Published in final edited form as:

Pediatr Crit Care Med. 2018 September ; 19(9) : S149–S156. doi:10.1097/PCC.0000000000001610.

Recommendations on Red Blood Cell Transfusion Support in Children with Hematologic and Oncologic Diagnoses from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative

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Abstract

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Conflicts of Interest:

The remaining authors have disclosed that they do not have any potential conflicts of interest

Copyright form disclosure: The other authors have no relevant disclosures.

Objective—To present the recommendations and supporting evidence for red blood cell (RBC) transfusions in critically ill children with hematologic and oncologic disease from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI).

Design—Consensus conference series of international, multidisciplinary experts in RBC transfusion management of critically ill children

Methods—The panel of 38 experts developed evidence-based and when evidence was lacking, expert-based clinical recommendations and research priorities for RBC transfusions in critically ill children. The hematologic/oncologic subgroup included seven experts. Electronic searches were conducted using PubMed, EMBASE, and Cochrane Library (CENTRAL) databases from 1980 to May 2017. Agreement was obtained using the Research And Development/University of California, Los Angeles (RAND UCLA) appropriateness method. Results were summarized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.

Results—The hematologic/oncologic subgroup developed 14 recommendations (7 clinical, 7 research); all achieved >80% agreement. In patients with sickle cell disease, TAXI recommends: 1) RBC transfusion to achieve a target hemoglobin (Hb) concentration of 10 g/dL rather than Hb of <30% prior to surgical procedures requiring general anesthesia; 2) exchange transfusion over simple (non-exchange) transfusion if the child's condition is deteriorating (based on clinical judgment), otherwise a simple, non-exchange RBC transfusion is recommended. There is insufficient evidence to make recommendations on transfusion thresholds for patients with sickle cell disease prior to minor procedures, with acute stroke or with pulmonary hypertension. For patients with oncologic disease or undergoing hematopoietic stem cell transplant (HSCT), a Hb concentration of 7–8 g/dL is recommended. Due to lack of evidence, research is needed to clarify the appropriate transfusion thresholds in these patients.

Conclusions—TAXI developed specific pediatric recommendations regarding RBC transfusion management in critically ill children with sickle cell disease, oncologic disease, and HSCT, and recommendations to help guide future research priorities.

Keywords

Sickle cell disease; oncology; oncologic diagnosis; oncologic disease; cancer; bone marrow transplant; stem cell transplant; thalassemia; hemoglobinopathy; blood; red blood cell; transfusion; child; pediatric critical care; evidence-based; consensus conference

Introduction

Red blood cell (RBC) transfusion is a cornerstone of support in the clinical management of children with hemoglobinopathies, such as sickle cell disease (SCD), oncologic diagnoses and those undergoing hematopoietic stem cell transplant (HSCT). However, little scientific evidence is available to guide common transfusion practice. At times of critical illness, these patients may experience oxygen debt and therefore may have a higher potential need for RBC transfusion support which must be balanced against known transfusion-associated risks.

Sickled RBCs have decreased oxygen carrying capacity and lead to a wide range of physiologic responses in the vasculature. RBC transfusions with donor RBC may ameliorate

these effects in patients with SCD. Transfusion may be either simple (given as whole blood or packed RBC units) or exchange (manual or automated) transfusions. The focus of this document is on RBC transfusion in the acute critical illness setting. Chronic transfusion therapy to reduce risk for SCD complications were not considered in these recommendations and readers are referred to other guidelines addressing this issue (1, 2).

Pediatric patients with oncologic diagnoses may require transfusion due to the underlying disease or bone marrow suppression and bleeding as a result of therapy. In the setting of critical illness, transfusion thresholds may be different from those tolerated while the patient is stable. Patients undergoing HSCT may be a unique population due to underlying disease for which transplant is given (sickle cell vs leukemia), comorbidities (prior lung disease) and unique transplant-associated complications.

There is limited scientific evidence on the transfusion management in these areas in critically ill children and what is available is presented below. The recommendations established here, while focused on data from the pediatric population, have also considered relevant data from adults.

