TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Red Blood Cell Transfusion
Evidence-Based Guideline

Definition: Red blood cell transfusion may be used in order to increase the supply of oxygen to the tissues, when the concentration of hemoglobin (Hb) is low and/or the oxygen carrying capacity is reduced, in the presence of inadequate physiological mechanisms of compensation. [(1)] Transfusion can be indicated for a variety of reasons, due to anemia, blood loss from trauma or surgical procedures, or congenital disease.

Inclusion Criteria
Hemodynamically stable children >4 months with clinical findings suggestive of anemia, such as hypotension, vital sign changes from baseline, significant decreases in functional status, etc. or low hemoglobin/hematocrit level.

Exclusion Criteria
Children who require massive transfusion, children who have conditions that require chronic transfusions, or pregnancy, autoimmune hemolytic anemia, and children who are hemodynamically unstable.

Diagnostic Evaluation
History: Assess
- Bleeding history
- Previous transfusion needs
- Underlying cause of anemia as applicable
- Willingness to consent to receipt of blood component
- Fatigue

Physical Examination
- Active bleeding
- Vital signs: respiratory rate, heart rate, blood pressure
- Oxygen saturation as indicated
- Pallor
- Mental status changes
- Inability to perform activities of daily living

Laboratory Tests
- Hemoglobin & hematocrit (H&H)—if known bleeding source (such as surgery or trauma)
- Type and screen (ABO/Rh and screen)
- Complete blood count (CBC), reticulocyte count, and peripheral smear—if etiology of anemia is unknown
- If hemolysis is suspected: Lactate Dehydrogenase (LDH), Bilirubin, Haptoglobin, Plasma Hemoglobin, Direct Antiglobin Test (DAT)

Critical Points of Evidence*

Evidence Supports
- The use of a 7 g/dL hemoglobin threshold in most hemodynamically stable pediatric patients aged 4 months and over, including patients with asymptomatic anemia, patients with oncologic diseases, patients undergoing surgery, and critically ill patients.[(2-9)] – Strong recommendation, moderate quality evidence

  Remarks: Clinical judgment may dictate a more liberal transfusion strategy depending on complicating factors or symptomatic anemia as evidenced by hypotension, vital sign changes from baseline, significant decreases in functional status, etc. For complex patients, consult the patient's primary team for threshold recommendations. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.
- The administration of red blood cells at a volume of 10-15 mL/kg (if the child is <35 kg) or one unit (if the child is ≥35 kg) for children who are not actively bleeding and who are hemodynamically stable and reassess after each transfusion.[(10-16)] – Weak recommendation, very low quality evidence

  Remarks: After each single-unit red blood cell transfusion (or equivalent volumes calculated based on body weight), clinically reassess and check hemoglobin levels, and give further transfusions if needed. After transfusions are administered, assess for fever or idiosyncratic reaction. In certain diagnoses, such as severe anemia, transfusing 5 mL/kg of RBCs at a time may be clinically necessary to prevent adverse events.
- The administration of red blood cells through a vein using a 25 gauge or larger catheter, unless otherwise ordered by the practitioner.[(17, 18)]– Strong recommendation, low quality evidence
- The use an infusion pump to administer a red blood cell transfusion. [(19, 20)] – Strong recommendation, low quality evidence
- The evaluation of each patient's plan of care to assess the necessity and frequency of laboratory studies and use the smallest volume necessary. [(21-27)] – Strong recommendation, low quality evidence
- The consideration of erythropoietin administration prior to surgery in select populations where a significant amount of blood loss is anticipated such as cardiovascular surgery, craniofacial procedures, neuromuscular scoliosis spinal instrumentation, organ transplant, and children with oncologic diseases. [(28-32)] – Weak recommendation, very low quality evidence
- The use of a Goal Directed Transfusion Pathway (thromboelastography or thromboelastometry, if available) can be employed successfully to decrease blood product transfusion in patients who are undergoing procedures with high levels of anticipated blood loss such as trauma, cardiovascular surgery, craniofacial procedures, neuromuscular scoliosis spinal instrumentation, organ transplant, and children with oncologic diseases. [(33)] – Strong recommendation, low quality evidence
- The use tranexamic acid or aminocaproic acid in patients who are undergoing procedures with high levels of anticipated blood loss such as trauma, cardiovascular surgery, craniofacial procedures, neuromuscular scoliosis spinal instrumentation, organ transplant, and children with oncologic diseases. [(35-43)] – Strong recommendation, moderate quality evidence

