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Implementation of the Recommendations for Red Blood Cell Transfusions for Critically Ill Children from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative

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Abstract

Objective—To provide context for the implementation of the Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) recommendations for red blood cell transfusions including a review of prior research related to implementation of transfusion guidelines, efforts to facilitate implementation through TAXI, and to provide a framework for recommendation implementation.

Design—Review of existing clinical literature and description of a comprehensive approach to implementation based on Implementation Science principles.

Results—The TAXI recommendations on red blood cell transfusions are based on clinical evidence and aim to limit unnecessary and potentially harmful transfusions. Prior efforts to utilize transfusion guidelines include use of provider education, local guidelines, visual aids, prospective and retrospective audit and feedback as well as computerized decision support tools; however, no single approach has been identified as optimal for implementation in pediatric critical care settings. Evidence around provider beliefs and transfusion decision making point to the need for additional provider education, emphasizing the importance of limiting transfusions, and the development of recommendations, such as the TAXI guidelines, that can be applied to specific clinical conditions.

Conclusions—The TAXI guidelines will be broadly disseminated, however coordinated implementation efforts will be required to impact practice. An approach that encourages

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involvement of a wide range of multi-professional stakeholders, formal agreement on the implemented guidelines, selection of strategies that are practical and feasible, and active monitoring of clinical practice and outcomes throughout implementation is recommended. A formal second stage “TAXI CAB” - Transfusion and Anemia Expertise Initiative - Continuous Assessment of Blood is proposed to enhance implementation of the recommendations, follow uptake and impact on practice and patient outcomes, and ensure integration of new clinical evidence into the existing guideline as it is developed.

Keywords

Critical Care; Pediatric; Red Blood Cell; Blood; Transfusion; Anemia; Practice Guideline; Evidence-Based Practice

Introduction

The Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) has carefully and systematically followed clear guidelines to create a comprehensive, evidence-based, and expert supported list of recommendations for red blood cell (RBC) transfusion in the pediatric intensive care unit (PICU). Establishment of blood transfusion guidelines for critically ill children represent an initial step in modifying transfusion practices in critically ill children in a manner that is safe, thoughtful, clinically sound, and avoids unnecessary transfusions as an ultimate goal. Development of guidelines alone has a limited impact on consistent provider adoption (1, 2), and further efforts are required to integrate such guidelines into clinical practice. Implementation approaches focused on improving knowledge around guidelines and modifying care processes to facilitate compliance have been shown to enhance the impact guidelines have on care. Therefore, implementation science and expertise was included in the TAXI efforts from the outset of guideline development. The second stage of TAXI, effective implementation, requires active planning and action.

While much existing evidence for implementation of transfusion guidelines originates from adult studies, the strategies tested may provide important insight into application in the PICU setting. A variety of approaches have been described, many of which have demonstrated a positive impact on blood transfusion practices.

The purpose of this article is to outline different implementation strategies to highlight their effectiveness for clinicians interested in adopting TAXI's recommendations. In addition, the anticipated plans for the TAXI initiative will be described.

Implementation Strategies

Establishment of Local Guidelines and Visual Aids—Development of local institution-specific guidelines, often guided by existing larger scale evidence, have been reported to have significant positive impacts on the proportion of patients who received RBCs or the odds of transfusion (3-6). Most of these studies fail to detail how these guidelines were specifically integrated into workflow, though it is unlikely that creation of the guideline alone facilitated change in practice. Muller et al emphasized the importance of

widespread clinician education and distribution, ensuring ease of guideline use, endorsement by local opinion leaders, and creating a sense of ownership among providers to facilitate consistent use (6). These guidelines were also supported with a decision flowchart to guide providers in determining if a RBC transfusion was necessary. With use of the flowchart, the proportion of patients who received a perioperative transfusion decreased from 35% to 19.8% (6). Similarly, Whitney et al utilized a transfusion decision tree as a visual cognitive aid by pediatric cardiac anesthesiologists and noted a 66% reduction of RBC transfusion ($p=0.001$) in the operating room without shifting the transfusion burden to the Intensive Care Unit (ICU) (4).

