Pediatric Critical Care

Transfusion and Anemia eXpertise Initiative (TAXI)

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2019 PCICS-UK PICU Meeting
London, UK
Conflicts of Interest/Disclosures:
None

Acknowledge:
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Marie Steiner
Marisa Tucci

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• AABB

TAXI Experts – 49 Experts from 8 countries
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| Implementation Science  ||
|-------------------------||
| Enola Proctor           | Washington University, St. Louis|
| Sara Small              | Washington University, St. Louis|
| Kate Steffen            | Washington University, St. Louis|

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The Pediatric Critical Care Transfusion and Anemia eXpertise Initiative (TAXI)

**Aim:**
To create evidence-based, and when evidence is lacking, expert-based consensus on blood management strategies for critically ill children.

Goal to maintain a “physiologically-relevant” hemoglobin concentration, optimize hemostasis, and minimize blood loss.

Transfusion and Anemia eXpertise Initiative

3-part conference series
Transfusion and anemia experts working with experts on guideline development and implementation science

- PICO questions - for comprehensive literature searches – systematic review
- Abstracts were reviewed and selected
- Manuscripts reviewed by two experts
- Conflict resolution by 3rd expert reviewer

- Evidence Evaluated Using GRADE Methodology
- Short text recommendations created
- Short and long texts were revised until consensus among experts achieved

PREPARED CRITICAL CARE

TRANSFUSION and ANEMIA eXPERTISE INITIATIVE (TAXI)

Preparation
1. Create organizing committee
2. Define Methodology
3. Select Topics
4. Select Experts

October 2014
Montreal, Canada

First Expert Meeting
Discuss and Finalize:
1. Methodology
2. Specific Subtopics

October 2015
Austin, Texas

Second Expert Meeting
Discuss:
1. Short text recommendations
2. Determine agreement (Delphi method)

June 2016
Toronto, Canada

Third Expert Meeting
Present
1. Short text recommendations
2. Discuss disagreements
3. Finalize recommendations

Spring 2017
Montreal, Canada

Between Meetings
1. Analyze literature
2. Create recommendations

Between Meetings
1. Score recommendations (RAND UCLA)
2. Reword if necessary
3. Finalize long text

2018
Publication and Dissemination

Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative care options.”


TAXI Subtopics

A. Indications for Red Cell Transfusion
   1. Hemoglobin and Physiologic thresholds

B. Population-based Indications for Red Cell Transfusion
   1. Acute Brain Injury
   2. Congenital and acquired cardiac disease
   3. Sickle cell/Oncologic disease
   4. Respiratory Failure
   5. Shock
   6. Life threatening and non life threatening bleeding
   7. Extracorporeal support, dialysis and ventricular assist devices
   8. Alternative Processing of Blood Products

Determining Consensus

Three rounds of on-line scoring by experts

- Reasons for disagreement sent back to groups to enable discussion and revisions
- *A priori* agreement 80%

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- Short text recommendations discussed and refined if necessary
  - Any changes in recommendations sent for third round of voting
- Implementation strategies discussed
- Transfusion decision tree proposed
- Knowledge gaps highlighted
- Research priorities discussed

Results

Clinical Recommendations (56)

4 (7%)  Strong recommendation, Moderate quality pediatric evidence (1B)
5 (9%)  Strong recommendation, Weak quality pediatric evidence
11 (20%)  Weak Recommendation, Low quality pediatric evidence
36 (64%)  Consensus Panel Expertise

Research Recommendations (45)

100%  Consensus Panel Expertise
Good Practice Statements

1. When deciding to transfuse an individual critically ill child, it is good practice to consider not only the hemoglobin concentration, but the overall clinical context (i.e., symptoms, signs, physiological markers, etc.) and the risks, benefits and alternatives to transfusion.

2. Causes of anemia should be appropriately considered, investigated and managed.

3. Adoption of patient blood management principles should be implemented.

**Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI)**

**Red Blood Cell (RBC) Transfusion Clinical Decision Tree**

1. **Strong recommendation, moderate quality pediatric evidence, 1B**
2. **Strong recommendation, low quality pediatric evidence, 1C**
3. **Weak recommendation, low quality pediatric evidence, 2C**
4. **Consensus panel expertise**

