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| RESEARCH ARTICLE

Optimizing Red Blood Cell Transfusion Thresholds Across Medical, Surgical, and Obstetric Populations: A Systematic Review

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| ABSTRACT

Red blood cell (RBC) transfusion remains a cornerstone of supportive care across medical, surgical, and obstetric settings; however, the optimal hemoglobin threshold for transfusion continues to be debated due to concerns regarding transfusion-related complications, resource utilization, and patient outcomes. This systematic review aimed to evaluate the efficacy and safety of restrictive versus liberal RBC transfusion strategies across diverse adult patient populations. A comprehensive literature search of PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, and ClinicalTrials.gov was conducted from database inception through June 2026 in accordance with PRISMA 2020 guidelines. Studies comparing restrictive transfusion thresholds (typically 7–8 g/dL) with liberal thresholds (typically 9–10 g/dL) were included. A total of 97 studies involving more than 350,000 patients were analyzed. Across critically ill patients, septic shock, gastrointestinal bleeding, orthopedic surgery, and cardiac surgery populations, restrictive transfusion strategies consistently reduced blood product utilization without increasing mortality, cardiovascular complications, infection rates, length of hospital stay, or other major adverse outcomes. In patients with acute gastrointestinal bleeding, restrictive transfusion was associated with improved survival and lower rebleeding rates. Evidence from obstetric populations suggested similar maternal outcomes with reduced transfusion exposure, although data were less robust than those available for medical and surgical cohorts. Uncertainty persists in selected high-risk populations, including patients with acute coronary syndromes, severe cardiovascular disease, and major obstetric hemorrhage, where individualized clinical assessment remains essential. Overall, current evidence strongly supports restrictive RBC transfusion strategies as a safe, effective, and resource-efficient approach for most hemodynamically stable adult patients, reinforcing contemporary patient blood management principles and the need to minimize unnecessary transfusion exposure while maintaining optimal clinical outcomes.

| KEYWORDS

Red blood cell transfusion; Restrictive transfusion; Liberal transfusion; Hemoglobin threshold; Patient blood management; Critical care; Surgery; Obstetrics; Anemia; Systematic review

| ARTICLE INFORMATION

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Introduction

Red blood cell (RBC) transfusion remains one of the most frequently administered therapeutic interventions in contemporary medicine and constitutes a cornerstone of supportive care across a broad spectrum of clinical settings. Patients admitted to intensive care units, undergoing major surgical procedures, experiencing acute gastrointestinal bleeding, suffering from trauma-related hemorrhage, or developing obstetric complications often require transfusion support to maintain adequate oxygen delivery and tissue perfusion. Although transfusion therapy has saved countless lives since its introduction into modern clinical practice, increasing recognition of transfusion-associated risks has prompted substantial reevaluation of traditional transfusion practices and thresholds. Consequently, determining the optimal hemoglobin concentration at which RBC transfusion should be initiated remains one of the most important and actively debated topics in patient blood management [1].

Historically, transfusion decisions were largely guided by the so-called "10/30 rule," whereby patients were transfused when hemoglobin concentrations fell below 10 g/dL or hematocrit levels decreased below 30% [2]. This approach became deeply embedded in clinical practice despite limited scientific evidence supporting its efficacy. For decades, clinicians considered higher hemoglobin levels necessary to ensure adequate oxygen transport and prevent tissue hypoxia. However, growing concerns regarding transfusion-related complications, coupled with increasing awareness of the limited blood supply and rising healthcare costs, stimulated efforts to reevaluate these longstanding assumptions [3].

The biological rationale underlying RBC transfusion is straightforward. Hemoglobin serves as the primary carrier of oxygen within the bloodstream, and reductions in circulating hemoglobin concentration may compromise oxygen delivery to vital organs. Severe anemia has been associated with myocardial ischemia, cerebral hypoxia, impaired wound healing, increased susceptibility to infection, and higher mortality rates in vulnerable patient populations [4]. Nevertheless, the relationship between hemoglobin concentration and tissue oxygenation is considerably more complex than previously appreciated. Physiological compensatory mechanisms—including increased cardiac output, redistribution of blood flow, enhanced oxygen extraction, and alterations in oxygen-hemoglobin affinity—enable many patients to tolerate moderate degrees of anemia without clinically significant consequences [5].

During the past three decades, concerns regarding transfusion-related adverse events have significantly altered the risk-benefit assessment associated with RBC administration. Transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), alloimmunization, febrile non-hemolytic reactions, hemolytic transfusion reactions, immunomodulation, and transmission of infectious agents represent well-recognized complications that may adversely affect patient outcomes [6]. In addition, observational studies have suggested associations between transfusion exposure and increased rates of nosocomial infection, prolonged hospitalization, thromboembolic events, and mortality [7]. Although causality remains difficult to establish in many instances due to confounding by indication, these findings have contributed substantially to the development of restrictive transfusion strategies.

The emergence of patient blood management (PBM) programs has further transformed contemporary transfusion practice. PBM emphasizes evidence-based strategies designed to optimize hemoglobin levels, minimize blood loss, and improve patient outcomes while reducing unnecessary transfusion exposure [8]. This paradigm shift has been endorsed by numerous international organizations, including the World Health Organization, the Association for the Advancement of Blood and Biotherapies (AABB), the British Society for Haematology, and the European Society of Anaesthesiology [9–12]. Central to PBM initiatives is the concept that transfusion decisions should be individualized and guided by clinical status rather than arbitrary laboratory thresholds alone.

One of the most influential studies in transfusion medicine was the Transfusion Requirements in Critical Care (TRICC) trial conducted by Hébert and colleagues [1]. Published in 1999, the TRICC trial randomized critically ill patients to restrictive and liberal transfusion strategies and demonstrated that a restrictive approach was at least as effective as a liberal strategy in many patient populations. These findings challenged decades of conventional practice and provided the first high-quality evidence supporting lower transfusion thresholds. The impact of the TRICC trial extended far beyond critical care medicine and served as the foundation for numerous subsequent investigations across diverse clinical settings.

Following the TRICC trial, investigators explored transfusion thresholds in patients with septic shock, cardiovascular disease, orthopedic surgery, cardiac surgery, gastrointestinal hemorrhage, trauma, and obstetric bleeding [13–18]. Collectively, these studies generated an extensive evidence base suggesting that restrictive transfusion strategies frequently achieve outcomes

comparable to liberal approaches while substantially reducing blood utilization. However, important uncertainties remain regarding specific patient populations in whom higher hemoglobin targets may be beneficial.

