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Perioperative Blood Conservation: Guidelines to Practice

Jenny Kwak, MD[a,*], Andrew L. Wilkey, MD[b], Mohamed Abdalla, MD[c], Ravi Joshi, MD[d], Philip E.F. Roman, MD, MPH[e], Philip E. Greilich, MD, MSc[f]

[a]Department of Anesthesiology and Perioperative Medicine, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153, USA; [b]Department of Anesthesia, Abbott Northwestern Hospital, 800 East 28th Street, Minneapolis, MN 55407, USA; [c]Department of Cardiothoracic Anesthesiology, Cleveland Clinic Lerner College of Medicine, Anesthesiology Institute, Cleveland Clinic, 9500 Euclid Avenue/J4-331, Cleveland, OH 44196, USA; [d]Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center - Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390-8894, USA; [e]Department of Anesthesiology, Centura St. Anthony Hospital, United States Anesthesia Partners, 11600 West 2nd Place, Lakewood, CO 80228, USA; [f]Cardiac Anesthesiology, Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center - Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390-8894, USA

Keywords

• Clinical practice guideline • Implementation • Anemia • Transfusion
• Patient blood management • Robust process improvement • Quality improvement
• Survey

Key points

- The formulation of clinical practice guidelines are complex, resource-intense processes for summarizing evidence-based best practices, yet alone are insufficient for translating guidelines to practice.
- The implementation of practice guidelines requires changing physician behaviors, engaging multiple stakeholders with flexible and persistent leadership effort.
- Identifying and responding to both barriers and facilitators of evidence-based best practices are vital to translating guidelines to practice.

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*Corresponding author.

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Continued

- Strategies for implementing patient blood management are emerging and represent and opportunity for robust process improvement.
- The coordinated use of a survey instrument for audit and feedback can align local, regional, and national efforts for translation of blood conservation guidelines to clinical practice.

INTRODUCTION

Translating guidelines for perioperative blood conservation and hemostasis to practice is an area of intense interest to anesthesiologists, administrators, patients, and surgeons. In addition to reviewing relevant evidence-based clinical practice guidelines for patient blood management, this article addresses how to overcome barriers and to facilitate the closure of the evidence-to-practice gap. The purpose of this article is to review the data and provide a framework for translating guidelines to practice. The use of a survey instrument to facilitate audit and feedback is highlighted.

FORMULATING CLINICAL PRACTICE GUIDELINES

According to the National Academy of Medicine, clinical practice guidelines are statements that include recommendations intended to optimize patient care and are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [1]. Although the rationale for creating clinical practice guidelines is sound, the formulation of objective, relevant, and easily applied recommendations currently faces many challenges. They are complex, resource-intense undertakings that may overlap with one another and struggle to stay current with new evidence. The number and complexity of guidelines has grown considerably over the past decade. In 2015, the US Agency for Healthcare Research and Quality National Guidelines Clearinghouse listed 2619 individual guidelines on its website [2].

The National Academy of Medicine has a clearly defined and rigorous definition of trustworthy guidelines that distinguishes clinical practice guidelines from other forms of advice such as consensus statements, position papers, practice bulletins, scientific statements, expert advice, quality measures, and evidence-based recommendations (Box 1). [1,3] "Clinical Practice Guidelines We Can Trust" is a 290-page publication from the Institute of Medicine. A summary of their "Standards for Developing Trustworthy Clinical Practice Guidelines" appears in Appendix 1 [1,4].

Clinical research: an early barrier

Early barriers to guideline formulation and dissemination are the planning and conduct of the clinical studies that form the bases for guideline development. Clinical research is burdened by a number of impediments including insufficient public participation, information systems, workforce training, and funding (Box 2) [5]. Sung and colleagues [5] contend that solutions to these

Box 1: Criteria for trustworthy guidelines according to the National Academy of Medicine

To be trustworthy, guidelines should:

Be based on a systematic review of the existing evidence

Be developed by a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups

Consider important patient subgroups and patient preferences, as appropriate

Be based on an explicit and transparent process that minimizes distortions, biases, and conflicts of interest

Provide a clear explanation of the logical relationships between alternative care options and health outcomes, and provide ratings of both the quality of evidence and the strength of recommendations

Be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations

Data from Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Graham R, Mancher M, Miller Wolman D, et al., editors. Clinical Practice Guidelines We Can Trust. Washington (DC): National Academies Press (US); 2011. Available from: https://www.ncbi.nlm.nih.gov/books/NBK209539/ https://doi.org/10.17226/13058

Box 2: Barriers to clinical practice guideline formulation

Translational steps

- Basic science to human studies
- New knowledge to clinical practice and health decision making

Translational blocks

- Lack of willing participants
- Regulatory burden
- Fragmented infrastructure
- Incompatible databases
- Lack of qualified investigators
- Career disincentives
- Practice limitations
- High research costs
- Lack of funding

Intended end point

- Improved health

From Sung NS, Crowley WF, Jr., Genel M, et al. Central challenges facing the national clinical research enterprise. JAMA. 2003;289(10):1278-1287; with permission.

problems are complex and involve the engagement of multiple stakeholders across the entire basic and clinical science research landscape as well as collaboration throughout the spectrum of participants in the health care system.

Cost and time considerations

Adherence to a comprehensive approach for developing guidelines comes at considerable cost. The Institute of Medicine publication cites a cost of $200,000, in 2003 dollars, per individual guideline developed in the United States [1]. An estimate of direct costs for a guideline consensus conference is around $82,000. This estimate does not include costs for other staff or volunteer efforts. The World Health Organization estimates a cost of $100,000 for development of one standard World Health Organization guideline [6].

Some costs for developing guidelines derive from the labor-intensive efforts of collecting, reviewing, evaluating, and collating appropriate published medical literature. Cost increases with the complexity of a topic, the number of pieces of literature reviewed, and the strategies used to complete the process. To establish a guideline for depression, a panel examined more than 90,000 peer-reviewed abstracts [1,7]. The cost and time required to produce a high-quality clinical practice guideline means that remaining current and applicable is an ongoing concern. The World Health Organization estimates that the time to develop a quality guideline can take 9 to 12 months if evidence has been already gathered and as long as 2 to 3 years for guidelines that deal with broad or complicated topics [8].

Conflict of interest

Another issue facing the formulation of clinical practice guidelines is conflict of interest (COI) and its potentially deleterious effects on clinical practice guideline objectivity. Statements to acknowledge and minimize potential COI exist in many methodology manuals for clinical practice guideline formulation [9–11]. A strategy for combatting COI influence has been set forth using the following 3 pillars [12]:

- Place equal emphasis on intellectual and financial conflicts and provide explicit criteria for both.
- A methodologist without important COI should have primary responsibility for each article.
- Experts with important financial or intellectual COI can collect and interpret evidence, but only panel members without important conflicts can be involved in developing the recommendation for a specific question.

Despite guidance from the Institute of Medicine, the problem of relationships with industry continue to plague guideline formulation [13,14].