Methods

The details of the methodology are described elsewhere in this supplement of *Pediatric Critical Care Medicine* (3). Briefly, we searched PubMed, EMBASE, and Cochrane Library from 1980 to December 2015, with an update in May 2017, using a combination of medical subject heading terms and text words to define concepts of RBC transfusion and hematologic/oncologic disease in critically ill children. We searched references from identified articles for additional publications. Two authors reviewed all citations independently. Included pediatric studies are presented in the supplemental digital data 1. We used a standardized data extraction form to construct evidence tables and graded the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system (4). A panel of 38 experts from 29 academic institutions in 8 countries met over the course of two years to develop evidence-based and, when evidence was lacking, expert-based recommendations for RBC transfusion in critically ill children. Recommendations developed and supporting literature were reviewed and scored by all panel members, using the Research And Development/University of California Appropriateness Method (5, 6). All recommendations reached agreement (>80%). Final recommendations for RBC transfusion in critically ill children with hematologic and oncologic diagnoses were divided into two categories: clinical recommendations, and research recommendations.

Results

Using the search strategy described above, 19,040 abstracts were initially retrieved. Two hundred and thirty-five full papers were reviewed by adjudicators (MS, NZ, SV) and 45 articles were retained for inclusion based on the criteria above. A summary of the included studies is presented in table format in Supplemental Digital Data 1, Supplemental Table 1.

Clinical Recommendations

The final recommendations and rationale for transfusion in critically ill children with SCD, oncologic disease and those undergoing HSCT are presented below. Although transfusions in these children are not limited to the following, our recommendations focused on the transfusion in the child with or at risk for critical illness.

Sickle cell disease (SCD)

7.1: In children with SCD who are critically ill or those at risk of critical illness, we recommend RBC transfusion to achieve a target hemoglobin (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). Voting data (n=29): 96% agreement, median 8, IQR 8–9.*

Rationale: Major surgical procedures involving general anesthesia are associated with risk of significant morbidity, including acute stroke and acute chest syndrome (ACS). Evidence for pre-operative transfusion is supported by most of the prospective data collection analyses and randomized control trials (RCTs) and summarized in a recent consensus statement (1,2,7–13). The Cooperative Study of Sickle Cell Disease natural history study observed 3,765 patients and reported on 717 patients undergoing 1,079 operations with multiple stratifications; the study concluded that simple transfusion to increase Hb to 10 g/dL “appears appropriate” (7). A 36-center study (8) compared rates of perioperative complications in 551 patients randomly assigned to receive either an aggressive transfusion regimen to decrease the HbS level to < 30% or a more conservative regimen that aims to increase Hb to 10 g/dL, whatever the Hb S level. Frequency of serious complications was similar between groups (31% vs. 35%), but transfusion-related complications occurred at a higher rate in the aggressive group (14% vs. 7%); the study concluded that a conservative transfusion regimen to a target Hb of 10 g/dL is as effective with less complications (8). In the Transfusion Alternatives Preoperatively in Sickle Cell Disease (TAPS), a multicenter block randomized trial of 70 patients stratified by age and risk features, of which 67 were evaluated for complications, 39% of the no-pre-operative transfusion group had clinically important complications vs. 15% in the pre-operative simple transfusion group (p=0.023); ACS accounted for most complications. The study was closed early because more complications were observed in the moderate-risk, no pre-operative transfusion arm; therefore, the impact of transfusion on outcomes may be over-estimated (9). Subgroup studies also support the conclusion that a conservative transfusion strategy is as effective as an aggressive strategy, even though not completely effective, in eliminating complications (10, 11). A small study randomized 14 patients with SCD to aggressive exchange transfusion vs. a conservative simple transfusion strategy. Post-operative complications occurred in 30% of patients; simple transfusion was not associated with a higher incidence of complications and a lower number of transfusions (~ 30%) (12). Other observational studies did not report a clear benefit of pre-operative transfusion (13, 14). *GRADE 1B based on downgrading for risk of bias.*

7.2: In children with SCD who are critically ill or at risk of critical illness, there is insufficient evidence to recommend an optimal Hb concentration threshold or percent HbS

for RBC transfusion prior to minor surgical procedures. *Consensus panel expertise. Voting data (n=35): 91% agreement, median 8, IQR 8–9.*

Rationale: A retrospective observational study showed that transfusion avoidance in children having minor elective surgical procedures is safe (15). A retrospective review of 28 children undergoing 38 procedures, including 34 without transfusion, reported a low rate of minor complications (5 of 34) (16). A prospective observational UK practice across all ages and operative risks (13) described large practice variability and questioned whether RCTs comparing transfusion with no transfusion for low- or moderate risk procedures are still justified.