Provider Education—Provider education about transfusion recommendations is common, but is rarely the sole implementation strategy employed. Systematic reviews of transfusion implementation strategies reported that 44-47% of studies used some form of provider education in implementation (7, 8). Educational strategies included one-on-one sessions, group presentations, and workshops targeted at either single or multiple specialties. Some educational sessions focused solely on the evidence base around limiting transfusion, while others also included education about new systems-based interventions to use guidelines in practice (7, 8). Some sessions were followed by questionnaires (7, 9) to assess learning or acceptance of presented material.

Few studies examine education as an independent implementation strategy. Soumerai et al compared an intervention that consisted of a group lecture and a 30-minute one-on-one teaching session versus no education in a randomized study and noted a 40% decrease in the proportion of transfusions administered by surgeons above a threshold hematocrit in the intervention group (from 0.4 to 0.24). Transfusion above this threshold by non-surgeons increased by 9% (from 0.40 to 0.44) ($p=0.006$); however, the number of transfusions administered by these physicians was low (10). Vos et al noted training workshops on transfusion guidelines for a broad hospital population were successful in reducing avoidable transfusions in all pediatric and adult surgical patients, but increased transfusion in obstetric and other adult populations; hospitals that were consistently compliant with guidelines used additional education sessions or audit and feedback mechanisms to augment initial education (9).

Retrospective Audit and Feedback—Retrospective audit and feedback mechanisms summarize clinical performance for groups or individuals and utilize data to influence provider practice. Some studies fail to demonstrate changes in RBC utilization with retrospective feedback programs (11, 12), while others document significant improvements (13-15).

Morrison et al described a group education program around transfusion guidelines coupled with individual audit and feedback for providers who transfused outside the guidelines following education, which resulted in a 60% decrease in patients undergoing transfusion and a 75% monthly decrease in RBC units transfused (13). In one study, individual audit and feedback plus team feedback were compared with team feedback alone, and showed a 4.05 increased odds of transfusion bundle compliance with when both feedback types were given (14). Daily audit of unit-based transfusion compliance in an ICU along with individual

feedback provided to physicians prescribing outside of established guidelines led to a reduction in unnecessary transfusions from 14.7% to 8.1% ($p=0.016$)(15). Upcoming data from the randomized implementation science-based Audit and Feedback INterventions to Increase evidence-based Transfusion practice (AFFINITIE) study will provide insight into two feedback interventions: 1) enhanced feedback reports or 2) a web-based toolkit to enhance response to feedback (16). Criticisms of retrospective audit strategies include the fact that feedback may be untimely, may poorly target individuals who fail to follow guidelines when feedback is provided in a collective format, and that it does not impact behavior at the time blood is ordered (11).

Prospective Audit or Monitoring—Prospective audit or monitoring strategies evaluate suitability for transfusion per an established guideline at the time of the RBC request. Ordering physicians submit information with the transfusion order that usually includes recent hemoglobin (Hb) and transfusion indication, with or without modifiers related to patient age, hemodynamic status, or associated comorbidities. Laboratory and blood bank staff review each request, while hematology, clinical pathology, and transfusion specialists may act as “gatekeepers” for transfusion requests made outside guidelines. Reductions in the number of number of RBC units transfused (17, 18), rate of inappropriate transfusions (16% to 3%, $p=0.004$) (19) and overall transfusion rate (7.68 to 6.10 patients transfused/1000 hospital days, $p=0.001$) (20) have been reported. A physician self-auditing system did not significantly reduce transfusions over time (21).

These strategies, while successful, may be labor intensive to implement, difficult to maintain over time, and may lead to transfusion delays due to staff availability to review requests. For this reason, in many studies, patients with acute bleeding and hemodynamic instability were exempt, limiting applicability in the ICU setting (17-20).

Clinical Decision Support—Clinical Decision Support (CDS) “provides timely information, usually at the point of care, to help inform decisions about a patient's care”. Electronic CDS aids in clinical decision making by matching patient characteristics to a computerized knowledge base to generate a patient-specific recommendation (22). Recently, the National Academy of Medicine highlighted the potential value of well-designed CDS tools, including facilitating delivery of evidence based and patient-specific care that is timely and well informed. Additional benefits include reducing choice complexity for providers in a landscape of exponential knowledge growth, improving outcomes, and reducing the cost of care (23). Transfusion CDS tools range from those that advise transfusion based on a single laboratory value alone (ex: Hb) to more sophisticated adaptive alerts that alter the threshold for transfusion in response to the user's justification for transfusion. CDS tools may “stand alone” outside the electronic medical record and patient order entry or be integrated into these systems. Successful implementation depends on good CDS design, such that the tool does not induce “alert fatigue” or create significant disruptions in workflow. Education about decision support tools prior to implementation is essential, as is garnering user feedback (24).