Differences in grading systems

Different clinical practice guidelines may use different standards by which to assess the quality of evidence found in literature searches. Examples include the Grading of Recommendations Assessment, Development and Evaluation

(GRADE), the Australian National Health and Medical Research Council approach, Formulating Recommendations Matrix, Strength of Recommendation Taxonomy, and the Scottish Intercollegiate Guidelines Network [15–18]. Although these guidelines share similarities, the GRADE system has gained popularity in the last few years [15].

Other barriers to clinical practice guideline formulation

Bias

Clinical practice guidelines are exposed to a high degree of bias. Approximately 75% of clinical studies published in *The Lancet*, the *New England Journal of Medicine*, and the *Journal of the American Medical Association* are industry sponsored. This can become a force multiplier for industry when scores of studies are compiled for inclusion in a clinical practice guideline [1,19].

Generalizability

A shortcoming of many clinical investigations is a lack of generalizability. For example, study participants are often relatively young, healthy, and not representative of many patient subgroups who will be treated using the studied intervention. Those frequently omitted from studies include older patients, those with comorbidities, racial minorities, and the socioeconomically disadvantaged [1,20].

Transparency

Many clinical practice guidelines do not adequately describe the processes used to develop and rate the recommendations they put forward. This shortcoming can have medical as well as legal implications [1,21]. For example, a perceived lack of transparency regarding potential conflicts of interest led to an investigation into the development of Lyme disease guidelines by the Infectious Diseases Society of America [22]. Ultimately, following "multiple meetings, a public hearing, and extensive review of research and other information, the Review Panel concluded that the recommendations contained in the 2006 guidelines were medically and scientifically justified on the basis of all of the available evidence and that no changes to the guidelines were necessary."

Conflicting guidelines and ratings

Conflicting recommendations may result from the use of differing literature search strategies and different evidence grading practices. As many as 70% of guideline developing groups do not reveal the method they use to rate the quality of evidence cited [1].

Implementation and patient outcome measures

Clinical practice guidelines rarely address sufficiently the processes for implementation of their recommendations or the tracking of patient outcomes as a result of guideline-based patient care improvement efforts. Although the words "implement(ation)" and "outcome(s)" may appear in a guideline or their methodology manuals, there are no sections that address implementation planning or patient outcomes measurement [9–11,23].

IMPLEMENTING CLINICAL PRACTICE GUIDELINES

Clinical practice guidelines have historically taken as long as 10 years to achieve even modest levels of adoption [24]. Barriers to the translation of guidelines to practice include the lack of an integrated strategy for implementation, resistance to change, and loss of autonomous decision making. Organizational infrastructure, resource constraints, inadequate support, and cultural factors within and between departments have also emerged as significant barriers to translating guidelines to practice [25]. With this growing awareness, some facilitators to translating guidelines to practice have emerged.

Successful translation of guidelines to practice must consider several variables such as the strength of evidence, superiority over existing practice, and the ease and practicality of trialing and observing the best practice (Table 1) [26–28]. Clinician age, time period of training, and country of training can also influence adoption, because younger clinicians are generally more inclined to modify their practices [29]. A practice setting that fosters improvement in the efficiency and effectiveness of treatments and values social norms can also contribute to more rapid adoption [30,31]. Financial incentives, policies and regulations, and the potential avoidance of litigation have had a variable impact changing physician behavior [32–34]. A hospital's commitment to responding to patient needs also contributes to the

Table 1
Variables affecting adoption of clinical practice guidelines

Guideline qualities	Incentives
Complexity of implementation	Legal
Compatibility with current values	Financial
Trialability of interventions	Overall compensation
Observability of other adopters	Reimbursement for procedures
Advantage over current care	
Individual professional characteristics	Regulation
Age	Accreditation
Country of training	Licensing
Effects on clinical autonomy	
Practice satisfaction	
Concern over health care costs	
Practice setting characteristics	Patient factors
Habit and custom	Demographics
Peer belief systems	Individual patient presentation
Social norms	Compliance patterns
System efficiency	
Implementation support	

Data from Davis DA, Taylor-Vaisey A. Translating guidelines into practice. A systematic review of theoretic concepts, practical experience and research evidence in the adoption of clinical practice guidelines. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne.* 1997;157(4):408-416 and Rogers EM. Lessons for guidelines from the diffusion of innovations. *The Joint Commission journal on quality improvement.* 1995;21(7):324-328.

implementation of change. For example, a patient population that includes Jehovah's Witnesses may be the driving force for the initiation of a bloodless surgery program, which in turn helps the hospital to support guidelines related to anemia management for all patients.

A summary of barriers and facilitators to guideline adherence are displayed in (Table 2) [35]. Effective implementation of clinical practice guidelines may suffer from multiple barriers, and the use of a single strategy to overcome them may not effective. A separate systematic meta-analysis highlighted a lack of institutional support and patient characteristics as the primary impediments to adoption of, and adherence to, clinical practice guidelines [28].

The complexities of translating guidelines to practice are formidable. The application of implementation science to health care is a recent development and has led to a better understanding of the barriers and facilitators that influence physician decision-making behaviors. Reluctance to modify existing practices, competing guidelines, and institutional culture have all played roles in delaying the adoption of transfusion guidelines [36–38].

Implementation science research focuses on how to translate evidence-based treatments to clinical practice with eventual assessment of outcomes stemming from the application of these treatments to practice [39]. Thus far, the most effective strategies emerging from this work have been audit and feedback, and educational outreach, which have consistently been shown to improve processes and outcomes in a variety of clinical settings [40,41]. Audit and feedback have been particularly helpful in changing physician behavior when individualized, and when practice data are shared in a group setting in a nonpunitive manner [42–47].

Table 2
Barriers and facilitators of guideline adherence

Barriers to Guideline Adherence	Facilitators of Guideline Adherence
Knowledge	Highly effective
Lack of familiarity	Reminder systems
Lack of awareness	Educational outreach
Attitudes	Academic detailing
Lack of agreement with specific clinical practice guidelines	Multiple interventions
Lack of agreement with clinical practice guidelines in general	Moderately effective
Lack of outcome expectancy	Audit and feedback, especially if:
Lack of elf-efficacy	Performed concurrently
Lack of motivation/inertia of practice	Provider specific
Behavior	By peers or opinion leaders
External barriers	Less effective
Guideline factors	Lecture-based didactic continuing medical education
Environmental factors	Mailed, unsolicited materials

Data from refs[26,28,35]

Peer, practice, and organizational influences

The impact of influential physician peers as levers for promoting change should not be underestimated [41,48]. Pollack and colleagues [49] showed that peer influence is a driver of physician practice styles. They raised the possibility of leveraging this peer influence to limit the adoption and use of low-value care models. Physicians generally respond much better to peer leadership, champions, and data shared from their local practice setting [50]. Physician champions are informal opinion leaders who are well-integrated in the medical community and are respected sources of information who serve as early adopters [51]. They work in similar environments and can influence their peers by serving as models and gatekeepers of information. Their colleagues reach out to them owing to their position, personality, knowledge, influence, and interpersonal skills [52].

Audit and feedback

Audit and feedback are widely used as strategies to improve professional practice, either on their own or as a component of multifaceted quality improvement interventions. In an audit and feedback process, an individual's professional practice or performance is measured and then compared with professional standards or targets. Audit and feedback generally leads to small but potentially important improvements in professional practice. The effectiveness of audit and feedback seems to depend on baseline performance and how the feedback is provided [53]. Factors that positively affect audit and feedback are summarized in Box 3. Audit and feedback is generally most effective when part of a multifaceted approach that includes educational outreach [40,41,54].