- The administration of iron intravenously for patients with iron-deficiency anemia who are either non-compliant or otherwise fail oral therapy to reduce or delay the use of blood products. [44, 45] – Weak recommendation, moderate quality evidence
- The administration of iron intravenously for patients with diseases that impair their ability to absorb oral preparations (such as short-gut, Crohn's disease, ileostomy, etc.) to reduce or delay the use of blood products. [44, 45] – Strong recommendation, moderate quality evidence
- The consideration of erythropoietin in selective patients, such as those who refuse transfusion, patients who are post-bone marrow transplant, patients for whom finding blood to match antibodies is difficult, in patients where blood transfusion is contraindicated or may lead to adverse events, and patients with renal failure. [46-52] – Weak recommendation, low quality evidence
- The utilization of irradiated blood products with any products donated by a blood relative, in patients who are candidates or recipients of allogenic or autologous bone marrow or hematoprogenitor cell transplantation, and immunocompromised patients. [53, 54] – Strong recommendation, very low quality evidence
- The use of the EDTA hemoglobin processed in the laboratory as the basis for determining need for transfusion with the use of whole blood hemoglobin/hematocrit from point of care blood gas levels as secondary (such as in the operating room or in emergency situations). [55, 56] – Strong recommendation, moderate quality evidence

Evidence Against

- The use of pulse co-oximetry to determine need for blood transfusion.[57-62] – Strong recommendation, low quality evidence
- The use of near-infrared spectroscopy to determine need for blood transfusion. [63, 64] – Strong recommendation, low quality evidence
- The routine use of erythropoietin.[46-52] – Strong recommendation, low quality evidence

Evidence Lacking/Inconclusive

- To use a higher hemoglobin threshold in pediatric patients aged 4 months and over meeting the following criteria:
    - Patients with portal hypertension: 8 g/dL
    - Patients undergoing radiation therapy: 10 g/dL
    - Patients undergoing hematopoietic stem cell transplant: 8 g/dL
    - Patients with pulmonary disease in the perioperative setting: 10 g/dL
    - Patients with hyperhemolysis
    - Patients with cardiovascular disease:
        - Cyanotic biventricular disease: 8 g/dL if well tolerated, otherwise 9 g/dL
        - Single ventricle: 10 g/dL if asymptomatic; 13 g/dL if symptomatic as evidenced by persistent desaturations, escalating respiratory or cardiovascular support, or persistent sinus tachycardia.
    - Acute respiratory dysfunction syndrome: a higher threshold may be indicated, evaluate the patient for evidence of decreased oxygen delivery (ex: lactate levels, mixed venous saturation, oxygen extraction ratio, etc.) before transfusion – Consensus recommendation

      Remarks: Clinical judgment may dictate a more liberal transfusion strategy depending on complicating factors or symptomatic anemia as evidenced by hypotension, vital sign changes from baseline, significant decreases in functional status, etc. For complex patients, consult the patient's primary team for threshold recommendations. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

Condition-Specific Elements of Clinical Management

General:
Assess for transfusion reactions during and after each unit of packed red blood cells are given.

Potential Risks of Blood Transfusion:

1. Infectious: HIV-1 (1 in 1.5 million), hepatitis C (1 in 1.1 million), hepatitis B (1 in 800,000-1,000,000), bacterial contamination (1 in 100,000 platelet units; 1 in 5 million red cell units)

2. Noninfectious: Wrong product given or mistransfusion

All suspected transfusion reactions must be reported to the TCH blood bank.