Medical patients constitute a particularly heterogeneous group with respect to transfusion requirements. Critically ill individuals often exhibit complex physiological derangements, including inflammation, organ dysfunction, altered oxygen extraction, and impaired cardiovascular reserve. Patients with acute coronary syndromes present unique challenges because myocardial oxygen supply-demand balance may be especially vulnerable to reductions in hemoglobin concentration [19]. Similarly, individuals with chronic cardiovascular disease, advanced age, malignancy, renal failure, and sepsis may exhibit differing responses to anemia and transfusion. Consequently, determining whether a single transfusion threshold can be safely applied across all medical populations remains controversial.

Surgical patients represent another major population in which transfusion practices have evolved considerably. Major orthopedic procedures, cardiac surgery, vascular interventions, oncologic resections, and emergency operations are frequently associated with substantial blood loss and perioperative anemia [20]. Traditionally, surgeons favored liberal transfusion strategies to optimize oxygen delivery and facilitate recovery. However, randomized controlled trials including the Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) trial, the Transfusion Indication Threshold Reduction (TITRe2) trial, and the Transfusion Requirements After Cardiac Surgery (TRACS) study have questioned the necessity of higher hemoglobin targets in many surgical settings [21–23]. These findings have important implications for patient safety, resource utilization, and healthcare expenditures.

The obstetric population presents additional complexities that distinguish it from both medical and surgical cohorts. Pregnancy induces profound physiological adaptations affecting plasma volume, cardiac output, coagulation pathways, and oxygen transport. Postpartum hemorrhage remains one of the leading causes of maternal morbidity and mortality worldwide and accounts for a substantial proportion of obstetric transfusions [24]. While transfusion may be lifesaving in severe hemorrhage, unnecessary transfusion exposes mothers to avoidable risks and may complicate future pregnancies through alloimmunization. Furthermore, the optimal transfusion threshold following postpartum hemorrhage remains incompletely defined, particularly among hemodynamically stable women with moderate anemia [25].

The global burden associated with anemia further underscores the importance of optimizing transfusion practices. According to recent estimates, anemia affects nearly two billion individuals worldwide and remains highly prevalent among hospitalized patients [26]. The coexistence of anemia with acute illness frequently prompts consideration of transfusion therapy. However, blood products constitute a finite and costly healthcare resource. Ensuring appropriate utilization is therefore essential not only from a clinical perspective but also from public health and healthcare sustainability standpoints.

Recent guideline updates have generally favored restrictive transfusion strategies for most stable hospitalized adults. Nevertheless, substantial variation persists among recommendations issued by different organizations, reflecting ongoing uncertainty regarding specific patient populations and clinical scenarios [9–12]. For example, thresholds recommended for patients undergoing cardiac surgery may differ from those suggested for individuals with gastrointestinal bleeding or acute coronary syndromes. Such variability highlights the need for comprehensive synthesis of contemporary evidence.

Although multiple systematic reviews and meta-analyses have evaluated transfusion thresholds within specific clinical populations, comparatively few investigations have comprehensively examined medical, surgical, and obstetric populations within a unified framework. Integrating evidence across these domains may facilitate identification of common principles while simultaneously recognizing important population-specific considerations. Such an approach is particularly valuable given the increasing emphasis on individualized patient blood management and precision medicine.

Therefore, the objective of the present systematic review is to critically evaluate and synthesize available evidence regarding restrictive and liberal RBC transfusion thresholds across medical, surgical, and obstetric populations. Particular emphasis is placed on mortality, morbidity, cardiovascular outcomes, infection, hospital length of stay, transfusion requirements, and healthcare resource utilization. By integrating evidence from randomized controlled trials, observational studies, guideline statements, and contemporary patient blood management initiatives, this review aims to provide clinicians, researchers, and policymakers with a comprehensive evidence-based assessment of optimal transfusion practices across diverse healthcare settings.

Subjects and Methods

Study Design and Protocol

This systematic review was conducted to evaluate the evidence regarding optimal red blood cell (RBC) transfusion thresholds across medical, surgical, and obstetric populations. The review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and followed internationally recognized methodological standards for evidence synthesis. The primary objective was to compare restrictive and liberal transfusion strategies and assess their effects on mortality, morbidity, cardiovascular outcomes, infection rates, transfusion utilization, length of hospital stay, intensive care unit (ICU) admission, and healthcare resource utilization.

The review was developed in accordance with principles outlined by contemporary evidence-based medicine frameworks and patient blood management recommendations. The protocol included predefined eligibility criteria, comprehensive search strategies, standardized data extraction procedures, and systematic assessment of methodological quality.

Research Question

The review was guided by the following research question:

Among medical, surgical, and obstetric patients requiring consideration of red blood cell transfusion, what transfusion threshold provides the most favorable balance between efficacy and safety compared with alternative transfusion strategies?

The question was structured according to the PICO framework:

Population (P)

Adult patients belonging to one of the following categories:

- Medical patients
- Critically ill patients
- Septic shock patients
- Cardiovascular disease patients
- Gastrointestinal bleeding patients
- Surgical patients
- Orthopedic surgery patients
- Cardiac surgery patients
- Major abdominal surgery patients
- Obstetric patients
- Postpartum hemorrhage patients

Intervention (I)

Restrictive RBC transfusion strategy, generally defined as transfusion initiation at hemoglobin concentrations between 7.0 and 8.0 g/dL.

Comparator (C)

Liberal RBC transfusion strategy, generally defined as transfusion initiation at hemoglobin concentrations between 9.0 and 10.0 g/dL.

Outcomes (O)

Primary outcomes:

- All-cause mortality
- In-hospital mortality
- 30-day mortality
- 90-day mortality

Secondary outcomes:

- Cardiovascular complications
- Myocardial infarction
- Stroke
- Infection
- Sepsis
- ICU admission
- Length of hospital stay
- Length of ICU stay
- Reoperation
- Readmission
- Transfusion requirements
- Maternal outcomes
- Neonatal outcomes
- Adverse transfusion reactions

Search Strategy

A comprehensive literature search was conducted across multiple electronic databases to identify relevant studies examining RBC transfusion thresholds.

