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Prehospital Trauma Compendium: Transfusion of Blood Products in Trauma – A Position Statement and Resource Document of NAEMSP

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ABSTRACT

Hemorrhagic shock remains the leading cause of potentially preventable death among injured patients with life-threatening bleeding. Prehospital resuscitation has been evolving with increasing use of blood product resuscitation. The impact of blood administration on patient outcomes remains poorly defined with significant heterogeneity in the quality of literature supporting prehospital blood product resuscitation after trauma. We completed a structured search of the literature using a rapid review framework based on three distinct PICO questions to develop systematic and consensus recommendations.

The National Association of Emergency Medical Services Physicians (NAEMSP) recommends, in EMS agencies/systems that can support a high-quality prehospital blood transfusion program:

- Use of blood components over crystalloids for the first-line treatment of patients with traumatic life-threatening bleeding in the prehospital phase of resuscitation
- Use of low titer group O whole blood (LTOWB) as the first-choice blood product for treatment of patients with traumatic life-threatening bleeding in the prehospital phase of resuscitation
- Use of a combination or composite of prehospital transfusion indications, focused on physiologic abnormalities and/or injury patterns with obvious significant blood loss.
- Use of active monitoring for transfusion-related adverse events.
- Developing a mechanism to recycle unused blood product units nearing their expiration date to a high-use hospital facility to minimize wastage.
- Engaging in a comprehensive longitudinal active collaboration between EMS agencies, trauma centers, and blood suppliers to ensure the success of a prehospital transfusion program.

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Introduction

Hemorrhagic shock from exsanguination is the leading cause of potentially preventable death after trauma (1,2). Prehospital treatment of traumatic hemorrhagic shock has evolved over time, with emphasis on bleeding control and minimizing crystalloid administration (3). Recently, access to prehospital blood product transfusion has expanded. Our objective was to review the literature on prehospital transfusion in the trauma patient and systematically develop recommendations supported by a resource document.

Methods

In collaboration with the National Association of Emergency Medical Services Physicians (NAEMSP) trauma compendium editorial board, our author team identified several content areas of interest regarding the role of prehospital administration of blood products for traumatic hemorrhagic shock. To inform this process, we organized our literature search and evidence review into three content areas:

1. Prehospital blood component transfusion.
2. Prehospital whole blood transfusion.
3. Best practices and outcome monitoring for prehospital transfusion programs.

We developed the three content areas into distinct PICO (Patients, Intervention, Comparison, Outcomes) questions to focus our literature review. The PICO questions were iteratively refined by the authors to ensure we captured important patient-centered outcomes around prehospital transfusion, as well as providing recommendations for prehospital transfusion programs that optimize efficiency and outcomes.

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PICO Questions

We developed the following three PICO questions:

1. In trauma patients with hemorrhagic shock, does the administration of blood products compared to crystalloid improve survival, reduce the need for subsequent transfusion, or improve physiologic measures?
2. In trauma patients with hemorrhagic shock, does the administration of whole blood compared to blood product components improve survival, reduce the need for subsequent transfusion, or improve physiologic measures?
3. For EMS agencies that have a blood product transfusion program, what storage and logistical approaches maximize blood product availability and minimize wastage?

Search Strategy

We performed a rapid review with a structured literature search using guidance developed for the National Association of EMS Physicians Trauma Compendium (4). The search strategy was built to broadly identify literature pertaining to emergency medical services and transfusion. We searched PubMed and OVID for articles published between January 2000 and February 2023. We excluded case reports and literature with non-human subjects as part of the search strategy. Included articles were uploaded to Ryyan software (https://www.rayyan.ai/) and automated duplication removal was applied to create a unique set of articles for manual screening (5) Our full search strategy is available in Appendix 1 (supplementary material).

Screening of Publications

We performed manual screening of titles and abstracts by individual authors using the Rayyan software, with single screening by individual authors divided by year of publication and no overlap. The first author (JBB) selected a random sample of 5% of articles to verify the results of the initial screen. We included articles if they were related to the prehospital transfusion of a blood product and evaluated at least one outcome relevant to any one of the three PICO questions above.

We performed Full-text evaluation of the articles included from the title and abstract screening phase using single review by the individual authors. Articles that were not published in English were excluded at the full-text review phase if an English translation could not be obtained through the University of Pittsburgh Health Services Library. Additional articles could be added by bibliographical review of articles reviewed in full-text.

All final articles included in the review were then grouped by the PICO question they addressed, allowing for an individual article to address more than one PICO question.