Types of Transfusion Reactions: [65]
Transfusion Associated Circulatory Overload (TACO): Acute onset or exacerbation of respiratory distress, fluid overload, pulmonary edema, evidence of left heart failure. Signs and symptoms include ↑BNP, ↑CVP, chest x-ray showing pulmonary edema, positive fluid balance, dyspnea, orthopnea, or cough.

Transfusion Related Acute Lung Injury (TRALI): Acute lung injury and hypoxemia resulting within 6 hours of transfusion with evidence of bilateral lung infiltrates and no evidence of circulatory overload. Signs and symptoms include PaO2/FiO2 less than or equal to 300 mm Hg, oxygen saturation less than 90% on room air, and bilateral infiltrates on x-ray.

Transfusion Associated Dyspnea (TAD): Acute respiratory distress occurring within 24 hours of transfusion without evidence of TACO, TRALI, or allergic reaction.

Allergic Reaction: Allergic sequelae within 4 hours of transfusion. Signs and symptoms include rash, urticaria, pruritus, bronchospasm/respiratory distress, angioedema, flushing, and or edema of lips/tongue/conjunctiva

Hypotensive Reaction: Hypotension during or within one hour of transfusion that does not meet criteria for other hypotensive reactions. Signs and symptoms in adults include drop in

systolic BP of greater than or equal to 30 mmHg and systolic BP less than or equal to 80 mmHg. Signs and symptoms in children include greater than 25% drop from baseline.

Febrile Non-Hemolytic Transfusion Reaction (FNHTR): Fever OR chills and rigors occurring within 4 hours of transfusion. Signs and symptoms include fever (greater than or equal to 38°C/100.4°F oral and a change of at least 1°C/1.8°F) from pre-transfusion value) or chills/rigors.

Acute Hemolytic Transfusion Reaction (AHTR): Hemolysis occurring within 24 hours of transfusion. Signs and symptoms include back/flank pain, chills/rigors, DIC, epistaxis, fever, hematuria, hypotension, oliguria/anuria, pain and/or oozing at IV site, renal failure, ↓fibrinogen, ↓haptoglobin, ↑bilirubin, ↑LDH, hemoglobinemia, hemoglobinuria, hemolysis of lab specimens, spherocytes.

Delayed Hemolytic Transfusion Reaction (DHTR): Positive direct antiglobulin test (DAT) for antibodies developed between 24 hours and 28 days after cessation of transfusion. Signs and symptoms include + DAT, new red blood cell alloantibody in recipient plasma, inadequate rise of post-transfusion Hgb level or rapid fall in Hgb back to pre-transfusion levels, spherocytes.

Transfusion Associated Graft vs. Host Disease (TAGVHD): Rare clinical syndrome occurring 2 days to 6 weeks after transfusion resulting from engraftment of donor lymphocytes in susceptible patients. Signs and symptoms include characteristic generalized erythema, diarrhea, fever, hepatomegaly, elevated liver enzymes, pancytopenia, marrow aplasia, characteristic skin biopsy findings.

Post-Transfusion Purpura: Thrombocytopenia occurring 5-12 days post-transfusion with antibodies to human platelet antigens (HPA). Signs and symptoms include thrombocytopenia (less than 80% of pre-transfusion value), HPA alloantibodies.

Premedication based on Transfusion Reaction History:

- Mild Allergic Diphenhydramine 0.5 mg/kg, max dose 50 mg
- Moderate to Severe Allergic (Respiratory Symptoms):
    - Diphenhydramine 0.5 mg/kg, max dose 50 mg,
    - Hydrocortisone 1-2 mg/kg max dose 250 mg,
    - Famotidine IV 0.25 mg/kg/dose every 12 hours
- Febrile Non-Hemolytic:
    - Acetaminophen* 10-15 mg/kg, max dose 650 mg

Note: *Premedication using acetaminophen may mask initial symptoms of an acute hemolytic transfusion reaction; patients will need to be carefully monitored for additional signs and symptoms

Patients with Heart Failure

Refer to Iron Deficiency in Heart Failure Patients Protocol.