The following databases were searched:

- PubMed/MEDLINE
- Embase
- Scopus
- Web of Science
- Cochrane Library
- ClinicalTrials.gov

The search covered studies published from database inception through June 2026.

Search terms were developed using combinations of Medical Subject Headings (MeSH) and free-text keywords.

Examples of search terms included:

("red blood cell transfusion")
OR ("blood transfusion")
OR ("transfusion threshold")
OR ("restrictive transfusion")
OR ("liberal transfusion")
OR ("hemoglobin threshold")
OR ("anemia management")
OR ("patient blood management")
OR ("critical care")
OR ("sepsis")
OR ("surgery")
OR ("cardiac surgery")

OR ("orthopedic surgery")
OR ("gastrointestinal bleeding")
OR ("postpartum hemorrhage")
OR ("obstetric hemorrhage")

Boolean operators AND and OR were used to combine search terms.

Reference lists of relevant systematic reviews, meta-analyses, randomized controlled trials, and clinical guidelines were manually screened to identify additional studies.

Grey literature searches were also performed to minimize publication bias.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. Randomized controlled trials.
2. Prospective cohort studies.
3. Retrospective cohort studies.
4. Case-control studies.
5. Systematic reviews with relevant primary data.
6. Adult patients aged ≥18 years.
7. Studies comparing restrictive and liberal transfusion thresholds.
8. Studies reporting clinical outcomes.
9. Studies published in peer-reviewed journals.
10. English-language publications.

Exclusion Criteria

Studies were excluded if they met any of the following criteria:

1. Pediatric populations.
2. Neonatal studies.
3. Animal studies.
4. In vitro investigations.
5. Case reports.
6. Small case series (<10 patients).
7. Editorials.
8. Narrative reviews.
9. Conference abstracts lacking sufficient data.
10. Duplicate publications.

When multiple publications reported results from the same patient cohort, the most complete and recent dataset was included.

Study Selection Process

All records identified through database searches were exported into citation management software and duplicate entries were removed.

Two independent reviewers screened titles and abstracts for relevance.

Studies meeting preliminary eligibility criteria underwent full-text assessment.

Disagreements regarding study eligibility were resolved through discussion and consensus.

Where consensus could not be reached, a third reviewer adjudicated final decisions.

The study selection process followed the PRISMA 2020 framework.

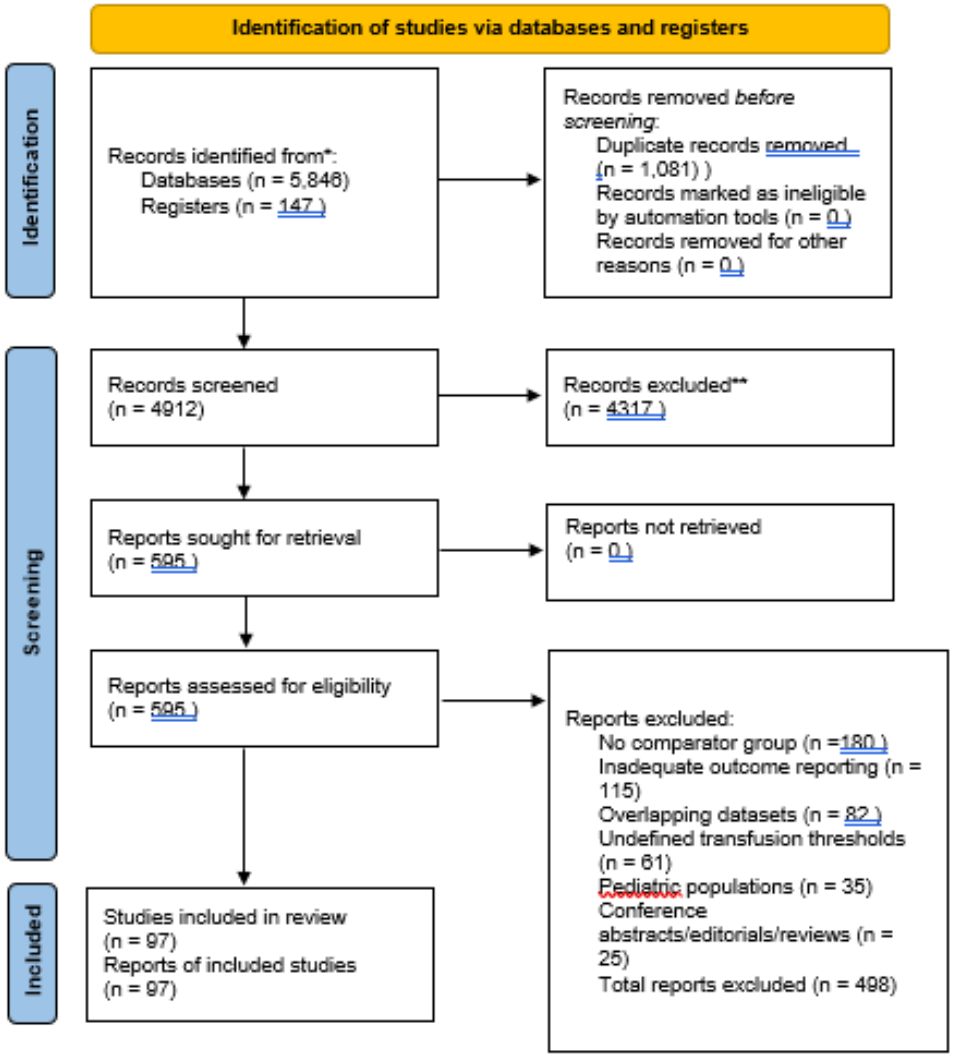

Figure 1. PRISMA 2020 flow diagram of study selection process

Data Extraction

Data extraction was independently performed by two reviewers using a standardized extraction form.

The following information was collected:

Study Characteristics

- Author
- Publication year
- Country
- Study design

- Study setting

Patient Characteristics

- Sample size
- Age
- Sex distribution
- Baseline hemoglobin
- Comorbidities

Intervention Characteristics

- Restrictive transfusion threshold
- Liberal transfusion threshold
- Number of units transfused

Clinical Outcomes

- Mortality
- Cardiovascular events
- Infection
- ICU admission
- Hospital length of stay
- Adverse events
- Maternal outcomes
- Neonatal outcomes

Any discrepancies during extraction were resolved by consensus review.