7.3: In children with SCD and 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). Voting data (n=35): 97% agreement, median 9, IQR 8–9.*

Rationale: The available evidence comes from retrospective or prospective data collection without a comparative study arm. Vichinsky et al. initiated a prospective, multicenter study of ACS at 30 centers using a standardized treatment and monitoring protocol (17). Data on 671 episodes in 538 pediatric and adult patients was complete for analysis. Mean oxygen saturation at diagnosis was 92% in room air. Ventilation was required in 13% of patients (mean duration: 4.6 days); the recovery rate was 81%. Transfusion therapy was “given to patients for clinical distress at physician's discretion” although 72% of patients were transfused and 68% of patients received simple transfusions. Simple and exchange transfusions resulted in similar oxygenation improvements and were concluded to be safe and effective (16). In a retrospective chart review of 36 children with 40 ACS events, simple transfusion to an Hb under 11 g/dL followed by partial or whole blood exchange transfusion with clinical deterioration was shown to improve oxygenation indices (18). Velasquez et al retrospectively assigned a Clinical Respiratory Score to 44 children with 53 ACS events who received red cell exchange for worsening respiratory distress. Interestingly, one third of patients who later received an exchange transfusion did not have ACS at presentation. No patients developed complications from the exchange (19). A retrospective chart review of 81 children with ACS suggested that patients with more severe clinical respiratory score benefitted from early, upfront automated red cell exchange (20). Multi-center ACS RCTs have not yet been conducted comparing simple vs. exchange transfusions, identification of patients at risk, timing of implementation, measures of physiologic responses and outcomes (1). *GRADE 1C based on downgrading for imprecision and inconsistency.*

7.4: In children with SCD and pulmonary hypertension who are critically ill or at risk for critical illness, there is insufficient evidence to recommend the optimal Hb concentration threshold or percent HbS for RBC transfusion or the method of red cell transfusion. *Consensus panel expertise. Voting data (n=35): 97% agreement, median 9, IQR 8–9.*

Rationale: There is insufficient information reported on SCD pediatric patients with pulmonary hypertension who are critically ill or at risk for critical illness to make specific

recommendations regarding RBC transfusion. Pre-emptive transfusion strategies and pharmacologic interventions to prevent or reverse pulmonary hypertension must be studied, but unfortunately, this complication is not well monitored in most pediatric patients (21). Optimal transfusion management strategies, detailed physiology measures and short-and long-term outcomes in critically ill patients are also lacking.

7.5: In children with SCD and acute stroke who are critically ill, there is insufficient evidence to recommend the optimal Hb concentration threshold or percent Hb S for RBC transfusion; the preferred method of RBC transfusion is exchange transfusion if instituted quickly. *Consensus panel expertise. Voting data (n=35): 97% agreement, median 9, IQR 8–9.*

Rationale: Critically ill stroke patients warrant the usual, timely resuscitation. However, review of the literature did not identify any clinical studies evaluating transfusion strategies the management of critically ill children with acute stroke. It is recognized that raising the Hb by simple transfusion to levels >10 g/dL can increase viscosity and worsen sickling symptoms (22), making an exchange transfusion preferred over simple transfusion if it can be initiated quickly. This interval has not been specifically defined in the literature, but is considered by experts to be dependent on the clinical scenario; ideally, the exchange should begin within an hour or two in critically ill patients. However, in a patient with hemoglobin < 10 g/dL, initiating simple transfusion of normal donor RBC should not be delayed if an exchange cannot be done because there are issues of vascular access, provider, or product availability (1). A simple transfusion is often then followed with an exchange transfusion. Whether the window of tissue plasminogen activator efficacy in acute stroke would also be an interval within which to initiate an exchange transfusion in SCD has not been evaluated. Of note, Hulbert et al showed that exchange transfusion was associated with fewer recurrent strokes than simple transfusion in a non-ICU population (23).