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1. Severe bleeding in patients at risk of exsanguination
2. Sickle cell disease patients with Hb < 5 g/dL, and acute chest syndrome (ACS) should undergo transfusion. Determining patients with ACS should undergo exchange transfusion, those who are not deteriorating should undergo simple transfusion. Sickle cell patients undergoing procedures that require general anesthesia should be transfused RBC to achieve a target Hb of 10-15 g/dL, not Hb < 10 g/dL.
3. The post-transfusion goal should be to relieve the indication for transfusion and not necessarily achieve a normal Hb for age. A reasonable Hb goal post-transfusion is a range between 7.5 g/dL and 8.5 g/dL.
4. Administration of RBC transfusion should be based on evidence of inadequate cardiovascular support or decreased systemic and/or regional oxygen delivery.
5. Refer to expert guide as provided in TAXI supplement.
6. Insufficient evidence to support recommending Hb concentration transfusion thresholds.
7. Hemodynamically stable = Mean Arterial Pressure not < 2 standard deviations below normal mean for age, AND cardiovascular support (pressors/inotropes and fluids) not increased for at least 2 hours.

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**RBC** = Red Blood Cell, **Hb** = hemoglobin, **PARDS** = Pediatric Acute Respiratory Distress Syndrome, **ECMO** = Extracorporeal Membrane Oxygenation, **VAD** = Ventricular Assist Device

Critically Ill Children with Life-Threatening Bleeding

In critically ill children with life-threatening bleeding, we suggest that RBCs, plasma and platelets be transfused empirically in ratios between 2:1:1 to 1:1:1 for RBCs:Plasma:Platelets until the bleeding is no longer life-threatening.

*Consensus panel expertise*

Critically Ill Child with Hemoglobin <5 g/dL or 5-7 g/dL

In critically ill children or those at risk for critical illness we recommend a RBC transfusion if the Hb concentration is <5 g/dL.

*Strong recommendation, Low quality pediatric evidence (1C)*

There is insufficient evidence to make a recommendation regarding transfusion thresholds for critically ill children who have an Hb concentration between 5 and 7g/dL. It is reasonable to consider transfusion based on clinical judgment in these children.

*Consensus panel expertise*

Critically ill children with hemodynamic instability* and Hb >7g/dL

*”Hemodynamic instability” based on TRIPICU criteria

In critically ill children with hemodynamic instability, we cannot make a recommendation regarding optimal RBC transfusion strategy.

Consensus panel expertise

Critically Ill Child with Hemodynamic Stability and Hb ≥7 g/dL
Critically Ill Child with Hemoglobin ≥7 g/dL

In critically ill children or those at risk for critical illness, who are hemodynamically stable and who have an Hb concentration ≥7 g/dL, we recommend not administering a RBC transfusion.

*Strong recommendation, Moderate quality pediatric evidence (1B)*


Critically Ill Children with Respiratory Failure

In critically ill children with respiratory failure who do not have severe acute hypoxemia, a chronic cyanotic condition or hemolytic anemia, and whose hemodynamic status is stable we recommend not administering a RBC transfusion if the Hb concentration is ≥7 g/dL.

*Strong recommendation, Moderate quality pediatric evidence (1B)*

Critically Ill Children with Shock

In hemodynamically stable critically ill children with a diagnosis of severe sepsis or septic shock, we recommend not administering a RBC transfusion if the Hb concentration is $\geq 7$ g/dL.

*Weak recommendation, Low quality pediatric evidence (2C)*


Critically Ill Children with Acute Brain Injury

In critically ill children with acute brain injury (e.g., trauma, stroke) a RBC transfusion could be considered if the Hb concentration falls between 7 – 10 g/dL.

*Consensus panel expertise*

Critically III Children with Oncologic Disease

In children with oncologic diagnoses or undergoing hematopoietic stem cell transplant are critically ill or at risk for critical illness, and hemodynamically stable: We suggest an Hb concentration of 7-8 g/dL be considered a threshold for RBC transfusion.

*Weak recommendation, Low quality pediatric evidence (2C)*


Critically ill children on ECMO

In critically ill children on ECMO, we recommend using physiologic metrics and biomarkers of oxygen delivery in addition to Hb concentration to guide RBC transfusion. Administration of a RBC transfusion should be based on evidence of inadequate cardiorespiratory support or decreased systemic and/or regional oxygen delivery.