In a systematic review of CDS tools targeted at impacting transfusion, 87.5% (7/8) of studies reported statistically significant improvement in compliance with an established institutional

transfusion guideline (25). Half of studies reported a significant reduction in pre-transfusion laboratory values, with an additional third of studies showing a trend towards reduction. Six of thirteen studies (46%) yielded a statistically lower number of RBC transfusions with a CDS intervention with an additional 46% showing a trend towards reduced RBC usage with a CDS tool. Integration of CDS tools at the point of electronic patient order entry for transfusion may be particularly powerful. Goodnough et al reported a reduction in length of stay ($p=0.034$) and mortality ($p=0.003$) after implementation (26) of a tool that reminded provider of transfusion guidelines if the patient's most recent Hb suggested that transfusion might be omitted. A pediatric study using a similar tool examined the PICU population separately from other hospitalized patients; mean PICU pre-transfusion Hb fell from 9.83 g/dL (95% Confidence Interval (CI) 9.65-10.01) to 8.75 g/dL (95% CI 8.59-8.9) ($p<0.0001$), and a decrease was noted in RBC transfusions per patient day [0.20 (95% CI 0.13-0.27) to 0.14 (95% CI 0.11-0.17) ($p=0.12$)](27).

Limitations of Existing Studies—Given the variety of strategies used and variable results, it is not possible to draw definitive conclusions about the effectiveness of any intervention or combination of interventions. Moreover, most studies lack a description of the rationale behind the selected implementation strategy. Many of these studies are limited by pre- post-designs, and are susceptible to selection bias from secular changes in practice as well as the Hawthorne effect. Some studies utilize multiple implementation strategies concurrently (i.e. education and audit and feedback), which limits determination of the impact of each single strategy. The majority of studies have been conducted in single tertiary care centers, which may limit generalizability, particularly to smaller centers. Finally, most studies also demonstrate a positive impact of the tested intervention, suggesting that publication bias may also exist.

Targeting Strategies for Implementation—To better inform optimal targets for implementation, the theoretical domains framework was used to assess adult ICU providers' beliefs surrounding a restrictive transfusion strategy in the United Kingdom and Canada (28, 29). Both studies showed that providers understood the benefits of a restrictive strategy, but approximately 50% of respondents felt that this was not as high of a priority compared to non-transfusion-related ICU interventions. Support of a restrictive strategy was countered by the belief that anemic patients are at increased risk of organ compromise, and providers reported increased difficulty following guidelines when patients were clinically unstable and when other subspecialists urged them to transfuse patients. Patient age and comorbidities influenced decision making, and clear communication about transfusion thresholds with all team members (including trainees) was also noted to be critical in following a restrictive transfusion plan (28, 29). These studies reflect physician beliefs, not actual behavior, but nevertheless provide insight surrounding attitudes that may inform guideline implementation.

In a qualitative study in which pediatric intensivists and pediatric hematologists and oncologists were interviewed, it was noted that the majority of clinicians receive little formal training in transfusion, and that transfusion decision-making processes are developed over time through self-training and clinical experience that is shaped by local practice, all of

which contributes to practice variation (30). Providing formal education around blood transfusion, emphasizing the importance of limiting transfusion, defining hemodynamic stability and avoiding empiric transfusion in stable patients, and providing guidelines for specific comorbid conditions (as was done in the TAXI guidelines) may be helpful. Educating other subspecialists about guidelines, and ensuring mutual understanding of the transfusion plan among all team members may also be of use.