Evidence Evaluation

A structured review of the included articles was conducted by all authors, with reporting of the included study details individually in evidence tables as well as in aggregate. Due to resource limitations assessment of bias and grading of evidence from the final text review was not performed. Authors reviewed the study design, description of the study setting, the PICO relevant study population, interventions, and outcomes, as well as overall conclusion of the study in single review for extraction to the evidence tables. From this review we developed systematic recommendations from the evidence for PICO questions 1 and 2, and consensus recommendations for PICO question 3 based on the less structured and diverse outcomes considered. The final recommendations were reviewed by the NAEMSP Standards and Clinical Practices Committee who provided commentary and recommendations for revisions. The authors made appropriate revisions based on that feedback, and the final recommendations were reviewed and approved by the NAEMSP board of directors.

Results

After executing our search strategy, we identified 2,435 PubMed articles and 2,038 OVID articles. Following duplicate removal, we identified 2,420 articles for screening. Second review of a random 5% sample (120 articles) resulted in 10 additional article exclusions and no additional inclusions. The title/abstract screening process resulted in 136 full-text articles for retrieval, with 71 excluded after full text review (Figure 1). One additional article was added based on full-text bibliography review resulting in 66 total articles in the final review. The remainder of the results are presented by PICO question below. Several articles addressed more than one PICO question.

We identified 32 articles that addressed PICO question 1 (Supplemental File Table 1) (6–37) and 6 articles that addressed PICO question 2 (Supplemental File Table 2) (36,38–42), each of which underwent a structured review for the development of systematic recommendations. We identified 37 articles that addressed PICO question 3 that underwent structured review (Supplemental File Table 3) (8,11,12,15,19,25,28,35,42–70) with development of consensus recommendations given the limited evidence, less structured outcomes, and greater heterogeneity for this PICO question. Among the articles addressing PICO question 1, 16 were retrospective cohort studies, 5 were randomized trials, 3 each prospective cohort, meta-analyses, and case-control studies, and one each of a systematic review and secondary analysis of a randomized trial. Among the articles addressing PICO question 2, 4 were retrospective cohort studies, 1 was a randomized trial, and 1 systematic review. Finally, among the articles addressing PICO question 3, 18 were retrospective cohort studies, 6 were cost-effectiveness/economic evaluations, 4 were cases series, 2 were narrative reviews, 1 was a randomized trial, and 6 were various guidelines, program descriptions, or other types of articles.

Discussion

Based on the results above, the following recommendations were developed for each PICO question among EMS agencies/systems that can support a high-quality prehospital blood transfusion program.

