each service can monitor its performance. In addition, services can be compared with each other. The champion or leader is responsible for providing feedback to colleagues. In addition, the report should be provided to hospital leadership, who will also have the opportunity to discuss the results with the service champions and to observe rates of compliance with transfusion guidelines.

Step 5: Other Blood Conservation Methods

Various other methods outlined in the Box[4,13-20,23,27,28,32-46] can be used to reduce blood loss and transfusion requirements. Diagnosing and treating anemia before elective surgery is an effective blood management strategy.[36] Oral or intravenous iron, for example, is cost-effective for patients with an iron deficiency,[51] and erythropoietin can be used in selected cases. Antifibrinolytic medications such a tranexamic acid can reduce blood loss and transfusion requirements for orthopedic and/or cardiac surgery by about 30%.[37] Autologous blood salvage (cell salvage) is useful for collecting and reinfusing shed blood during surgery and is a valuable blood conservation strategy for cardiac, major vascular, and specific orthopedic and spine surgical procedures.[38] This method is preferred instead of preoperative autologous blood donation,[52] as patients are not rendered anemic prior to their surgery, and the blood is not subjected to storage, which is associated with reduced RBC quality.[53,54] Methods of blood conservation involving anesthetic management include acute normovolemic hemodilution,[39,40] maintaining normothermia,[41] and controlled hypotension.[42] Surgeons can use newer methods of electrocautery[43] as well as topical hemostatics and sealants to reduce blood loss.[44] As blood loss from phlebotomy can be substantial, especially in critical care units, smaller phlebotomy tubes and less frequent laboratory testing can both be effective methods of blood management.[45] Point of care testing, or any laboratory test with a rapid turnaround time, can reduce blood use,[46] since the clinician is not left waiting and wondering if the patient needs a transfusion.

Conclusions

Although transfusions can be a lifesaving therapy in patients who are hemorrhaging or severely anemic, unnecessary transfusions expose patients to added risk and costs without the provision of benefit. Given that most of the evidence supporting a restrictive transfusion strategy has been published in the past decade, patient blood management programs have only recently gained popularity. A recent survey by the AABB reported that 38% of hospitals had a formal patient blood management program,[55] indicating room for growth in this area to promote patient safety, improve quality of health care, and reduce unnecessary expenditure.

Although transfusion guidelines are based primarily on quantitative laboratory value measurements as the threshold for transfusion, it is important to keep in mind that these guidelines are not intended as an absolute standard and may not apply in all situations. Clinical judgment must be used, as we recognize that clinicians treat patients, not laboratory values. For RBCs, factors such as active bleeding, intravascular volume depletion (eg, tachycardia or hypotension), signs of end organ ischemia (eg, cardiac chest pain), or symptomatic anemia (eg, dyspnea) must be considered. With this in mind, adherence to transfusion guidelines should be an institutional priority at every medical center in the United States. Using the information and the implementation blueprint outlined above, we aim to facilitate widespread compliance with guidelines, resulting in increased quality as well as cost savings for patients, payers, and medical centers, as well as preservation of the blood supply for patients who truly need transfusions. By increasing quality and reducing costs, a successful patient blood management program achieves the goals set forth by the High Value Practice Academic Alliance.

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