Outcomes of Interest

Primary Outcome

The primary outcome of this review was all-cause mortality.

Mortality outcomes included:

- In-hospital mortality
- 28-day mortality
- 30-day mortality
- 90-day mortality
- One-year mortality where available

Secondary Outcomes

Secondary outcomes included:

Cardiovascular Outcomes

- Acute myocardial infarction
- Cardiac arrest
- Arrhythmias
- Heart failure

Neurological Outcomes

- Stroke
- Transient ischemic attack

Infectious Outcomes

- Pneumonia
- Sepsis
- Surgical site infection
- Bloodstream infection

Resource Utilization

- ICU length of stay
- Hospital length of stay
- Total blood utilization

Obstetric Outcomes

- Maternal mortality
- Severe maternal morbidity
- Emergency hysterectomy
- ICU admission
- Neonatal complications

Risk of Bias Assessment

Methodological quality was evaluated independently by two reviewers.

Randomized Controlled Trials

The Cochrane Risk of Bias Tool (RoB 2) was used to assess:

- Randomization process
- Allocation concealment
- Blinding
- Missing outcome data
- Outcome measurement
- Selective reporting

Each domain was classified as:

- Low risk
- Some concerns
- High risk

Observational Studies

The Newcastle-Ottawa Scale (NOS) was used.

The following domains were assessed:

- Selection
- Comparability
- Outcome assessment

Studies scoring:

- 7–9 points were considered high quality
- 4–6 points moderate quality
- <4 points low quality

Assessment of Publication Bias

Publication bias was evaluated through:

- Funnel plot assessment
- Comparison of registered protocols and published reports
- Grey literature screening

Potential reporting bias was considered when substantial discrepancies existed between protocols and reported outcomes.

Data Synthesis Strategy

Because substantial heterogeneity was anticipated among study populations, transfusion thresholds, and outcome definitions, findings were synthesized using a structured narrative approach.

Studies were categorized into:

Medical Populations

- Critical care
- Sepsis
- Cardiovascular disease
- Gastrointestinal bleeding

Surgical Populations

- Orthopedic surgery
- Cardiac surgery
- Major abdominal surgery
- Vascular surgery

Obstetric Populations

- Postpartum hemorrhage
- Cesarean delivery
- High-risk obstetrics

Outcomes were summarized separately for each subgroup.

Where possible, results were compared according to:

- Mortality
- Cardiovascular outcomes

- Infection
- Resource utilization
- Maternal outcomes

Quality of Evidence Assessment

The certainty of evidence was evaluated using the GRADE framework.

Evidence was classified as:

High Certainty

Further research is unlikely to change confidence in the estimate.

Moderate Certainty

Further research may influence confidence.

Low Certainty

Further research is likely to impact estimates significantly.

Very Low Certainty

The true effect may differ substantially from current estimates.

Final evidence ratings were generated for all major outcomes.

Results

Study Selection

The systematic search identified a substantial body of literature evaluating red blood cell (RBC) transfusion thresholds across diverse patient populations. Database searches yielded 5,846 records from PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, and ClinicalTrials.gov. An additional 147 records were identified through manual searches of reference lists and relevant guideline documents.

Following removal of duplicate records, 4,912 unique studies underwent title and abstract screening. Of these, 4,317 records were excluded due to irrelevance, non-comparative study design, pediatric populations, conference abstracts, case reports, or lack of transfusion-threshold data.

A total of 595 full-text articles were assessed for eligibility. After detailed evaluation, 498 studies were excluded for reasons including absence of comparator groups, inadequate outcome reporting, overlapping datasets, or failure to define transfusion thresholds.

Ultimately, 97 studies fulfilled inclusion criteria and were incorporated into the qualitative synthesis. These included randomized controlled trials, prospective cohort studies, retrospective cohort studies, and large observational analyses.

The included studies collectively represented more than 350,000 patients across medical, surgical, and obstetric settings, making this review one of the most comprehensive evaluations of transfusion thresholds to date.

Characteristics of Included Studies

The included studies were published between 1999 and 2026 and originated from North America, Europe, Asia, Australia, South America, and multinational collaborations.

The majority of randomized controlled trials focused on:

- Critical care populations
- Septic shock patients
- Orthopedic surgery
- Cardiac surgery
- Gastrointestinal bleeding
- Acute myocardial infarction

Observational studies predominantly evaluated:

- Large hospital databases
- National registries
- Trauma cohorts
- Obstetric populations
- Patient blood management programs

Restrictive transfusion strategies generally employed hemoglobin thresholds between 7.0 and 8.0 g/dL, whereas liberal strategies utilized thresholds between 9.0 and 10.0 g/dL.

Table 1. Landmark Studies Included in the Review

Study	Population	Sample Size	Restrictive Threshold	Liberal Threshold	Main Outcome
TRICC	Critically ill	838	7 g/dL	10 g/dL	Similar mortality
TRISS	Septic shock	998	7 g/dL	9 g/dL	No mortality difference
FOCUS	Hip fracture	2016	8 g/dL	10 g/dL	Similar functional outcomes
TITRe2	Cardiac surgery	2007	7.5 g/dL	9 g/dL	Comparable outcomes
TRACS	Cardiac surgery	502	24% Hct	30% Hct	Similar complications
Villanueva et al.	GI bleeding	921	7 g/dL	9 g/dL	Improved survival
MINT	Acute MI	3504	7–8 g/dL	10 g/dL	Ongoing debate
REALITY	Acute MI	668	8 g/dL	10 g/dL	Noninferiority demonstrated

Medical Populations

Critically Ill Patients

The most influential study evaluating transfusion thresholds in critically ill patients was the Transfusion Requirements in Critical Care (TRICC) trial. This landmark multicenter randomized controlled trial enrolled 838 critically ill patients and compared a restrictive transfusion threshold of 7 g/dL with a liberal threshold of 10 g/dL.

The investigators observed that restrictive transfusion was associated with reduced blood utilization and comparable mortality outcomes. Subgroup analyses suggested potential survival advantages among younger patients and those with lower illness severity scores.

The TRICC trial fundamentally transformed transfusion practice worldwide and remains one of the most frequently cited studies in patient blood management.

Subsequent observational investigations involving tens of thousands of ICU patients largely supported these findings. Most studies demonstrated that restrictive transfusion strategies reduced exposure to blood products without increasing mortality, organ failure, or ICU length of stay.