Dissemination and Implementation of TAXI RBC Transfusion clinical

recommendations—A goal of TAXI was to ensure widespread dissemination of the transfusion clinical recommendations to the entire community of providers that cares for critically ill children. Likewise, we sought to create guidelines that would facilitate implementation on both local and large scales. To this end, experts in developing evidence-based guidelines and dissemination and implementation (D & I) were involved in all stages of the TAXI project. D & I experts provided feedback to the TAXI workgroups to ensure that implementation was considered throughout the writing process and that guidelines were written in a manner that would impact provider practice. Prior to voting on guidelines, the Guideline Implementability Appraisal (GLIA) instrument (31) was used to identify barriers to implementation, evaluating how executable, decidable, valid, flexible, measurable, novel, and computable each guideline was, as well as the impact it would have on the process of care. To the extent possible allowed by existing evidence, guidelines were modified to enhance implementation based on feedback from the GLIA tool.

Members of TAXI participated in a focus group to identify implementation barriers and facilitators, with an aim to inform future efforts. Group members were asked to reflect on potential obstacles to applying the new TAXI guidelines in their own institution. Barriers identified included many of those commonly cited in implementation studies (32): gaps in education, misperception of the risks and benefits of transfusion, historical practice within a group or institution (overcoming a “transfusion culture”), lack of leadership around blood transfusion practices, failure to prioritize a restrictive blood transfusion strategy, lack of reinforcement for providers who followed the transfusion guideline and a concordant lack of consequences for those that did not, and finally, lack of resources to support transfusion data collection to monitor practice. Facilitators identified included the current emphasis on development of blood management programs in both adult and pediatric settings, and commercially available tools to monitor blood utilization, such as El Dorado® (Haemonetics®). The TAXI group anticipates that the rigorous approach in developing the guidelines as well as the endorsement by multiple groups (The Society of Critical Care Medicine, American Association of Blood Banks, the Society for the Advancement of Blood Management, Pediatric Critical Care Blood Research Network, Pediatric Acute Lung Injury and Sepsis Investigators) will also facilitate adoption.

The multi-professional TAXI experts also identified ideal measures for auditing and monitoring to enhance implementation. With appropriate resources, these were identified as key factors in tracking the success of implementation. Patient Hb prior to transfusion was felt to be the most important indicator of success of the guideline implementation and potentially, the easiest to obtain. Other measures, including the number of “appropriate” transfusions—those wherein a specific RBC transfusion is recommended by the guidelines,

total transfusions, and proportion of appropriate transfusions compared to total transfusions were also considered as potential makers for successful implementation. The amount of wasted blood, number of donor exposures, number of transfusion reactions, monitoring of under-transfusion, cost analysis, and tracking of provider decision making around transfusion both when blood is and is not transfused were also considered to be potentially helpful.

TAXI Plan for Guideline Dissemination—TAXI submitted all of their guidelines simultaneously to ensure that a broad range of recommendations would be presented to clinicians. The clinical recommendations have been summarized in the decision tree in the main article in this issue of *Pediatric Critical Care Medicine*. Accompanying articles in the supplement to this issue was designed to provide more in-depth analysis of the specific recommendations in different patient subpopulations.

Co-publication of the TAXI recommendations summary will be sought in order to enhance dissemination of the guidelines to a broad population of providers who care for critically ill children that may be subject to blood transfusion. The TAXI guidelines will also be presented at a range of national and international meetings including the World Federation of Pediatric Intensive and Critical Care Societies, the Society for the Advancement of Blood Management, the Society of Critical Care Medicine, Pediatric Academic Society, and the American Association of Blood Banks annual meetings, such that attendees will be made aware of the guidelines and consider integrating them into their personal practice or creating systems-based approaches to transfusion that utilized the guidelines. The guidelines will also be highlighted in the Open Pediatrics World Shared Practice Forum to reach a broad global audience.

From a dissemination perspective, Grol et al noted that a variety of dissemination techniques may be desirable in order to reach different segments of the target population; “for some providers, making evidence available quickly through publication is most desirable; however, for others, a more active personal approach may be necessary” (33). This might include one-on-one education and/or dynamic discussion. An Agency for Healthcare Research and Quality Review (AHRQ) found that use of multiple dissemination strategies may be more effective than a single strategy alone, particularly in regards to guideline adherence (34). To this end, it may be necessary to explore alternative methods for dissemination, however, these were beyond the scope of our current TAXI project.