Educational outreach

Educational outreach is best performed by physician peers in a multidisciplinary group setting. Alternatively, outside experts can provide concise and relevant information about an approach that has had previous success. These visits should be interactive, provide the practitioner with evidence and rationale

Box 3: Factors positively affecting audit and feedback in changing physician practice

- A significant evidence to practice gap is present at baseline.
- The individual responsible for the audit and feedback is a colleague.
- Serial reporting is completed at regular intervals.
- Audit and feedback is provided for both individual reflection and group discussion.
- Actionable metrics of meaning are selected.

Data from Ivers N, Jamtvedt G, Flottorp S, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *The Cochrane database of systematic reviews.* 2012(6):Cd000259.

for the proposed change, and be an opportunity to discuss any concerns [55]. Soumerai and colleagues [56] showed that a brief, focused educational visit by a transfusion specialist can substantially improve the appropriateness and cost effectiveness of blood product use in surgery.

Academic detailing uses educational outreach experts from outside the institution and has been used to update physicians and support adoption to practice [57,58]. Academic detailing has typically been delivered face to face, but web-based and other technologies are being explored as alternative channels. It has been successfully applied to increase adherence of health care professionals to guidelines for screening [59,60] and to decrease inappropriate use of medicines [26]. Finally, clinical decision support using electronic medical records has been shown to be effective in improving processes of care, with variable effects on improving outcomes [61].

Clinical decision support

Reminders provided at the time and in the context of clinical decision-making can be effective in changing physician behaviors [41]. Whether reminders are provided verbally, on paper, or on a computer screen, they are designed to prompt health professionals to recall relevant information at the point-of-care. Immediate electronic reminders can trigger physicians to adhere to guidelines and therefore assist in behavior change. For example, Schwann and colleagues [62] increased antibiotic administration compliance according to Surgical Care Improvement Project core measures using point-of-care electronic prompts. The use of electronic communication technology provides instantaneous availability of guidelines, which may be particularly crucial for busy physicians [61,63]. This strategy is generally most useful when physicians are in agreement with the information being prompted.

TRANSLATING BLOOD CONSERVATION GUIDELINES TO PRACTICE

There are many guidelines related to perioperative bleeding, coagulopathy, and blood management. The most relevant guidelines with the highest class recommendations are summarized in Table 3 [23,64–66]. Several methods exist to evaluate and describe clinical practice guidelines [67–71]. A critical evaluation of these guidelines falls outside the scope of this review. A simplified framework to aid in comparison of the selected clinical practice guidelines is shown in Table 4.

The experience surrounding the care of patients for cardiac surgery, a clinical area in which there is a high incidence of blood product transfusion, illustrates the shortcomings of focusing solely on guidelines. A publication of blood conservation guidelines developed jointly by The Society of Thoracic Surgeons, the Society of Cardiovascular Anesthesiologists (SCA) and American Society of Extracorporeal Technology was published in 2007 [72], and was assessed using a survey instrument in 2010 [73]. Despite the recommendations, limited adoption had occurred.

Table 3
Guidelines and publication qualities for blood management in cardiac surgery

Category	Society of Thoracic Surgeons/SCA (Ferraris et al, [64] 2011)	EACTS/EACTA (Pagano et al, [23] 2018)	American Society of Anesthesiologists Task Force [65] (2015)	ESA (Kozek-Langenecker et al, [66] 2016)
Publication year	2011	2018	2015	2016
Number of class I recommendations	11	14	16	76[a]
Number of class IIa recommendations	20	17	12	2[b]
Total number of recommendations	35	61	50	153[e]
Class I/IIa: total	88.5%	50.8%	56%	50.9%
Methodology for assessing strength of evidence	AHA/ACCF Task Force on Practice Guidelines Methodology Manual[c]	Scottish Intercollegiate Guidelines Network	Self-developed (specified in guideline text)	GRADE
Guidance for implementation	No	No	No	No
Conflict of interest disclosure	Yes	Yes	No	Yes
Outside review	No	No[d]	Yes	Yes
Summary of recommendations	Yes	No	No	Yes

Abbreviations: ACCF, American College of Cardiology Foundation; AHA, American Heart Association; EACTA, European Association of Cardiothoracic Anesthesiologists; EACTS, European Association for Cardio-Thoracic Surgery; ESA, European Society of Anaesthesiologists.

[a] Includes 1A, 1B, and 1C recommendations.

[b] Additional grade 2 recommendations: 2B = 26, 2C = 110.

[c] http://www.americanheart.org/downloadable/heart/1260477059730120 9Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf.

[d] External review method (Scottish Intercollegiate Guidelines Network).

[e] Does not include statements without a recommendation level but only indication of evidence quality.

Table 4
Class of recommendation/level of evidence by guideline

Category	Society of Thoracic Surgeons/SCA (Ferraris et al [64], 2011)	EACTS/EACTA (Pagano et al [23], 2018)	American Society of Anesthesiologists Task Force [65] (2015)	ESA (Kozek-Langenecker et al [66], 2017)[m]
Stop antiplatelet and/or anticoagulants preoperatively	I(B)	IIa(B) – DAPT IIa(C) – DOAC	A2-E[f] B1-E[g]	1C
Evaluation/treatment of preoperative anemia	IIa (B)	IIa(B)[a] IIb(C)[b]	A1-B[h]	1C
Blood management or conservation program	IIa (B)	I (C)	A2-E	N/C[n]
Intraoperative antifibrinolytic therapy	I(A)	I (A)	A1-B	1A
Low volume cardiopulmonary bypass circuit	I(A)	IIA(B)	N/C	N/C
Acute normovolemic hemodilution	IIb(B)	IIb(B)	A1-B	2C
Retrograde autologous priming	IIb(B)	IIa(A)	N/C	N/C
Modified ultrafiltration	N/C	IIb(B)	N/C	N/C
Intraoperative cell salvage	IIa(A)	IIa(B)	N/C	1B
Restrictive transfusion/use of transfusion triggers	IIa	I (B)[d] IIb(B)[e]	A1-B[i] A2-E[i]	1A
Use of transfusion guideline/algorithm	I (A)	IIA(B)	A2-B[l]	1B
POC hemostatic/viscoelastic testing	I (A)	III(C)[c]	A1-B[k] A2-B[l]	1C

Abbreviations: DAPT, dual antiplatelet therapy; DOAC, direct acting oral anticoagulant; EACTA, European Association of Cardiothoracic Anesthesiologists; EACTS, European Association for Cardio-Thoracic Surgery; ESA, European Society of Anaesthesiologists; N/C, no comment in the guideline.

[a] Erythropoietin with iron for non–iron deficiency anemia.

[b] Oral or intravenous iron for mildly or severely anemic patients.

[c] POC testing not recommended.

[d] Packed red blood cell transfusion based on clinical condition versus fixed hemoglobin threshold.

[e] Hematocrit of 21% to 24% during cardiopulmonary bypass is adequate if the DO_2 is maintained.