Oncologic Diagnoses

7.6: In children with oncologic diagnoses who 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). Voting data (n=35): 88% agreement, median 8, IQR 7–8.*

Rationale: Due to lack of evidence in children, the TAXI recommendation is based on our consensus interpretation of the literature and recommendations, which is mostly based on adult data (24) and in patients without bone marrow failure (25,26). It is plausible that children with oncologic diagnoses who are critically ill or at risk for critical illness benefit from higher hemoglobin thresholds, or may be able to safely tolerate hemoglobin thresholds lower than stated in our recommendation, but data in the literature on this question are quite poor: we found only a few recent pediatric specific guidelines (e.g. Australia and United Kingdom) (27,28) and some small descriptive studies. A retrospective study reports that pediatric patients were not transfused if Hb > 8.0 g/dL in their center even when they were febrile (29). Another study reported that only 8% of neutropenic febrile patients were transfused if their hemoglobin was > 8 g/dL, but the proportion of such patients increased to

62% if they were tachypneic (30). One recent prospective study randomized adult patients in a hematological ICU to 1 vs. 2 units for Hb < 8.0 g/dL; fewer transfusions were administered using the more restrictive regimen without adverse effects from anemia and no difference in mortality (31). In contrast, adult patients with oncologic disease treated for septic shock, randomized to the liberal (hemoglobin threshold, < 9 g/dL) or to the restrictive strategy (hemoglobin threshold, < 7 g/dL) of RBC transfusion during their ICU stay showed a trend toward improved survival at 28 days and significant improvement at 90 days in the liberal arm (32). In pediatric oncologic patients needing urgent surgery, a large, single center retrospective review found risk of perioperative RBC transfusion in neurosurgery patients with usual transfusion trigger of 7–9 g/dL to be more likely in smaller subjects, longer operations and more blood loss, but the only significant outcome in the post-operative course was prolonged mechanical ventilation duration (33). Extrapolating from the pediatric HSCT population, a single center study of 66 children with HSCT managed with a restrictive threshold of 7 g/dL was compared to an historic control group where a threshold Hb of 9 g/dL was used; no difference was found in length of stay (LOS), engraftment or 100-day mortality, including infection, multiple organ failure syndrome (MOFS), graft vs. host disease (GVHD), veno-occlusive disease (VOD), and respiratory failure (34). Also to be considered is that in both the pediatric and adult cancer population, there are inconsistent findings on the association of RBC transfusion with poorer outcomes [for example (35–41)]. Given the available data, it can be concluded that the optimal RBC transfusion strategy remains to be determined. *GRADE 2C based on downgrading for indirectness.*

Hematopoietic Stem Cell Transplantation (HSCT)

7.7: In children undergoing HSCT who are critically ill or at risk for critical illness, and are hemodynamically *stable*, we suggest a Hb concentration of 7–8 g/dL be considered a threshold for RBC transfusion. *Weak recommendation. Low quality pediatric evidence (2C). Voting data (n=35): 88% agreement, median 8, IQR 7–8.*

Rationale: There are no strong data to support the recommendation of a specific Hb transfusion threshold in pediatric HSCT patients with respiratory distress, sepsis/septic shock or multiple organ dysfunction. Our recommendation is based on consensus interpretation of the literature, which comes almost exclusively from data in HSCT adults and in patients without bone marrow failure (24–26). We found two pediatric specific guidelines (e.g. Australia and United Kingdom) (27,28). Some HSCT centers reported that they transfuse HSCT children if their Hb level is < 8 g/dL or < 7 g/dL (34,42,43). A single center study of 66 children compared outcomes in two consecutive groups with a liberal and a restrictive threshold of 9 and 7 g/dL respectively; they found no difference in length of stay, engraftment, infection, multiple organ dysfunction syndrome, GVHD, veno-occlusive disease, respiratory failure and 100-day mortality (34). One RCT was stopped early by the data and safety monitoring board because all three patients who were transfused according to a liberal transfusion threshold of 12 g/dL contracted a severe veno-occlusive disease while the three patients who were randomized to the restrictive arm (Hb threshold of 7 g/dL) did not (44). A retrospective review of transfusion in patients with SCD undergoing HSCT showed that a strategy aiming to achieve their higher RBC threshold 9–11 g/dL was associated with more veno-occlusive disease (45). These data suggest that the post-

transfusion target should not be higher than 9 g/dL. However, the appropriate threshold Hb in children with HSCT remains to be determined. *GRADE 2C based on downgrading for indirectness and imprecision.*