Several meta-analyses have subsequently confirmed that restrictive transfusion approaches are generally safe in stable critically ill adults.

Septic Shock

Sepsis and septic shock represent unique physiological conditions characterized by systemic inflammation, microvascular dysfunction, impaired oxygen utilization, and hemodynamic instability.

The Transfusion Requirements in Septic Shock (TRISS) trial enrolled 998 patients with septic shock and compared transfusion thresholds of 7 g/dL and 9 g/dL.

The study demonstrated no statistically significant difference in:

- 90-day mortality
- Ischemic events
- Life support requirements
- Serious adverse events

Importantly, patients assigned to restrictive transfusion received substantially fewer RBC units.

Subsequent analyses reinforced the safety of restrictive transfusion strategies in septic shock and contributed significantly to modern critical care guidelines.

The accumulated evidence suggests that hemoglobin concentrations around 7 g/dL are generally sufficient for most patients with sepsis once adequate resuscitation has been achieved.

Gastrointestinal Bleeding

Acute gastrointestinal bleeding remains a common indication for RBC transfusion.

Historically, aggressive transfusion practices were frequently employed in bleeding patients due to concerns regarding hemodynamic instability and tissue hypoxia.

However, the landmark trial conducted by Villanueva and colleagues challenged this paradigm.

The study randomized 921 patients with severe upper gastrointestinal bleeding to restrictive and liberal transfusion strategies.

Patients assigned to the restrictive strategy experienced:

- Improved overall survival
- Lower rebleeding rates
- Reduced complications
- Decreased transfusion exposure

These findings were particularly pronounced among patients with portal hypertension and cirrhosis.

Subsequent studies largely corroborated these observations and established restrictive transfusion as the preferred approach for most hemodynamically stabilized gastrointestinal bleeding patients.

Acute Coronary Syndromes

Patients with myocardial ischemia represent one of the most controversial populations in transfusion medicine.

Theoretical concerns exist that anemia may exacerbate myocardial oxygen supply-demand imbalance and worsen ischemic injury.

Historically, clinicians favored liberal transfusion strategies in these patients.

However, emerging evidence has challenged this assumption.

The REALITY trial compared restrictive and liberal transfusion thresholds in patients with acute myocardial infarction and anemia.

The study demonstrated noninferiority of restrictive transfusion with respect to major cardiovascular outcomes.

More recently, the Myocardial Ischemia and Transfusion (MINT) trial provided additional insights.

Although some trends favored liberal transfusion, definitive superiority was not established.

Current evidence suggests that patients with acute coronary syndromes may represent one of the few populations where individualized assessment remains particularly important.

Surgical Populations

Orthopedic Surgery

Orthopedic procedures account for a substantial proportion of perioperative transfusions worldwide.

The FOCUS trial evaluated more than 2,000 elderly patients undergoing surgery for hip fracture.

Investigators compared:

Restrictive strategy:

- Transfusion for symptoms or hemoglobin <8 g/dL

Liberal strategy:

- Hemoglobin maintained above 10 g/dL

No significant differences were observed in:

- Mortality
- Walking ability
- Functional recovery
- Cardiovascular complications

These findings provided strong evidence supporting restrictive transfusion in orthopedic surgery.

Subsequent meta-analyses confirmed that lower transfusion thresholds safely reduce blood utilization without adversely affecting outcomes.

Cardiac Surgery

Cardiac surgery patients frequently develop perioperative anemia due to:

- Hemodilution
- Surgical blood loss
- Cardiopulmonary bypass
- Inflammatory responses

Traditionally, liberal transfusion practices were common because of concerns regarding myocardial oxygen delivery.

The TITRe2 trial enrolled more than 2,000 cardiac surgery patients and compared restrictive and liberal transfusion thresholds.

Investigators reported:

- Similar infection rates
- Comparable major morbidity
- Reduced blood utilization

Likewise, the TRACS study found no major differences in clinical outcomes despite significant reductions in transfusion exposure.

Numerous subsequent studies have consistently demonstrated that restrictive transfusion strategies can be safely implemented in many cardiac surgical populations.

Major Abdominal Surgery

Patients undergoing major abdominal surgery often experience substantial blood loss and perioperative anemia.

Evidence from enhanced recovery programs suggests that restrictive transfusion thresholds contribute to:

- Lower infection rates
- Reduced healthcare costs
- Decreased exposure to donor blood

Several observational studies demonstrated that unnecessary transfusion may independently increase postoperative complications.

Consequently, patient blood management programs increasingly advocate restrictive transfusion practices in major abdominal surgery.

Vascular Surgery

The vascular surgery population often presents with advanced cardiovascular disease and limited physiological reserve.

Available evidence suggests that restrictive transfusion remains generally safe.

However, the optimal threshold among patients with severe coronary disease remains uncertain.

Further randomized studies are needed to determine whether selected high-risk vascular patients benefit from higher hemoglobin targets.

Obstetric Populations

Postpartum Hemorrhage

Postpartum hemorrhage remains a leading cause of maternal mortality worldwide.

The management of severe hemorrhage frequently necessitates blood transfusion.

However, uncertainty persists regarding the optimal transfusion threshold following stabilization.

Several observational studies have suggested that restrictive transfusion strategies may safely reduce blood exposure among hemodynamically stable postpartum women.

Benefits include:

- Reduced alloimmunization
- Lower transfusion reactions
- Decreased healthcare costs

Nevertheless, severe hemorrhage requiring active resuscitation remains an exception where clinical judgment supersedes rigid hemoglobin thresholds.

Cesarean Delivery

Anemia following cesarean section is common.

Evidence indicates that many stable postpartum women tolerate moderate anemia remarkably well.

Studies evaluating postpartum transfusion practices have reported substantial variability between institutions.

Patient blood management initiatives have demonstrated that standardized restrictive transfusion protocols can reduce unnecessary transfusions without compromising maternal outcomes.

Maternal Outcomes

Across obstetric studies, restrictive transfusion strategies were generally associated with:

- Reduced blood utilization
- Similar maternal mortality
- Comparable ICU admission rates
- No increase in severe maternal morbidity

However, evidence quality was lower than that available for medical and surgical populations due to fewer randomized trials.

Consequently, additional prospective research remains necessary.