Blood Product Administration:

See Blood or Blood Component Transfusion Policy and Blood or Blood Component Transfusion Procedure.

Consults/Referrals

- The patient's primary team is to determine transfusion threshold recommendations.
- For patients with chronic symptomatic anemia, consult hematology for transfusion and/or medication strategies.
- For suspected transfusion reactions, consult transfusion medicine.

Follow-Up Care

- Assess for signs of transfusion reaction
- Repeat H/H or CBC before ordering repeat blood components
- Assess for clinical improvement such as vital signs and physical activity

Measures

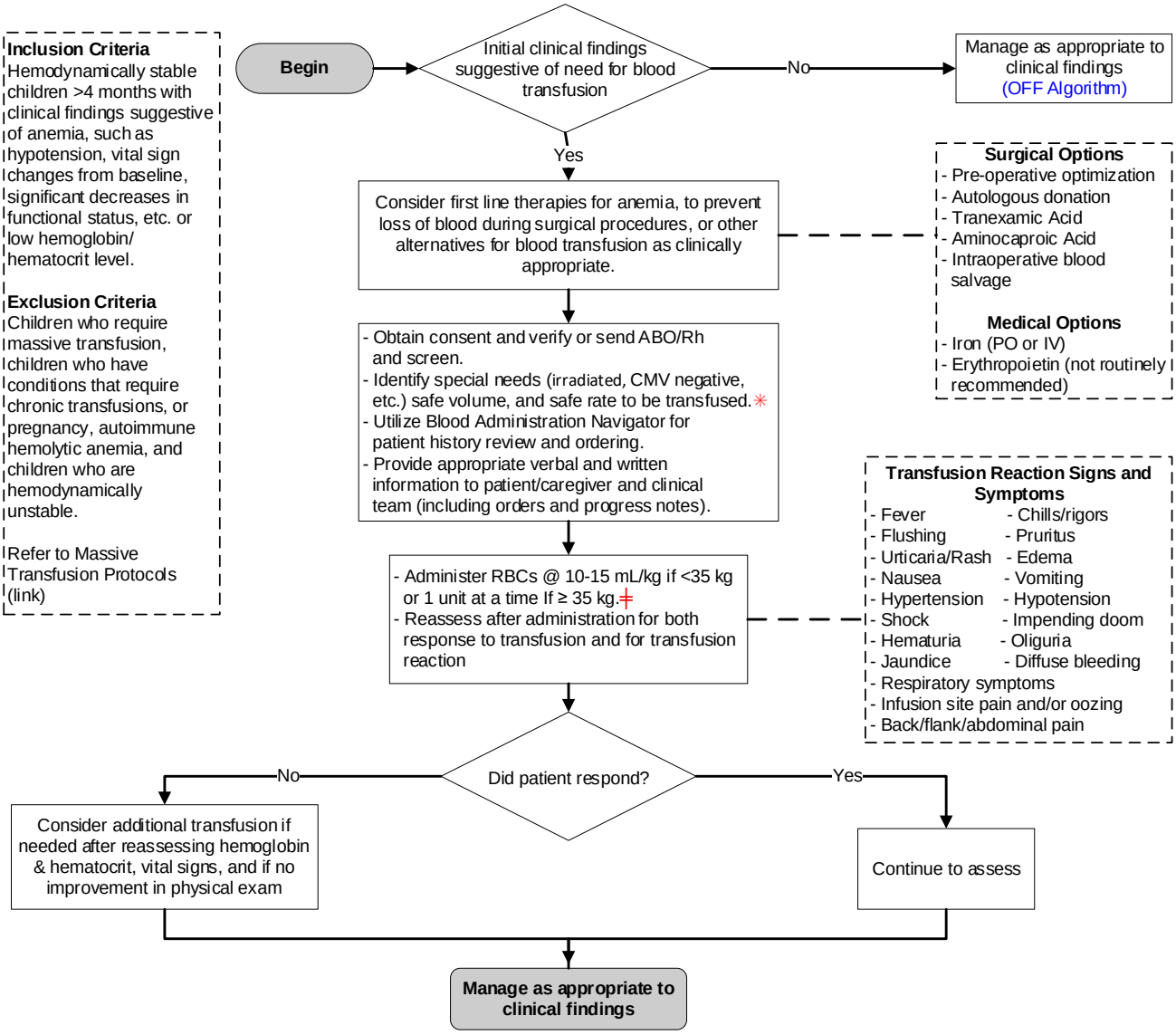
Process

- Number of orders for hemoglobin >7 g/dL
- Number of orders with indication of symptomatic anemia without supporting documentation
- Number of orders with dosing >15 mL/kg for patients weighing <35 kg
- Number of orders requesting >1 unit for patients weighing <35 kg

Outcome

- Number of days between over-transfusion events
- Transfusion reaction rate
- Number of transfusion reactions with transfusions outside of recommended dosing or hemoglobin threshold.

Texas Children's Hospital Evidence-Based Outcomes Center
Red Blood Cell Transfusion Management Algorithm



✳**Recommended Transfusion Hemoglobin Thresholds**

Strong recommendation with **moderate quality evidence** to use the 7 g/dL hemoglobin threshold in most hemodynamically stable pediatric, including newborns, patients with asymptomatic anemia, patients with oncologic diseases, patients undergoing surgery, and critically ill patients.

Consensus recommendation to use a higher hemoglobin thresholds in pediatric patients aged 4 months and over meeting the following criteria:

- Patients with portal hypertension: 8 g/dL
- Patients undergoing radiation therapy: 10 g/dL
- Patients undergoing hematopoietic stem cell transplant: 8 g/dL
- Patients with pulmonary disease in the in perioperative setting: 10 g/dL
- Patients with cardiovascular disease:
  - Cyanotic biventricular disease: 8 g/dL if well tolerated, otherwise 9 g/dL