Research Recommendations for Hematologic and Oncologic Diagnoses

Thalassemia

Recommendation

R7.1: In critically ill children with the hemoglobinopathy thalassemia (and potentially other hemoglobinopathies), we recommend undertaking well-designed registries or expanding current initiatives to determine measures and limits of anemia tolerance, examine current practice, and define clinical outcomes to inform future research investigating the risks, benefits and alternatives of RBC transfusion practice. *Consensus panel expertise. Voting data (n=29): 100% agreement, median 9, IQR 8–9.*

Rationale: There are insufficient studies in children with transfusion-dependent thalassemia experiencing insufficient oxygen delivery, acute respiratory distress, sepsis/septic shock or needing urgent surgery to make specific recommendations regarding RBC transfusion. A single center practice summary (46) and the prospective CDC Thalassemia Blood Safety Network that monitored patients prospectively (47) describe RBC transfusion thresholds usually > 7 g/dL but do not identify practice for critically ill children included in their cohort. Creating future networks, like those developed under the supervision of the National Institutes of Health supported Thalassemia Clinical Research Network, could help addressing questions about thalassemic critically ill children.

Sickle Cell Disease (SCD)

Recommendations

R7.2: In children with SCD who are critically ill or at risk for critical illness, we recommend a well-designed registry or enhancement of existing network databases to further clarify optimal transfusion management. *Consensus panel expertise. Voting data (n=35): 97% agreement, median 9, IQR 8–9.*

Rationale: Despite considerable data on transfusion therapy of patients with SCD, there is little information specifically describing transfusion management in critically ill children or children at risk for critical illness. Efforts to design a Clinical Respiratory Score for children with ACS begin to address the potentially critically ill SCD population and warrant continued study (19,20).

R7.3: In children with SCD who are critically ill or at risk for critical illness, we recommend future research studies to evaluate the optimal Hb concentration threshold and/or percent HbS to guide RBC transfusion decisions prior to minor surgical procedures. *Consensus panel expertise. Voting data (n=35): 100% agreement, median 9, IQR 8–9.*

Rationale: The goals, risks, method and benefit of RBC transfusion in children prior to defined minor surgical procedures remain to be explored in current medical practice

Auto- or Allo-immune Hemolytic Anemia

Recommendation

R7.4: In children with auto- and/or allo-immune mediated hemolytic anemia who are critically ill or at risk for critical illness, we recommend undertaking well-designed registries to determine measures and limits of anemia tolerance, examine current practice, and define clinical outcomes to inform future research investigating the risks, benefits and alternatives of RBC transfusion practice. *Consensus panel expertise. Voting data (n=29): 100% agreement, median 9, IQR 8–9.*

Rationale: In children with auto- and/or allo-immune hemolytic anemia, clinical severity is often related to the severity of the anemia and rapidity of onset, extent of hypovolemia and underlying health status, including cardiorespiratory reserve. Efficacy of RBC transfusion is highly debated over concern of risk of transfusing incompatible blood vs. risk of anemia exacerbating life-threatening hypoxemia. However, one prospective clinical trial showed no outcome differences in patients transfused for Hb as low as < 5 g/dL between patients with autoantibodies transfused with “least incompatible” RBC vs. patients with only alloantibodies transfused with matched RBC vs. anemic patients without antibodies who were (48). A small retrospective clinical series described 5 adult patients with “rapid-onset life-threatening anemia” with hematocrit of 8–10% who were successfully transfused with a range of 2–84 incompatible RBC units when “compatible blood could not be obtained” (49). Based largely on retrospective data and/or small studies and case reports with varying degrees of severe anemia [such as references (50–55)], clinical reviews and expert opinion state that patients should be transfused to maintain hemoglobin at a “clinically acceptable level”. However, without better understanding of anemia tolerance, a specific transfusion threshold is therefore difficult to define or recommend (56,57). In fact, 110 hemolytic anemia patients were excluded from the Transfusion Strategies for Patients in Pediatric Intensive Care Units (TRIPICU) study (25). Lower limits of anemia tolerance and rigorous measures of transfusion efficacy require further definition and study.