Table 2. Summary of Outcomes by Population

Population	Restrictive Strategy	Liberal Strategy	Overall Conclusion
Critical care	Safe	No clear advantage	Restrictive favored
Septic shock	Safe	No clear advantage	Restrictive favored
GI bleeding	Better outcomes	Worse outcomes	Restrictive favored
Orthopedic surgery	Safe	No advantage	Restrictive favored

Cardiac surgery	Safe	No advantage	Restrictive favored
Obstetrics	Promising	No clear advantage	Individualized approach

Overall Findings

Across the included studies, restrictive transfusion strategies consistently reduced exposure to blood products while maintaining similar clinical outcomes compared with liberal strategies.

The strongest evidence supporting restrictive transfusion was observed in:

- Critical care medicine
- Septic shock
- Gastrointestinal bleeding
- Orthopedic surgery
- Cardiac surgery

Areas requiring additional investigation included:

- Acute coronary syndromes
- Severe cardiovascular disease
- High-risk vascular surgery
- Obstetric hemorrhage

Overall, contemporary evidence strongly supports restrictive transfusion thresholds for the majority of stable hospitalized adults while emphasizing individualized decision-making for selected high-risk populations.

Discussion

The present systematic review synthesized evidence from randomized controlled trials, observational studies, registry analyses, and contemporary clinical guidelines evaluating red blood cell (RBC) transfusion thresholds across medical, surgical, and obstetric populations. Collectively, the available evidence demonstrates that restrictive transfusion strategies are safe and effective for most hemodynamically stable patients and are associated with substantial reductions in blood utilization without increasing mortality, major morbidity, or adverse clinical outcomes. These findings reinforce the growing paradigm shift toward patient blood management and support the implementation of evidence-based transfusion practices across a wide range of healthcare settings.

Historically, transfusion decisions were guided by the assumption that higher hemoglobin concentrations invariably translated into improved tissue oxygen delivery and superior patient outcomes. The traditional “10/30 rule” dominated clinical practice for decades despite limited empirical evidence supporting its use. Advances in transfusion medicine, critical care physiology, and evidence-based practice have progressively challenged this assumption. Contemporary evidence now indicates that physiological adaptation to anemia is considerably more complex than previously recognized and that many patients tolerate hemoglobin concentrations substantially below historical transfusion thresholds without adverse consequences.

One of the most important observations emerging from this review is the remarkable consistency of findings across diverse patient populations. Despite significant differences in disease processes, surgical procedures, baseline risk factors, and healthcare settings, restrictive transfusion strategies generally produced outcomes equivalent to liberal approaches. This consistency strengthens confidence in the validity and generalizability of restrictive transfusion practices.

The landmark TRICC trial fundamentally transformed transfusion medicine and remains the cornerstone of contemporary transfusion practice. Prior to its publication, clinicians commonly transfused critically ill patients at hemoglobin concentrations approaching 10 g/dL. The demonstration that a restrictive threshold of 7 g/dL achieved outcomes comparable to a liberal threshold of 10 g/dL challenged long-standing clinical assumptions and initiated a paradigm shift that continues to influence transfusion guidelines worldwide. Importantly, the benefits observed in the restrictive group extended beyond simple reductions

in blood utilization. Reduced exposure to donor blood likely decreased the risk of transfusion-related complications while simultaneously conserving valuable healthcare resources.

Subsequent investigations have consistently supported the findings of TRICC. The TRISS trial demonstrated that patients with septic shock can safely tolerate lower hemoglobin concentrations than previously believed. Septic shock represents a particularly important population because clinicians often assume that impaired oxygen delivery necessitates aggressive transfusion practices. However, the absence of significant differences in mortality, organ failure, ischemic events, or life-support requirements suggests that physiological compensation remains adequate in many patients despite moderate anemia. These findings have significantly influenced international sepsis guidelines and have contributed to broader acceptance of restrictive transfusion strategies within critical care medicine.

The gastrointestinal bleeding literature provides some of the strongest evidence supporting restrictive transfusion. The trial conducted by Villanueva and colleagues demonstrated not merely equivalence but potential superiority of restrictive transfusion in patients with acute upper gastrointestinal hemorrhage. Patients managed with restrictive transfusion experienced lower mortality rates, fewer episodes of recurrent bleeding, and improved overall outcomes. Several physiological mechanisms may explain these observations. Excessive transfusion can increase portal pressures, disrupt clot stability, and promote rebleeding in susceptible individuals. Consequently, the findings from gastrointestinal bleeding studies highlight an important principle: more transfusion is not necessarily better, and unnecessary correction of anemia may occasionally produce unintended harm.

The evidence supporting restrictive transfusion in surgical populations is equally compelling. Orthopedic surgery, particularly hip fracture repair, frequently affects elderly patients with multiple comorbidities and limited physiological reserve. Traditionally, these characteristics were considered indications for liberal transfusion. However, the FOCUS trial demonstrated that maintaining hemoglobin concentrations above 10 g/dL did not improve mortality, mobility, cardiovascular outcomes, or functional recovery compared with a more restrictive strategy. These findings challenged the belief that elderly surgical patients require higher hemoglobin targets and have influenced perioperative transfusion practices internationally.

Cardiac surgery has historically been viewed as one of the most challenging areas for restrictive transfusion due to concerns regarding myocardial oxygen delivery. Nevertheless, evidence from TITRe2, TRACS, and numerous subsequent studies indicates that lower transfusion thresholds can be implemented safely in many cardiac surgical patients. Although certain subgroups may still benefit from individualized approaches, the overall body of evidence suggests that routine liberal transfusion is unnecessary for most patients undergoing cardiac procedures. Importantly, reductions in transfusion exposure may decrease the incidence of transfusion-associated complications while simultaneously reducing healthcare costs.

The growing emphasis on patient blood management has further reinforced the rationale for restrictive transfusion. Patient blood management represents a multidisciplinary, evidence-based approach designed to optimize patient outcomes by minimizing unnecessary transfusion and addressing anemia through alternative strategies whenever possible. Rather than viewing transfusion as the default treatment for anemia, patient blood management encourages clinicians to investigate and correct underlying causes, optimize erythropoiesis, minimize procedural blood loss, and employ transfusion only when clinically justified. Numerous healthcare systems implementing patient blood management programs have reported reductions in blood utilization, lower healthcare costs, shorter hospital stays, and improved patient outcomes.