[f] Discontinue aspirin preoperatively.

[g] Bridge warfarin with low-molecular-weight heparin.

[h] Erythropoietin with or without iron.

[i] Fewer red blood cell transfusions.

[i] Equivocal findings for mortality, cardiac, neurologic or pulmonary complications, and hospital length of stay.

[k] Thromboelastography versus standard coagulation testing.

[l] Rotational thromboelastometry-guided algorithm versus no algorithm.

[m] Entries without grade of recommendation excluded.

[n] No specific recommendation is given regarding a patient blood management program. Patient blood management programs are referenced in different sections (eg, anemia management).

USE OF AN IMPLEMENTATION SCIENCE-BASED APPROACH

Until recently, effective strategies for bridging the evidence-to-practice gap in health care have been largely underused [74,75]. Implementation science focuses on identifying and targeting factors that are critical for successful implementation. It seeks to "understand factors that determine why an evidence-based intervention may or may not be adopted within specific health care or public health settings and uses this information to develop and test strategies to improve the speed, quantity and quality of uptake" [76]. Implementation science-based approaches have the potential to translate evidence-based patient blood management into practice.

The application of implementation science requires an appreciation of 3 key principles (Table 5) [77]. First is the appreciation of the importance of changing the behaviors of clinicians, patients, and policymakers. Most change strategies are designed to improve the capability, opportunity, and motivation of the affected individuals. For patient blood management, this means knowing the guidelines, having ready access to the clinical and laboratory data needed to make transfusion decisions, and believing that one can influence changes in practice. Second is the need to engage a wide range of stakeholders whose influence is imperative to achieving sustained improvements in outcomes. In addition to frontline physicians, this group includes blood bank leadership and institutional executives, because the change strategies likely require alterations to process and policy as well as to priorities and resources. Finally, the physician leader or champion must be flexible and willing to tolerate the iterative and nonlinear nature of the process of addressing barriers and discovering the enablers needed to adapt guidelines to the real-world situation.

In many cases, a readiness assessment conducted before an intervention reveal conditions or behaviors (mediators) that need to be incorporated into implementation strategy. For patient blood management, a systematic,

Table 5
Essential principles in implementation science

Principle	Change strategies
Focus on changing provider behaviors	COM-B model Capability/opportunity/motivation Plus behavior change wheel
Engage all stakeholders affected by new intervention or behavior	Community-engaged research Individuals (patients and providers) Delivery (health system) Others (government, regulators)
Provide flexible commitment to implementation	Iterative, cyclical processes Long-term planning and expectations

Abbreviation: COM-C, capability, opportunity, motivation and behaviour.

Data from Handley MA, Gorukanti A, Cattamanchi A. Strategies for implementing implementation science: a methodological overview. Emergency medicine journal: EMJ. 2016;33(9):660-664

step-by-step process should include 3 major phases. The preimplementation or planning phase starts with making the case for the implementation strategy by clearly establishing its relation to a health problem. Once assembled, the case can be further improved as the leadership team makes stakeholder rounds. Their presentation should delineate the performance gap (between the current and the ideal practice or behavior) and the outcome gap (between the current and the expected health outcomes). For blood conservation, the performance gap will likely be unnecessary blood transfusions with an outcome gap of reduced safety, effectiveness, and patient centeredness. The intervention or behavior change might be adherence to a point-of-care (POC)-driven transfusion algorithm.

Designing the implementation strategy is the next phase and should focus on identifying mediators that represent barriers and facilitators of the desired behavior change. In the case of a POC-driven transfusion algorithm, examples of barriers include availability of laboratory analyzers at the point of care, increased cost of tests and personnel, as well as the risk of being cited for noncompliance (of an ancillary site) by external regulatory agencies. Examples of enablers would be support from a multidisciplinary change team with performance reviews and shared goals supported by the chief operating officer. Careful selection of the implementation strategy is critical, and guidance by experts in quality improvement, human factors and/or implementation science are recommended [78].

Finally, evaluate the implementation strategy by assessing:

1. The process: Is it acceptable and feasible?
2. The mediators of change: Do components modify targeted barriers and enhance targeted enablers?
3. The outcomes: How do they affect the institution (eg, reduced transfusions, cost) and patients (eg, reduced morbidity)?

The design and evaluation of an implementation strategy for increasing adherence to a POC-driven transfusion algorithm in the operating room is shown in Table 6, and a similar display for approaching preoperative anemia management is summarized is shown in Table 7. Additional support and resources that can be used to help close the evidence-to-practice gap are summarized in Table 8.

IMPLEMENTATION STRATEGY FOR PATIENT BLOOD MANAGEMENT

The Society for the Advancement of Patient Blood Management defines patient blood management as "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis, and minimize blood loss in an effort to improve patient outcomes" [88]. Implementation of a patient blood management program requires significant collaboration between clinicians and administrators. These programs touch almost every specialty in medicine. A transfusion specialist plays a key

Table 6
Evaluating implementation strategy for a transfusion algorithm

Performance gap	Unnecessary blood transfusions gap between current and ideal practice/behavior	
Outcome gap	Reduced safety, effectiveness, and patient-centeredness gap between current and expected health outcomes	
Intervention (behavior change)	Adhere to POC-driven transfusion algorithm in the operating room	
Process	*Dimension*	*Measurement*
Acceptability	Transfusion triggers	Survey, focus group discussions
Feasibility	Laboratory TAT	% of sample TAT of <5–10 min
Fidelity	Transfusion algorithm	% protocol adherence
Mediators		
Modify barriers	POC analyzers	Yes/no analyzer in OR # CAP citations per inspection
	CLIA/CAP certification	
	Net cost of intervention	Yes/no hospital ROI determination
Enhance enabler	Multidisciplinary patient blood management team performance review	Yes/no presence of unit-based team
	Collective discussion of results	Number of audit and feedback per year
		Number of group conferences per year
Outcomes		
Transfusions	Restrictive transfusion	Percent transfused
		Units per 1000 patient-days
Cost	Operating margin	AP-DRG-adjusted direct costs
Safety	Patient	Risk-adjusted morbidity

Abbreviations: AP-DRG, all patient-diagnosis related groups; CAP, College of American Pathologists; CLIA, Clinical Laboratory Improvement Amendments; POC, point of care; TAT, turnaround time.

role in the coordination of multiple different specialties (medical and surgical) as well as laboratory and nonclinical staff.

The first national patient blood management program was implemented in Australia following the World Health Assembly's resolution WHA63.12 [89]. Australia adopted the "3 pillar model" of optimizing red cell mass: minimizing blood loss and bleeding and optimizing physiologic reserve to anemia. Guidelines were developed in 6 modules, including critical bleeding and massive transfusion, perioperative, medical, intensive care, obstetrics, and pediatrics and neonates. Other countries, including the UK, Spain, and Switzerland, have established similar programs.