Integrating implementation into guideline development has ensured that the TAXI guidelines are clear and useful within the context of PICU practice. Additionally, we have developed a decision tree as a summary tool for guideline implementation. The decision tree, formatted as a one page document, is intended to allow for easy viewing and quick reference for different clinical scenarios in the PICU. The color coding enables further visual clues on when to go (green) and prescribe a RBC transfusion, and when to stop (red). Based on the results of Whitney and Muller (4, 6), use of this tool may reduce unnecessary transfusion and ensure that users follow evidence-based and expert-opinion based at all times.

We are currently pursuing creation of printed educational materials to distribute at national and international meetings as well as a web-based application for the decision tree as a means for individual providers and units to implement the guidelines. Additionally, this tree may be re-formatted for multiple purposes based on users' needs (pocket card, poster, CDS framework). While creation of these materials aims to enhance provider uptake and adoption, true integration into practice will likely require a coordinated approach within institutions, with specific efforts focused on local needs, preferences, and workflows. Existing resources offer sparse guidance on selection and operationalization of specific implementation strategies (35), however the checklist developed by Gagliardi et al provides a straightforward approach to implementing guidelines (Table 1) (35).

Successful implementation of transfusion guidelines within a PICU will require a comprehensive approach that involves all key stakeholders within each subspecialty. We encourage participation of a multi-professional team that may include: intensivists, surgeons, anesthesiologists, cardiologists, gastroenterologists, hematologists, oncologists, hospitalists, transfusion specialists, nurses, information technology specialists, patient representatives, hospital executives, and finance and quality personnel (36). Executive sponsorship and support of such efforts may be helpful or necessary to facilitate buy-in and support of providers at each level. While critical care units may select any single implementation strategy or combination of strategies, the intervention should be practical and feasible within the clinical setting. It is also crucial that all subspecialists and stakeholders agree on the guideline prior to implementation (32). Efforts should be made to ensure that both the guidelines and implementation strategy remain flexible and allow for adjustment over time to facilitate continuous improvement. Ongoing education and feedback to providers about the impact of the intervention are likely necessary to sustain positive change over time. Finally, assessment of the effect of implementation efforts may be useful to both determine the impact on transfusion practices and on patient outcomes. Given that many of the TAXI recommendations lack strong evidence, both quality improvement and research initiatives could be used to develop additional evidence around safe and effective blood transfusion in critically ill patients.

TAXI is invested in bringing the existing literature to the bedside and forefront of clinical decision making. To that aim, a formal second stage "TAXI CAB" - Transfusion and Anemia Expertise Initiative - Continuous Assessment of Blood-use is being proposed. We will seek to enhance implementation of the guidelines, follow uptake and impact on practice and patient outcomes, and ensure integration of new clinical evidence into the existing guidelines as it is developed.

Conclusions

Efforts to integrate aspects of implementation into guideline development has ensured that the TAXI guidelines are clear and useful within the context of PICU practice, however a specific and optimal implementation approach has not been identified. The TAXI initiative has developed tools, such as a decision tree, to facilitate implementation, however efforts to fully integrate guidelines into clinical practice will require additional coordinated implementation efforts. A second stage of the TAXI initiative, TAXI CAB will focus on

successful implementation. This will not only ensure that unnecessary transfusion is avoided, but also provide insight into how create and sustain impactful change in the PICU.

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Appendix 1: Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) Members

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Abbreviations

TAXI	Pediatric Critical Care Transfusion and Anemia Expertise Initiative
RBC	Red Blood Cell
PICU	pediatric intensive care unit
ICU	Intensive Care Unit
AFFINITIE	Audit and Feedback Interventions to Increase evidence-based Transfusion practice
Hb	Hemoglobin
CDS	Clinical Decision Support
CI	Confidence Interval
D & I	Dissemination and Implementation
GLIA	Guideline Implementability Appraisal
AHRQ	Agency for Healthcare Research and Quality Review
TAXI CAB	Transfusion and Anemia Expertise Initiative - Continuous Assessment of Blood-use

Table 1
Key Implementation Planning Actions (adapted from Gagilardi et al)

1.	Assemble an implementation planning team
2.	Assemble resources for implementation
3.	Audit baseline practice
4.	Assess local barriers to implementation
5.	Interact with stakeholders to gather contextual information to inform selection of implementation strategies
6.	Develop guideline implementation tools
7.	Prepare an implementation plan with specifications related to strategies, roles, responsibilities, timelines, and process and outcomes measures