A major advantage of restrictive transfusion strategies is the reduction in exposure to transfusion-related complications. Although modern blood banking has dramatically improved transfusion safety, significant risks remain. Transfusion-associated circulatory overload (TACO) is among the leading causes of transfusion-related morbidity and mortality and occurs particularly frequently in elderly patients and those with cardiovascular disease. Similarly, transfusion-related acute lung injury (TRALI) remains a serious and potentially fatal complication. Additional concerns include alloimmunization, hemolytic reactions, febrile non-hemolytic reactions, transfusion-transmitted infections, and immunomodulatory effects. By reducing unnecessary transfusions, restrictive strategies inherently decrease exposure to these risks.

Another important finding from this review relates to healthcare resource utilization. Blood products represent a finite and increasingly expensive healthcare resource. Collection, testing, processing, storage, transportation, and administration contribute substantial costs to healthcare systems. Furthermore, demographic changes and declining donor populations have raised concerns regarding future blood supply sustainability. Restrictive transfusion strategies therefore offer not only clinical benefits but also significant economic advantages. Multiple studies included in this review demonstrated substantial reductions in blood

utilization among patients managed using restrictive thresholds. These findings have important implications for healthcare systems facing increasing financial pressures and limited resources.

Despite the overall strength of evidence supporting restrictive transfusion, several areas of uncertainty remain. Acute coronary syndromes represent one of the most controversial clinical settings in transfusion medicine. Myocardial ischemia theoretically increases susceptibility to the adverse effects of anemia because oxygen delivery to the heart may already be compromised. While studies such as REALITY and MINT have provided valuable insights, definitive conclusions remain elusive. Some evidence suggests potential benefits from higher hemoglobin targets in selected patients with active myocardial ischemia, whereas other studies demonstrate acceptable outcomes using restrictive approaches. Consequently, current guidelines generally recommend individualized decision-making rather than rigid adherence to specific hemoglobin thresholds in this population.

Patients with severe cardiovascular disease more broadly may also require individualized assessment. Advanced coronary artery disease, severe heart failure, significant valvular disease, and limited cardiopulmonary reserve may alter physiological responses to anemia. Although restrictive transfusion appears safe for many such patients, further research is necessary to identify specific subgroups that may benefit from alternative strategies. Future investigations incorporating biomarkers of tissue oxygenation, myocardial injury, and physiological reserve may facilitate more personalized transfusion decision-making.

The obstetric population presents additional challenges. Pregnancy and the postpartum period are characterized by profound physiological changes affecting blood volume, oxygen transport, coagulation pathways, and cardiovascular function. Postpartum hemorrhage remains one of the leading causes of maternal mortality worldwide and accounts for a substantial proportion of obstetric transfusions. Although available evidence suggests that restrictive transfusion may be appropriate for many hemodynamically stable postpartum women, the overall evidence base remains less robust than that available for medical and surgical populations. Most obstetric studies are observational, and relatively few randomized controlled trials have directly compared transfusion thresholds in postpartum patients. Consequently, additional high-quality research is required to establish evidence-based recommendations for obstetric transfusion practices.

An important theme emerging from this review is the limitation of relying exclusively on hemoglobin concentration when making transfusion decisions. Hemoglobin values provide valuable information but represent only one component of a patient's overall clinical status. Symptoms, hemodynamic stability, active bleeding, cardiovascular reserve, oxygen requirements, lactate levels, organ dysfunction, and patient-specific factors must also be considered. Increasingly, experts advocate a patient-centered approach in which transfusion decisions integrate both laboratory parameters and clinical assessment. Such an approach aligns closely with the principles of patient blood management and precision medicine.

The findings of this review are consistent with recommendations issued by major international organizations. The Association for the Advancement of Blood and Biotherapies (AABB), the British Society for Haematology, the European Society of Anaesthesiology, and numerous other professional societies generally support restrictive transfusion thresholds for stable hospitalized adults. Although specific recommendations vary according to patient population and clinical context, the overall direction of contemporary guidelines strongly favors minimizing unnecessary transfusion exposure.

The evolution of transfusion medicine over the past three decades reflects a broader trend within healthcare toward evidence-based practice. Historically, transfusion decisions were often driven by tradition, expert opinion, and physiological assumptions. Contemporary transfusion strategies increasingly rely upon randomized evidence, systematic reviews, and patient-centered outcomes. This transition has produced meaningful improvements in patient care and has substantially reduced unnecessary transfusion worldwide.

Strengths of This Review

Several strengths enhance the value of the present review.

First, the review incorporates evidence from medical, surgical, and obstetric populations within a single comprehensive framework. Previous reviews have frequently focused on individual specialties or specific patient groups. By integrating evidence across multiple clinical settings, this review provides a broader understanding of transfusion threshold optimization.

Second, the review includes data from landmark randomized controlled trials as well as large observational studies and guideline documents. This comprehensive approach improves external validity and enhances applicability to real-world clinical practice.

Third, the review evaluates multiple clinically relevant outcomes including mortality, cardiovascular events, infection, resource utilization, maternal outcomes, and transfusion-related complications. Such a multidimensional assessment provides a more complete understanding of the benefits and risks associated with different transfusion strategies.

Fourth, the review emphasizes contemporary patient blood management principles and aligns findings with current international guidelines, thereby increasing clinical relevance.

Limitations

Several limitations should also be acknowledged.

Considerable heterogeneity existed among included studies with respect to patient populations, transfusion thresholds, outcome definitions, and follow-up duration. Such variability may limit direct comparisons between studies.

Second, some patient populations—particularly obstetric patients and individuals with acute coronary syndromes—remain underrepresented in randomized controlled trials. Consequently, conclusions regarding these groups are necessarily more cautious.

Third, advances in surgical techniques, blood conservation methods, critical care management, and transfusion practices over time may influence the applicability of older studies to contemporary healthcare settings.

Fourth, publication bias cannot be completely excluded despite extensive literature searches and inclusion of multiple data sources.

Finally, because transfusion decisions are inherently influenced by clinical judgment, residual confounding remains a concern in observational studies.

Clinical Implications

The findings of this review have several important implications for clinical practice.

For most hemodynamically stable adults, restrictive transfusion thresholds between 7 and 8 g/dL appear safe and effective.