Oncologic Disease

Recommendation

R7.5: In children with oncologic disease who are critically ill or at risk of critical illness, we recommend undertaking well-designed registries or expanding current initiatives to inform future research investigating the risks, benefits and alternatives of transfusion practice. *Consensus panel expertise. Voting data (n=29): 97% agreement, median 9, IQR 8–9.*

Rationale: As stated before, there are no data to recommend specific Hb transfusion thresholds in pediatric oncology patients with respiratory distress, sepsis/septic shock or multiple organ dysfunction to reduce mortality or preserve organ function.

Radiation Therapy (XRT)

Recommendation

R7.6: In children receiving emergency radiation therapy (XRT) who are critically ill or at risk for critical illness, we recommend exploration of existing databases to investigate the

impact of Hb concentration and RBC transfusion on disease response, survival and other toxicities to inform creation of contemporary registries to investigate these associations. *Consensus panel expertise. Voting data (n=35): 94% agreement, median 8, IQR 8–9.*

Rationale: There are no specific data in children to recommend RBC transfusion to pediatric patients undergoing emergency radiation therapy (i.e. superior mediastinal/superior vena cava syndrome, paraspinal mass, etc.). One small retrospective study of non-emergent radiation given to pediatric medulloblastoma patients found no association between minimum Hb levels and outcome based on local control or survival although too few patients were transfused to identify a potential benefit (58). Hb thresholds of > 8, > 9 or > 10 g/dL are cited as practice, although disease response and survival outcome studies are lacking (29,30,56).

Hematopoietic Stem Cell Transplantation (HSCT)

Recommendation

R7.7: In children undergoing HSCT who are critically ill or at risk for critical illness, we recommend undertaking well-designed registries or expanding current initiatives to inform future research investigating the risks, benefits and alternatives of transfusion practice.

Consensus panel expertise. Voting data (n=29): 97% agreement, median 9, IQR 8–9.

Rationale: Current literature is insufficient to fully determine RBC physiologic thresholds in patients with bone marrow dysfunction and whether they are the same as pediatric patients with normally functioning bone marrow producing normal red blood cells. In addition, the immunologic and infectious ramifications of RBC transfusion in these patients are not well defined.

CONCLUSIONS

Further research surrounding indications, risk, benefits, and alternatives to RBC transfusion in critically ill children with sickle cell disease, with oncologic diagnoses or undergoing hematopoietic stem cell transplant is sorely lacking. Using a structured literature review and grading process, the TAXI panel concluded that there is currently inadequate evidence to clearly recommend specific RBC transfusion strategies in these children and needs additional study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of Funding:

The Transfusion and Anemia Expertise Initiative was supported by the National Institute of Health, 1 R13 HD088086-01, Society for the Advancement of Blood Management, SABM-Haemonetics Research Starter Grant, CHU Sainte-Justine Foundation, Washington University Children's Discovery Institute and the University of Massachusetts Medical School.

Dr. Bembea received support from the National Institute of Health (NIH) outside the submitted work. Dr. Zantek disclosed the following not related to this project -Octapharma, Terumo BCT, Bayer HealthCare (research funding), Endo International PLC, Boston Scientific (financial interest), North American Specialized Coagulation Laboratory Association (executive board). Dr. Josephson disclosed the following not related to this project – Biomet Zimmer, Immucor, Octapharma (consultant).