The Simplified International Recommendations for the Implementation of Patient Blood Management described by Meybohm and colleagues [79] recommends the use of bundles to improve adoption. Bundles are "a straightforward set of evidenced-based interventions for a defined patient population that, when implemented together, will result in significantly better, more penetrating and sustainable outcomes than when implemented individually" [90]. Broken down into separate "blocks," an individual hospital can more easily determine

Table 7
Evaluating implementation strategy for preoperative anemia management

Performance Gap	Avoidable red blood cell transfusions gap between current and ideal practice/behavior	
Outcome Gap	Reduced safety, effectiveness, and patient-centeredness gap between current and expected health outcomes	
Intervention (behavior change)	Active management of preoperative anemia	
Process	*Dimension*	*Measurement*
Acceptability	Patients and surgeons	Survey, focus group discussion
Feasibility	Cost and logistics	Yes/no approved clinical pathway
Fidelity	Treatment algorithm	Percent protocol adherence
Mediators		
Modify barriers	Patient inconvenience	Number of additional patient visits
	Reimbursement by payer	Yes/no hospital ROI determination
	Care coordination	Yes/no part of preoperative process
	Net cost of intervention	Yes/no hospital ROI determination
Enhance enabler	Bloodless surgery program	Number of referrals for program
Outcomes		
Untreated anemia	Anemia on morning of surgery	Percent with preoperative anemia
Transfusion	Red blood cells	Red blood cells per 1000 patient-days
Cost	Moderate/severe anemia on discharge	Readmission rate
Safety	Patient	Risk-adjusted morbidity

Abbreviation: ROI, return on investment.

which components would be most realistic and beneficial to implement (Table 9).

Block 1 of recommendations by Meybohm and colleagues includes a patient blood management project manager with a "central role in charge of communication, education, and documentation" who continually informs hospital administrators and medical staff. They also recommend an education program that includes standard operating procedures, clinical protocols, and checklists. Block 2 begins with anemia management, which includes early identification of anemic patients and those undergoing operations with greater than a 10% probability of transfusion and optimization of red cell mass. Block 3 ensures optimization of hemostasis. Before red blood cell transfusion, the use of a coagulation algorithm in accordance with local standards and practice should be adopted. Block 4 introduces a multidisciplinary approach to blood conservation. This approach consists of early anemia detection, restricted laboratory testing with small phlebotomy volumes, and decreasing waste volume. Block 5 focuses

Table 8
Additional support and resources

Source	Content
Agency for Healthcare Quality and Research (AHRQ website) [2]	Formation of unit-based safety programs
American College of Cardiology and American Heart Association (Chan 2017) [41].	Clinical practice guideline implementation strategies
Meybohm et al [79], 2017	Implementation strategy for patient blood management
Proctor et al [80], 2011	Measuring implementation outcomes
Greilich et al [81], 2018	Diffusing successful pilots
Frank et al [82], 2017	System-wide spread of patient blood management
Haynes et al [83], 2017; and Haugen et al [84], 2019	Use of implementation-based approach to reducing mortality using surgical checklists
Journal of Implementation Science [85] (https://implementationscience.biomedcentral.com)	General resources
Annual Conference on the Science of Dissemination and Implementation in Health [86] (https://www.academyhealth.org/events)	General resources
UCSF Department of Epidemiology and Biostatistics [87] (https://epibiostat.ucsf.edu/certificate-programs)	Online training programs in implementation science for leaders in quality improvement

on optimal resource management, particularly adopting a restrictive transfusion practice. Emphasis on single-unit transfusion and specification of indications for transfusion help reduce overall transfusion. Block 6 is benchmarking. Data should be collected on all aspects of a patient blood management program, both administrative and clinical. Data can be reported by service line as well as by individuals. The adoption of bundles facilitates implementation of patient blood management programs in a stepwise fashion without requiring immediate major changes that may not be well-received.

Support from executives, at the hospital and system levels, is imperative for a patient blood management program's success [81]. Also imperative is using a clinical community approach, consisting of physician-led, self-governing stakeholders to improve quality in health care. The Johns Hopkins Health System adopted a patient blood management program across 5 hospitals [82]. The largest hospital in the system, The Johns Hopkins Hospital, began an educational program in each department. Focusing on abundant high-quality evidence, an educational program initially targeted surgical services and transfusion triggers and thresholds. Data acquisition was initially provided via a commercial system (IMPACT Online, Haemonetics Corp, Braintree, MA). Equally important to the clinical education component was a formal business plan that included salary support for transfusion specialists (including 1

Table 9
Summary of blood management bundles

Block 1	
Patient blood management project management	Patient blood management stakeholder involvement Education Local standards of practice/protocols
Block 2	
Manage patient's anemia	Preoperative management of anemia (subgroup of surgical patients) Improve cardiovascular and pulmonary tolerance of anemia Anemia management in postoperative/hospitalized patients
Block 3	
Optimizing coagulopathy	Preoperative management of coagulopathy Hemostasis management in hospitalized patients
Block 4	
Interdisciplinary blood conservation modalities	Reduction of diagnostic-associated blood loss Reduction of surgery-related blood loss (subgroup of surgical patients)
Block 5	
Optimal blood use with patient-centered decision making	Patient-centered decision making
Block 6	
Patient blood management-related metrics, patient's outcome, benchmark	Patient blood management–related metrics Patient's outcome Benchmarking Program budget for patient blood management Hospital audit for patient blood management Hospital accreditation for patient blood management

Data from Meybohm P, Richards T, Isbister J, et al. Patient Blood Management Bundles to Facilitate Implementation. Transfusion medicine reviews. 2017;31(1):62-71.

anesthesiologist), a nurse coordinator, and a data manager. Peer comparison was accomplished with rank-order bar graphs with individual identifiers available within departments but not between departments. Blood acquisition cost savings were $2,102,273 per year, a 400% return on investment.

HIGH OPPORTUNITY AREAS FOR PERIOPERATIVE BLOOD CONSERVATION: LESSONS FROM CARDIAC SURGERY

Although much of the evidence base discussed in this article derives from cardiac surgery, the broader goal is to provide a framework for translating guidelines to an improved practice of perioperative blood conservation for patients with anemia and/or patients at risk for at least moderate blood loss (>500 mL).

Implementation of a preoperative anemia management program

Anemia is a predictor of long-term mortality in patients undergoing cardiac surgery (Fig. 1) [91–95]. It is also an independent risk factor for postoperative