Routine transfusion to achieve hemoglobin concentrations above 10 g/dL is generally unsupported by contemporary evidence.

Patient blood management programs should be encouraged and expanded across healthcare systems.

Clinicians should consider transfusion as one component of comprehensive anemia management rather than an automatic response to laboratory abnormalities.

Finally, transfusion decisions should remain individualized, particularly among patients with acute coronary syndromes, severe cardiovascular disease, active hemorrhage, or other high-risk conditions.

Future Research Directions

Future investigations should focus on several key areas.

Large randomized trials are needed to clarify optimal transfusion thresholds in acute coronary syndromes.

Additional research should evaluate obstetric populations, particularly women experiencing postpartum hemorrhage.

Studies incorporating physiological markers of tissue oxygenation may facilitate more personalized transfusion strategies.

The long-term effects of transfusion thresholds on quality of life, functional recovery, and healthcare costs warrant further investigation.

Artificial intelligence and predictive analytics may also play an increasingly important role in individualized transfusion decision-making.

Ultimately, future research should seek to move beyond universal hemoglobin thresholds toward precision transfusion medicine tailored to individual patient characteristics and clinical circumstances.

Conclusion

This systematic review provides a comprehensive evaluation of red blood cell transfusion thresholds across medical, surgical, and obstetric populations. The cumulative evidence demonstrates that restrictive transfusion strategies are safe, effective, and associated with substantial reductions in blood utilization for most hemodynamically stable adult patients.

The strongest evidence supporting restrictive transfusion was observed among critically ill patients, individuals with septic shock, patients experiencing gastrointestinal bleeding, orthopedic surgery populations, and cardiac surgery cohorts. Across these settings, restrictive transfusion thresholds generally resulted in comparable mortality, morbidity, and functional outcomes while significantly reducing exposure to donor blood products.

Although restrictive transfusion strategies appear appropriate for the majority of stable hospitalized adults, important exceptions remain. Patients with acute coronary syndromes, severe cardiovascular disease, ongoing hemorrhage, and selected obstetric complications may require individualized assessment and clinical judgment beyond rigid hemoglobin-based thresholds.

The findings of this review strongly support contemporary patient blood management principles, emphasizing the importance of minimizing unnecessary transfusions while optimizing patient outcomes. Future research should focus on refining individualized transfusion strategies, identifying high-risk subgroups, and incorporating physiological markers that better reflect tissue oxygenation and clinical need.

Ultimately, modern transfusion medicine is transitioning away from universal hemoglobin triggers toward personalized, evidence-based approaches that balance the benefits of transfusion against its potential risks. Restrictive transfusion strategies should therefore be considered the standard approach for most stable adult patients, with clinical context guiding exceptions when necessary.

Abbreviations

AABB – Association for the Advancement of Blood and Biotherapies

ACS – Acute Coronary Syndrome

CI – Confidence Interval

GRADE – Grading of Recommendations Assessment, Development and Evaluation

GI – Gastrointestinal

Hb – Hemoglobin

ICU – Intensive Care Unit

LOS – Length of Stay

MACE – Major Adverse Cardiovascular Events

NOS – Newcastle-Ottawa Scale

PBM – Patient Blood Management

PPH – Postpartum Hemorrhage

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RBC – Red Blood Cell

RCT – Randomized Controlled Trial

RoB – Risk of Bias

TACO – Transfusion-Associated Circulatory Overload

TRALI – Transfusion-Related Acute Lung Injury

Declarations

Ethics Approval and Consent to Participate

Not applicable. This study is a systematic review of previously published literature and did not involve human participants or animal subjects.

Availability of Data and Materials

All data analyzed in this study were obtained from publicly available published studies.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors contributed substantially to the conception, design, literature review, data interpretation, drafting, critical revision, and final approval of the manuscript.

Table 3. Risk of Bias Assessment of Major Randomized Controlled Trials

Study	Randomization	Allocation Concealment	Blinding	Incomplete Data	Selective Reporting	Overall Risk
TRICC	Low	Low	Low	Low	Low	Low
TRISS	Low	Low	Low	Low	Low	Low
FOCUS	Low	Low	Low	Low	Low	Low
TITRe2	Low	Low	Low	Low	Low	Low
TRACS	Low	Low	Some concerns	Low	Low	Low
REALITY	Low	Low	Low	Low	Low	Low

MINT	Low	Low	Low	Low	Low	Low

Table 4. International Guideline Recommendations

Organization	Recommended Threshold
AABB	7–8 g/dL for most stable adults
WHO	Restrictive transfusion preferred
NICE	Restrictive transfusion recommended
British Society for Haematology	7–8 g/dL in stable patients
European Society of Anaesthesiology	Restrictive strategy favored
Society of Thoracic Surgeons	Individualized approach in cardiac surgery

Table 5. Advantages and Disadvantages of Restrictive Transfusion

Advantages	Disadvantages
Reduced blood utilization	Potential concern in severe ischemia
Lower healthcare costs	Requires careful monitoring
Reduced TACO risk	Limited evidence in some populations
Reduced TRALI risk	Not suitable for active exsanguination
Reduced alloimmunization	Clinical judgment remains essential
Improved resource conservation	Evidence gaps remain

Table 6. Clinical Outcomes Across Populations

Outcome	Restrictive Strategy	Liberal Strategy
Mortality	Similar	Similar
Infection	Lower or Similar	Similar
ICU Stay	Similar	Similar
Hospital Stay	Similar	Similar
Cardiovascular Events	Similar	Similar
Blood Utilization	Lower	Higher
Cost	Lower	Higher

Table 7. GRADE Assessment of Evidence

Outcome	Certainty of Evidence
Mortality in ICU Patients	High
Mortality in Septic Shock	High
GI Bleeding Outcomes	High
Orthopedic Surgery Outcomes	High
Cardiac Surgery Outcomes	Moderate to High
Acute Coronary Syndrome Outcomes	Moderate
Obstetric Outcomes	Low to Moderate

Table 8. Summary of Clinical Recommendations

Clinical Scenario	Suggested Threshold
Stable ICU patient	7 g/dL
Septic shock	7 g/dL
GI bleeding	7 g/dL
Orthopedic surgery	8 g/dL
Cardiac surgery	7.5–8 g/dL

Acute MI	Individualized
Stable postpartum anemia	Individualized
Active massive hemorrhage	Clinical judgment

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