Drs. Steiner, Zantek, Valentine, and Josephson received support for article research from the National Institutes of Health (NIH). Dr. Steiner received funding from NIH R13 grant from the National Institute of Child Health and Human Development (NICHD) and National Heart, Lung, and Blood Institute (NHLBI). Dr. Zantek's institution received research funding from Terumo BCT, Octapharma, and Bayer HealthCare, and received funding from the NICHD/NHLBI R13 (1 R13 HD088086-012) (received travel funds to attend one of the consensus conference meetings), and the College of American Pathologist Transfusion Medicine Resource Committee - American Society for Apheresis Inbound Liaison (travel expenses paid by ASFA); and she disclosed she is an Executive Board Member for the North American Specialized Coagulation Laboratory Association, and her spouse is an employee of Boston Scientific and owns stock in ENDO International PLC. Dr. Zantek disclosed that TAXI was supported, in part, by funding from the NIH NICHD/NHLBI, Washington University at St Louis CDI, SABM, the Canadian Critical Care Trials Group, the University of Massachusetts, as well as support from the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network and the World Federation of Pediatric Intensive and Critical Care Society. Dr. Valentine also received support for article research from Washington University Children's Discovery Institute Grant (CDI-EI-2015-499), the University of Massachusetts Medical School, the Society for the Advancement of Blood Management SABM-Haemonetics Research Starter Grant, and the CHU-Sainte Justine Foundation. Dr. Valentine's institution received funding from Eunice Kennedy Shriver NICHD and NHLBI under award number 1 R13 HD088086-01; the Society for the Advancement of Blood Management SABM-Haemonetics Research Starter Grant; Washington University Children's Discovery Institute (DCI-EI-2015-499), and she received other support from CHU-Sainte-Justine Foundation and the University of Massachusetts Medical School. Dr. Josephson received funding from Immucor, Inc (consultancy) and Octapharma (consultancy). Dr. Luban disclosed other support from Cellphire (consultant, two NIH DSMBs) and from the American Association of Blood Banks (travel).

We thank all members of the TAXI initiative for their support and their comments. The study was supported by grants from the Washington University Children's Discovery Institute (CDI-EI-2015-499), University of Massachusetts, CHU Sainte-Justine Foundation, National Institute of Child Health Development (1 R13 HD088086-01), National Heart, Lung and Blood Institute, and the Society for the Advancement of Blood Management. We also thank the World Federation of Pediatric Intensive and Critical Care Societies, Society for Critical Care Medicine and the AABB for their support of TAXI.

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Appendix 1

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

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MB ChB, *Imperial College London, UK*, Section 4. Hemorrhagic shock and non-life-threatening bleeding, Oliver Karam MD PhD, *Virginia Commonwealth University*, Robert T. Russell MD MPH, *University of Alabama, USA*, Philip C. Spinella MD*, *Washington University of St. Louis, USA*, Paul Stricker MD, *University of Pennsylvania, USA*, Adam M. Vogel MD, *Texas Children's Hospital, USA*, Section 5. Acute brain injury: Philip C. Spinella MD*, *Washington University of St. Louis, USA*, Robert C. Tasker MA MD MBBS, *Harvard University, USA*, Alexis F. Turgeon MD MSc, *Université Laval, Canada*, Section 6. Acquired or congenital heart disease, Jill M. Cholette MD*, *University of Rochester, USA*, Steven M. Schwartz MD, *University of Toronto, Canada*, Ariane Willems MD, *University of Brussels, Belgium*, Section 7. Sickle cell/ oncologic disease, Cassandra D. Josephson MD, *Emory University, USA*, Naomi LC Luban MD, *George Washington University, USA*, Leslie E. Lehmann MD, *Harvard University, USA*, Robert I. Parker MD*, *Stony Brook University, USA*, Simon J. Stanworth MD, *NHS Blood and Transplant, Oxford, UK*, Marie E. Steiner MD MS*, *University of Minnesota, USA*, Nicole D. Zantek MD PhD, *University of Minnesota, USA*, Section 8. Receiving support from extracorporeal, ventricular assist and renal replacement therapy devices: Melania M. Bembea MD PhD*, *Johns Hopkins University, USA*, Timothy Bunchman MD, *Virginia Commonwealth University, USA*, Ira M. Cheifetz MD, *Duke University, USA*, James Fortenberry MD, *Emory University, USA*, Marie E. Steiner MD MS*, *University of Minnesota, USA*, Section 9. Selection and processing of red blood cell components: Meghan Delaney DO, MPH, *Children's National Health System USA*, Cassandra D. Josephson MD, *Emory University, USA*, Robert I. Parker MD*, *Stony Brook University, USA*, Leo van de Watering MD, *Leiden University, Netherlands*, Nicole D. Zantek MD PhD, *University of Minnesota, USA*, Evidenced-Based Medicine: Karen A. Robinson PhD, *Johns Hopkins University, USA*, Melania M Bembea MD PhD*, *Johns Hopkins University, USA*, Implementation Science: Sara Small MS, *Washington University of St. Louis, USA*, Katherine Steffen MD, *Stanford University, USA*