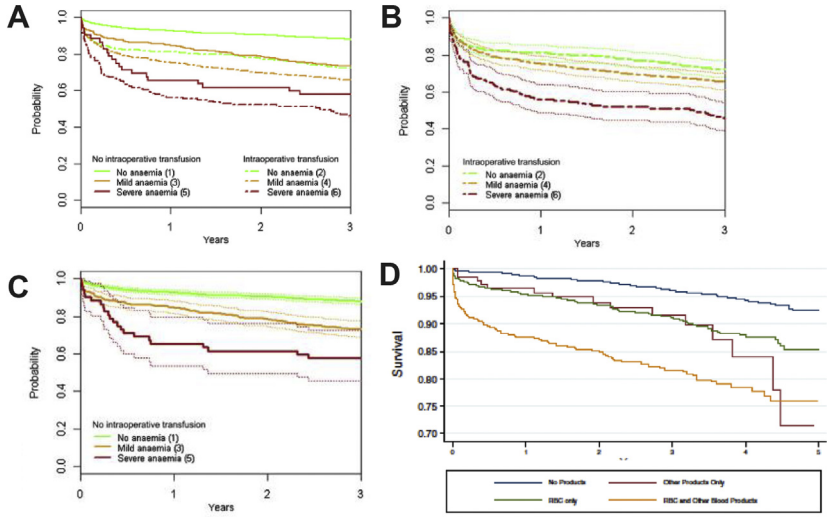

Fig. 1. Association of transfusion of blood and blood products with long-term survival. (*A, B*) Anemia severity, transfusion, and survival. (*C*) Anemia severity and survival. (*D*) Transfusion and survival. ([*A–C*] *From* von Heymann C, Kaufner L, Sander M, et al. Does the severity of preoperative anemia or blood transfusion have a stronger impact on long-term survival after cardiac surgery? *The Journal of Thoracic and Cardiovascular Surgery.* 2016;152(5):1412-1420; with permission. [*D*] *From* Bhaskar B, Dulhunty J, Mullany DV, Fraser JF. Impact of blood product transfusion on short and long-term survival after cardiac surgery: more evidence. *The Annals of Thoracic Surgery.* 2012;94(2):460-467.)

renal dysfunction, stroke, and prolonged hospital length of stay [93]. Although there are conflicting data, preoperative administration of erythropoietin plus iron or a single dose of erythropoietin, have been shown to reduce transfusion requirements, improve survival, and shorten hospital length of stay [96,97]. This management program can stand alone or be part of a larger, institution-wide patient blood management bundle as recently described by Meybohm and colleagues [79].

The initial step in establishing such a program requires assessing the institutional need for decreasing transfusion rates in cardiac surgery. Gathering information about the number of anemic patients undergoing surgery and transfusion rates for those with varying degrees of anemia and their outcomes can help an institution assess the potential impact of an anemia management program. These data can be collected from enterprise databases and clinical registries such as the Society of Thoracic Surgeons National Database. After determining whether a cardiac surgical program would benefit from a preoperative anemia management program, the next phase is to conduct an assessment of readiness, which includes a determination of feasibility and acceptability of a program proposal. Resources vary among hospital systems, and it is advisable to survey the availability of infrastructure, funding, personnel, equipment, and

other services (ie, laboratory, pharmacy) necessary for successful implementation. Based on the initial investigations into the feasibility of a project, realistic goals or milestones should be determined. Even if a comprehensive preoperative anemia program may not be possible, elements of the program may still be implemented on a smaller scale.

Development of a management team and engagement with stakeholders

Successful implementation of a preoperative anemia management program requires a central management team to coordinate patient selection, determine treatment pathways, and evaluate quality outcomes such as transfusion rates and perioperative adverse events. This management team also needs to engage with hospital leadership and primary stakeholders, including patients, surgeons, anesthesiologists, hematologists, blood bank personnel, laboratory medicine leadership, and perioperative physicians. It is critical that the benefits to patients and the cost-to-benefit ratio be emphasized to all major stakeholders and hospital leaders. The cost effectiveness of anemia management programs has been shown for patients with chronic kidney disease, and recent simulations of patient blood management bundles have revealed the potential for reduced hospital length of stay and associated cost savings. Leadership awareness and support are crucial to overcoming barriers to implementation of an anemia treatment program.

Planning the intervention

Factors important for designing an anemia treatment program are summarized in Table 10 and include patient eligibility criteria, the treatment regimen, overall cost, monitoring for patient safety, and performance evaluation. Patients referred for cardiac surgery can be flagged for predetermined hemoglobin or hematocrit levels. The level at which significant anemia is defined can be either an institutional decision or based on national and international guidelines. Once a patient is identified with preoperative anemia, it is important for the preoperative clinical staff to investigate the cause of the anemia.

Treatment pathway

Although oral iron supplementation is the most common treatment for iron deficiency anemia, normalization of hemoglobin levels can take weeks [98]. Intravenous iron supplementation can improve hemoglobin levels safely and more rapidly than oral supplements, making it more appropriate in the context of cardiac surgery [99]. Intravenous iron therapy needs to be administered and monitored by health care professionals, which may lead to increased cost and facility use. Using hospital outpatient chemotherapy infusion centers may help to decrease costs and, in some systems, provide a source of revenue. Patients with coagulopathies, a history of stroke, or hypersensitivity to intravenous iron should be excluded from this treatment.

A recent meta-analysis found that preoperative erythropoietin treatment for anemia in cardiac surgical patients leads to a 50% decrease in the incidence of perioperative blood transfusions [100]. In addition, preoperative administration

Table 10
Factors important for designing an anemia management program

Factors	Special Considerations
Patient eligibility criteria	Level of anemia (hemoglobin or hematocrit)
	Underlying causes of anemia
	Identification of patients
Treatment regimen	Treatment (iron and/or erythropoietin)
	Timing and duration of treatment
	Surveillance of patients (follow-up visits and tests)
Cost of implementation	Medications
	Laboratory tests
	Staffing
	Identification and follow-up of patients (clinic?)
Monitoring for patient safety	Side effects
	Complications
	Rate of increase of hemoglobin
Performance evaluation of program	Cost
	Acceptance of program
	Number of patients screened
	Number of patients screened
	Annual transfusion rates
	Other outcomes

of erythropoietin with iron has been shown to be as safe as iron therapy alone in a variety of surgical populations including cardiothoracic surgery [101]. Dosing regimens vary and even ultrashort courses (0–5 days) of erythropoietin with or without intravenous iron have been shown to be effective [96,97,102,103]. Some treatment regimens include postoperative doses of erythropoietin during patient hospitalization. Scheduling and logistical barriers may make it difficult to adhere to established treatment regimens, so shorter courses may be preferable.

Strategy for surveillance and monitoring

Previous experience in patients with chronic kidney disease provides a framework for monitoring erythropoietin therapy [104–106]. Regardless of the dose or administration schedule, erythropoietin therapy should be accompanied by formal monitoring for the development of venous thrombosis or pulmonary embolism. It is recommended to use venous thromboembolism prophylaxis during erythropoietin therapy. Contraindications to erythropoietin treatment include known malignancy, significant hypertension, thrombophilia, or a high risk of stroke. Although the risks of parenteral iron administration have been reduced with new iron formulations, the risks of anaphylaxis, thrombosis, or iron overload still exist. During the preoperative treatment period, the patient should have 1 to 2 visits for surveillance of side effects or adverse events. The rate of increase in hemoglobin should not exceed 1 g/dL per week. Diastolic blood pressures should not exceed 100 mm Hg. Therapy should also

be halted in those patients who display allergic reactions or complications at any time during the course of treatment.

Infrastructure and cost

Major costs include laboratory studies, cost of medications, and hospital or clinic staff. Facilities should be able to provide space and equipment for the intravenous administration of iron. For example, in 2015 at the University of Texas Southwestern Medical Center in Dallas, the average anemic patient undergoing cardiac surgery received 3.07 units of packed red blood cells, compared with 1.3 units for nonanemic patients. These anemic patients also had longer ICU stays resulting in an average additional cost of $10,282. Acquisition cost of 1 unit of packed red blood cells is $155. However, the total cost of packed red blood cells units may be as much as 4 times higher owing to costs associated with testing, storage, administration and complications [88]. The cost of an EPOGEN (Amgen, Thousand Oaks, CA) injection plus FERAHEME (AMAG Pharmaceuticals, Waltham, MA) for an 80-kg patient is about $2232. If preoperative anemia therapy is instituted, the predicted cost savings may approach $8000 per patient.