  - Single ventricle: 10 g/dL if asymptomatic, 13 g/dL if symptomatic as evidenced by persistent desaturations, escalating respiratory or cardiovascular support, or persistent sinus tachycardia.
- Acute respiratory dysfunction syndrome: a higher threshold may be indicated, evaluate the patient for evidence of decreased oxygen delivery (ex: lactate levels, mixed venous saturation, oxygen extraction ratio, etc.) before transfusion

Remarks: Clinical judgment may dictate a more liberal transfusion strategy depending on complicating factors or symptomatic anemia as evidenced by hypotension, vital sign changes from baseline, significant decreases in functional status, etc. For complex patients, consult the patient's primary team for threshold recommendations. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.

╪***Note:*** In certain diagnoses, such as severe anemia, transfusing 5 mL/kg of RBCs at a time may be clinically necessary to prevent adverse events.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts

2. Review of Existing External Guidelines
   - AABB Red Blood Cell Transfusion Threshold and Storage Clinical Practice Guideline, National Blood Authority of Australia Patient Blood Management Guidelines, American Society of Anesthesiologists Practice Guidelines for Perioperative Blood Management, National Institute of Clinical Excellence Blood Transfusion, Society of Thoracic Surgeons Blood Conservation Clinical Practice Guidelines

3. Literature Review of Relevant Evidence
   - Searched: PubMed, CINAHL, and Cochrane

4. Critically Analyze the Evidence
   - Fifteen of meta-analyses, nine randomized controlled trials, and thirty-eight nonrandomized studies

5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a blood transfusion evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline. This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.
"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*
The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management of red blood cell administration in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Action	Comments
March 2018	Guideline created	
Oct 2018	Revision	
July 2023	Update	