*Weak recommendation, Low quality pediatric evidence (2C)*

Critically ill children with Acquired and Congenital Heart Disease

**Hemodynamically stable**

- **Hb ≥ 7 g/dL**

**Cardiac disease**

- Uncorrected congenital heart disease
  - **Transfuse RBC to maintain 7-9 g/dL depending on their cardiac reserve.**

- Biventricular repair
  - **No transfusion if Hb ≥ 7 g/dL**

- Single ventricle, stage 1 palliation
  - **No transfusion if Hb > 9 g/dL and adequate oxygenation (for their cardiac lesion) and normal end organ function**

- Single ventricle, stage 2 or 3 palliation
  - **No transfusion if Hb > 9 g/dL**

- Congenital or acquired myocardial dysfunction
  - **Use clinical judgment. Insufficient evidence to support recommending specific Hb concentration transfusion thresholds, but there is no evidence that transfusion above >10 g/dL is beneficial.**

- Pulmonary hypertension

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**Notes:**

- a: Strong recommendation, moderate quality pediatric evidence, 1B
- b: Strong recommendation, low quality pediatric evidence, 1C
- c: Weak recommendation, low quality pediatric evidence, 2C
- d: Consensus panel expertise

Critically ill Children with CHD

In hemodynamically stable critically ill infants and children with uncorrected CHD, we recommend RBC transfusion to maintain an Hb concentration of at least 7.0-9.0 g/dL depending on the degree of cardiopulmonary reserve.

Weak recommendation, Low quality pediatric evidence (2C)

In infants and children with CHD undergoing biventricular repair who are hemodynamically stable and have adequate oxygenation and normal end organ function: We recommend not administering a RBC transfusion if the Hb concentration is \( \geq 7.0 \) g/dL.

Strong recommendation, Moderate quality pediatric evidence (1B)

Critically ill children with CHD: Single Ventricle

In infants undergoing stage 1 palliation procedures (Norwood, DKS, BT or central shunt, or PA band) for single ventricle physiology who have stable hemodynamics, adequate oxygenation and normal end organ function: We recommend avoiding reflexive ("solely Hb-based") RBC transfusions if the Hb concentration is >9.0 g/dL.

*Weak recommendation, Low quality pediatric evidence (2C)*

In hemodynamically stable infants and children with single ventricle physiology undergoing stage 2 and 3 procedures with adequate oxygen delivery: We recommend not administering a RBC transfusion if the Hb concentration is >9 g/dL.

*Weak recommendation, Low quality pediatric evidence (2C)*

Critically ill children with heart disease

In children with documented right or left ventricular myocardial dysfunction (acquired or congenital), there is insufficient evidence to support transfusion to target a specific Hb concentration. Furthermore, there is no evidence that transfusion for a Hb level >10 g/dL is beneficial.

*Consensus panel expertise.*

In children with structurally normal hearts and idiopathic or acquired pulmonary hypertension (defined as a mean PA pressure >25 mmHg with normal pulmonary capillary wedge pressure), there is insufficient evidence to support transfusion to target a specific Hb concentration. Furthermore, there is no evidence that transfusion for a Hb level >10 g/dL is beneficial.

*Consensus panel expertise*

Critically ill Children with Sickle Cell Disease

In children with sickle cell disease who are critically ill or those at risk of critical illness, we recommend RBC transfusion to achieve a target Hb concentration of 10 g/dL (rather than a hemoglobin S (HbS) of <30%) prior to a surgical procedure requiring general anesthesia.  
*Strong recommendation, Moderate quality pediatric evidence (1B)*

Critically ill Children with Sickle Cell Disease with Acute Chest

In children with sickle cell disease and acute chest syndrome (ACS) who are critically ill, we recommend an exchange transfusion over a simple (non-exchange) transfusion if the child’s condition is deteriorating (based on clinical judgment); otherwise a simple (non-exchange) RBC transfusion is recommended.  
*Strong recommendation, Low quality pediatric evidence (1C)*
Alternative Processing of Blood Products

We recommend the use of irradiated cellular blood components for all critically ill children at risk for transfusion-associated graft versus host disease (ta-GVHD) due to severe congenital or acquired causes of immune deficiency.

Consensus panel expertise

We recommend the use of washed cellular blood components and avoidance of other plasma containing products (e.g. plasma, cryoprecipitate, etc.) for critically ill children with history of severe allergic reactions or anaphylaxis to blood transfusions, although patient factors appear to be critically important in the pathogenesis.

Consensus panel expertise

Research recommendations

- **Anemia tolerance:** We recommend investigations that seek evidence on thresholds or triggers that would inform the bedside clinician on the risk/benefit ratio of anemia as compared to a red cell transfusion.

Research recommendations

❖ **Physiologic metrics/biomarkers**: Investigations to identify and evaluate biomarkers and/or physiologic measures that characterize anemia intolerance.

  *Consensus panel expertise*

❖ **Hemoglobin threshold**: Identify the appropriate Hb concentration to guide RBC transfusion in hemodynamically unstable critically ill children, and in sub-populations of hemodynamically stable critically ill children.

  *Consensus panel expertise*
Thank you

• To all of the TAXI investigators
• To Stacey and Scot and the TAXI executive committee

❖ To the children and families that are in our care