Performance evaluation

When initiating any quality improvement or treatment program, it is important to develop methods to test performance. It is also important to evaluate how well the program is implemented at set intervals after program initiation. Stakeholder acceptance of a blood conservation program can be measured through feedback surveys, a feedback hotline or website, and interval group feedback sessions, particularly of the major clinical providers (cardiac surgeons, cardiac anesthesiologists, critical care physicians, and the perioperative and intensive care unit staff). Adoption of the program can be measured with a variety of methods, including a review of pharmacy administration logs for erythropoietin and parenteral iron supplementation, a count of patients referred for anemia treatment, and a system for reporting staff use. Reevaluation on a monthly basis is recommended after program implementation to assess for areas of waste or possible avenues for improvement. Finally, penetration of the program can be calculated by looking at the number of anemic cardiac surgical patients enrolled in the treatment program divided by the total number of anemic cardiac surgical patients diagnosed or screened in the preoperative setting.

At some point after a program has been implemented, service metrics should be evaluated. In the case of blood conservation, the service metrics are well-defined. Annual transfusion rates in cardiac surgery cases (typically excluding aortic surgery, ventricular assist devices, transplants, or other procedures with very high blood loss) should be monitored. Other variables that should be recorded include preoperative and postoperative complication including prolonged ventilation, stroke, acute kidney injury, renal failure, infection, sepsis, and death. Length of stay, cost of care, and staff work-hours can also be used. The metrics should be analyzed with reference to clinical providers including surgeon and anesthesiologist. Results of the analysis can hopefully

provide enough data to indicate the cost benefit and/or outcomes benefit of the program.

USE OF A SURVEY INSTRUMENT TO DRIVE LOCAL AND NATIONAL PERIOPERATIVE BLOOD CONSERVATION

As described elsewhere in this article, audit and feedback is one of the most reliable methods for improving process and clinical outcomes. Surveys have long been used to collect, compare, and analyze information from either the general population or targeted groups. A well-designed questionnaire can provide valid and actionable information about behaviors, practices, and unjustified variations in practices. One approach in quality improvement is the use of a survey as a mechanism for audit and feedback. Audit and feedback methods have been shown to be useful tools in implementation science to promote the adoption of clinical recommendations or consensus policies [41]. Surveys can evaluate the efficacy of particular clinical interventions, identify knowledge gaps among providers and reveal impediments to adoption of best clinical practices. Surveys performed by the American Society of Anesthesiologists Committee on Transfusion Medicine in 1981 and 2002 have been used to demonstrate notable reductions in hemoglobin triggers, increased use of POC coagulation testing, and increased availability of autologous blood salvage equipment [107]. Previously mentioned was the clinical practice guideline for blood conservation published in 2007 [37,73,108,109]. Although both surveys provided useful information, the prolonged interval between surveys and lack of serial data limited their usefulness as instruments for audit and feedback. The biennial hospital survey on patient safety created by the Agency for Healthcare Research and Quality is more representative of how a validated survey might be used for audit and feedback for patient blood management [110].

Survey instruments can also be used by medical societies to support the development of quality metrics and champion efforts to close evidence-to-practice gaps. For example, the SCA, American Society of Anesthesiologists, and Anesthesia Quality Institute's (AQI) recently created a metric for blood conservation during cardiopulmonary bypass (AQI49). The 4 components of this composite metric include the (1) use of lysine analogues, (2) use of minicircuits, retrograde autologous priming, ultrafiltration, (3) use of red cell salvage, and (4) use of a transfusion algorithm with POC testing [111]. This composite metric has been added to the AQI's Qualified Clinical Data Registry and has provisional acceptance by the National Quality Forum as an allowable measure for merit-based incentive payment system. Concurrent with this work, the SCA Blood Conservation Work Group designed a serial survey instrument for audit and feedback both locally and nationally. The potential role of a serial survey in translating guidelines to practice is shown in Fig. 2. The survey addresses (1) preoperative preparation, (2) intraoperative techniques, (3) transfusion avoidance and algorithms, (4) POC testing, (5) hemostatic agents and factor concentrates, and (6) massive bleeding and transfusion. Locally, a serial survey could

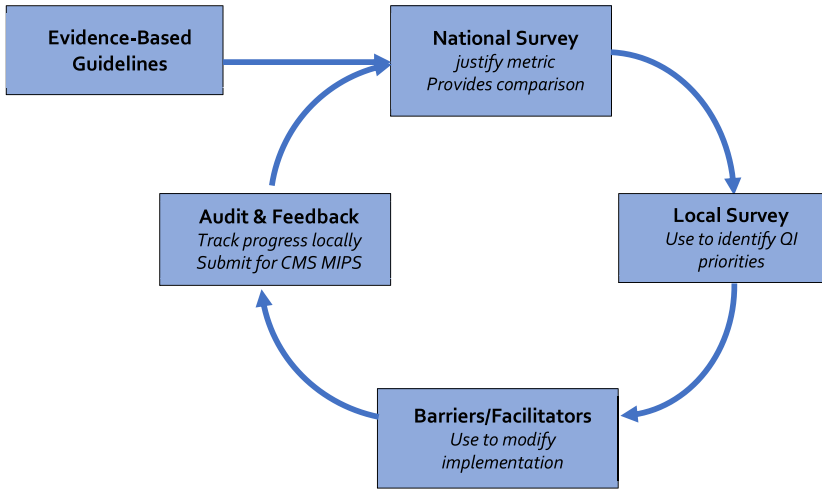

Fig. 2. Role of SCA serial blood conservation survey in support of efforts to translate guidelines to practice. CMS, Centers for Medicare and Medicaid Services; MIPS, merit-based incentive payment system; NQF, National Quality Foundation; QI, quality improvement; SCA, Society of Cardiovascular Anesthesiologists.

be tailored for use as an audit and feedback tool focusing on their greatest priority. Comparative data from the national survey (conducted every 2–4 years) could be used help local champions with policymakers and promote a common language among a peer-to-peer collaboration. Aligning local, regional, and national efforts has the potential to increase the capacity and effectiveness of blood conservation champions. The 2017 SCA Survey of Blood Conservation in Cardiac Surgery had 525 respondents. It demonstrated the AQI49 composite is justified, because fewer than 30% of the practices reported conformance with all 4 components. Although low, the National Quality Forum prefers metrics supported by Class I evidence with large evidence-to-practice gaps. In the beginning, top decile performance could be as low 40% to 60% until wider adoption occurs.

Although survey research does have some inherent difficulties, including assessing the validity of the survey data, assessing for the presence of survey bias, and acquiring adequate response rates, a survey is a relatively simple and cost-effective tool to help promote and assess the implementation of quality standards in health care [112]. The designation of local champions, working in conjunction with regional and national efforts to provide meaningful metric and comparative data, is essential. The maintenance of survey response rates should ideally be more than 30% to maintain validity of the audit and feedback system. The development of a peer-to-peer network capable of sharing barriers and facilitators to perioperative blood conservation is vital to program success.

TRANSFUSION ALGORITHMS

Despite the lack of practice change observed owing to the Society of Thoracic Surgeons/SCA 2007 guideline [73], there is evidence that reduction in practice variation can improve the process and structure of care [113]. Evidence also exists that decreased interhospital variation decreases red blood cell transfusion and maintains patient safety [114–116]. Further, the use of an algorithm or protocol for the evaluation and treatment of coagulopathy is associated with decreased perioperative use of red blood cells and other blood products, decreased blood product reactions and thrombotic events, improved 6-month mortality, and decreased hospital cost [117–120].

POC hemostatic testing, particularly when used in conjunction with an algorithmic approach to treatment of hemostatic lesions, decreases red blood cell and platelet transfusions. Additionally, POC testing decreases major bleeding after cardiac surgery, postoperative mechanical ventilation time, intensive care unit length of stay, and 6-month mortality [121–123].

LEVERAGING COMMON INTEREST IN RESTRICTIVE TRANSFUSION

Lessons learned from cardiac surgery are used in this article to provide examples for the implementation of blood conservation to practice. However, blood management is an area of common interest and focus of quality improvement for many groups (eg, different medical specialties, hospital leadership, quality and safety organizations) at the local, regional, national, and international levels. This common interest can be a driving force for collaboration and leverage to implement change. Mazer and colleagues [124] recently confirmed restrictive transfusion to be noninferior to liberal transfusion in cardiac surgery. Transfusion data are monitored by the Society of Thoracic Surgeons National Database and the American College of Surgeons National Surgical Quality Improvement Program. Thus, restrictive transfusion is a high opportunity area for implementing change and a topic that lends itself to be the topic of a survey. A survey instrument can assess transfusion thresholds and restrictive strategies being used to provide a window into practice behaviors and gaps. This use of audit and feedback can be used to drive collaboration for change and quality improvement. Further, this process can be expanded to different service lines (eg, orthopedic surgery, spine surgery, and surgical oncology) to improve perioperative blood conservation beyond cardiac surgery.

PEER-TO-PEER LEARNING COLLABORATIVES

These approaches can be combined with an institution-wide blood conservation program. These programs have been effective in reducing blood use and improving patient outcomes in both academic and private practice settings [114,116,125–127].

SUMMARY

Multiple guidelines exist for perioperative blood management [23,64–66,128,129]. Implementation science can be applied to the translation of patient blood management to practice. Meybohm and colleagues [79] describes an implementation strategy using comprehensive bundles of patient blood management that illustrates the breadth of this endeavor. The process of establishing a preoperative anemia management is an example for the implementation of 1 component of a patient blood management program. Blood conservation efforts in cardiac surgery are described, but lessons learned can be applied more broadly. Barriers and facilitators for adoption to practice are provided in this article to help provide a framework for strategy. Patient blood management requires a proactive, patient-centered, and multidisciplinary approach with the goal of decreasing cost, decreasing harm, and improving outcomes in cardiac surgery.

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APPENDIX 1: STANDARDS FOR DEVELOPING TRUSTWORTHY CLINICAL PRACTICE GUIDELINES

STANDARD 1

Establishing transparency

1.1 The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible.

STANDARD 2

Management of conflict of interest (COI)

2.1 Prior to selection of the Guideline Development Group (GDG), individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity, by written disclosure to those convening the GDG.
- Disclosure should reflect all current and planned commercial (including services from which a clinician derives a substantial proportion of income), noncommercial, intellectual, institutional, and patient/public activities pertinent to the potential scope of the CPG.

2.2 Disclosure of COIs within GDG
- All COI of each GDG member should be reported and discussed by the prospective development group prior to the onset of their work.
- Each panel member should explain how their COI could influence the CPG development process or specific recommendations.

2.3 Divestment
- Members of the GDG should divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by CPG recommendations.

2.4 Exclusions
- Whenever possible GDG members should not have COI.
- In some circumstances, a GDG may not be able to perform its work without members who have COIs, such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the CPG.
- Members with COIs should represent not more than a minority of the GDG.
- The chair or co-chairs should not be a person(s) with COI.
- Funders should have no role in CPG development.

STANDARD 3

Guideline development group composition

3.1 The GDG should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG.

3.2 Patient and public involvement should be facilitated by including (at least at the time of clinical question formulation and draft CPG review) a current or former patient and a patient advocate or patient/consumer organization representative in the GDG.

3.3 Strategies to increase effective participation of patient and consumer representatives, including training in appraisal of evidence, should be adopted by GDG.

STANDARD 4

Clinical practice guideline–systematic review intersection

4.1 CPG developers should use systematic reviews that meet standards set by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research.

4.2 When systematic reviews are conducted specifically to inform particular guidelines, the GDG and systematic review team should interact regarding the scope, approach, and output of both processes.

STANDARD 5

Establishing evidence foundations for and rating strength of recommendations

5.1 For each recommendation, the following should be provided:

- An explanation of the reasoning underlying the recommendation, including:
  - A clear description of potential benefits and harms.
  - A summary of relevant available evidence (and evidentiary gaps), description of the quality (including applicability), quantity (including completeness), and consistency of the aggregate available evidence.
  - An explanation of the part played by values, opinion, theory, and clinical experience in deriving the recommendation.
- A rating of the level of confidence in (certainty regarding) the evidence underpinning the recommendation.
- A rating of the strength of the recommendation in light of the preceding bullets.
- A description and explanation of any differences of opinion regarding the recommendation.

STANDARD 6

Articulation of recommendations

6.1 Recommendations should be articulated in a standardized form detailing precisely what the recommended action is and under what circumstances it should be performed.

6.2 Strong recommendations should be worded so that compliance with the recommendation(s) can be evaluated.

STANDARD 7

External review

7.1 External reviewers should comprise a full spectrum of relevant stakeholders, including scientific and clinical experts, organizations (e.g., health care, specialty societies), agencies (e.g., federal government), patients, and representatives of the public.

7.2 The authorship of external reviews submitted by individuals and/or organizations should be kept confidential unless that protection has been waived by the reviewer(s).

7.3 The GDG should consider all external reviewer comments and keep a written record of the rationale for modifying or not modifying a CPG in response to reviewers' comments.

7.4 A draft of the CPG at the external review stage or immediately following it (i.e., prior to the final draft) should be made available to the general public for comment. Reasonable notice of impending publication should be provided to interested public stakeholders.

STANDARD 8

Updating

8.1 The CPG publication date, date of pertinent systematic evidence review, and proposed date for future CPG review should be documented in the CPG.

8.2 Literature should be monitored regularly following CPG publication to identify the emergence of new, potentially relevant evidence and to evaluate the continued validity of the CPG.

8.3 CPGs should be updated when new evidence suggests the need for modification of clinically important recommendations. For example, a CPG should be updated if new evidence shows that a recommended intervention causes previously unknown substantial harm, that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective, or that a recommendation can be applied to new populations. (Standards for Developing Trustworthy Clinical Practice Guidelines, 2011)

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