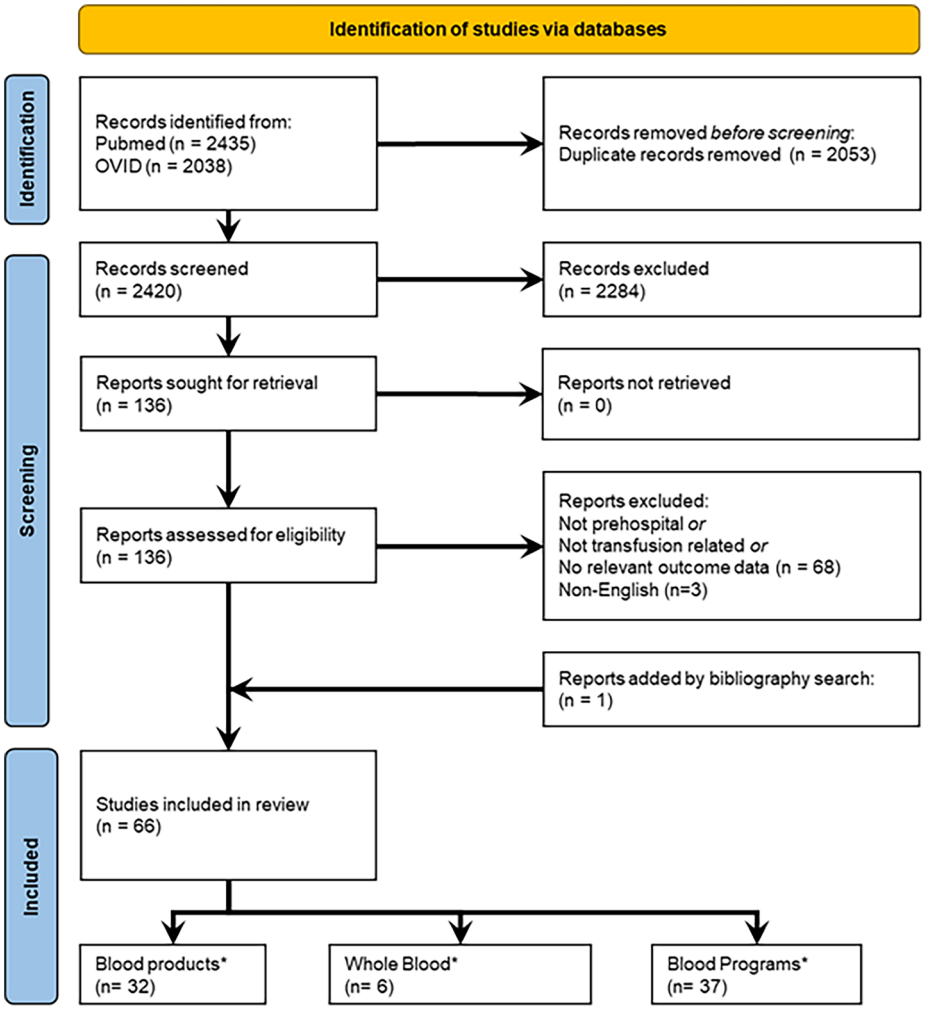


Figure 1. PRISMA flow diagram of literature search results and included articles by PICO question.
*Total number of articles by topic is greater than 66 because several individual studies include information on blood product outcomes and blood program considerations covering more than one PICO (Patients, Intervention, Comparison, Outcomes) question.

Table 1. Suggested indications* for prehospital transfusion in civilian trauma.

- Hemorrhagic shock indicated by:
  - ❖ Systolic blood pressure < 90mmHg *or*
  - ❖ Shock index >1 (e.g. heart rate > systolic blood pressure) *or*
  - ❖ Point of care lactate >4mmol/L
- Major traumatic amputation or limb injury with significant external blood loss requiring tourniquet application
- Penetrating injury to the neck/chest/abdomen/pelvis
- Positive FAST ultrasound for intraperitoneal fluid in the setting of appropriate mechanism of injury

*These criteria represent those in the literature with the strongest and/or most consistent association with need for on-going transfusion requirement. A combination of these criteria or others should be considered in the context of the individual prehospital transfusion program resources for use in a prehospital transfusion protocol. The presence of any one of these criteria has been associated with the need for blood product transfusion..

Prehospital Blood Transfusion versus Usual Care

We Recommend the Use of Blood Components over Crystalloids for the First-Line Treatment of Patients with Traumatic Life-Threatening Bleeding in the Prehospital Phase of Resuscitation

Many crystalloid formulations have non-physiological compositions and they neither carry oxygen nor support hemostasis, but do contribute to acidosis and coagulopathy (71,72). Injured patients who are resuscitated with a large volume of crystalloids have worse outcomes, including higher mortality, compared to patients who received a smaller volume of crystalloids (73–78). Thus, prehospital resuscitation strategies are shifting toward using blood products instead of crystalloids based on military and civilian data.

In the military setting, patients who received red blood cells (RBC), plasma, or a mix of both components before they arrived at a care facility had significantly reduced 24-h mortality (hazard ratio 0.26%, 95% CI:0.08–0.84, $p = 0.02$) and 30-day mortality (hazard ratio 0.39, 95% CI: 0.16–0.92, $p = 0.03$) compared to usual care (32). In fact, this study found that only the transfusions that were administered within the first 15 min after evacuation (median 36 min after injury) were associated with reduced 24-h mortality.

In the civilian setting, the resuscitation with prehospital blood products (RePHILL) randomized controlled trial (RCT) found that the administration of prehospital RBCs and lyophilized plasma to injured patients did not improve in-hospital mortality compared to those who received saline alone. However, despite this study's methodological limitations, including long out-of-hospital times, very high mortality, and nonstandard composite outcome of mortality or

impaired lactate clearance (79), there was a 6% absolute, and a 25% relative risk reduction in 3-h mortality amongst the patients who received prehospital blood products (9). This is likely the more relevant of the two mortality time points when studying the effects of prehospital transfusion (80).

The cluster-randomized trial Prehospital Air Medical Plasma (PAMPer) evaluated outcomes for patients treated by a helicopter air medical service and compared usual care (crystalloid resuscitation plus packed red blood cells if available at the agency) for prehospital trauma resuscitation versus the agency's usual care supplemented with up to two units of plasma. This study found that patients who received plasma first had improved 30-day survival compared to those who received usual care alone (23.2% vs. 33.0%, 95% CI: −18.6 to −1.0%, $p = 0.03$). Secondary analyses of this trial found that the benefit of prehospital plasma transfusion was primarily in those with blunt injuries (30), those with traumatic brain injury and a certain metabolomic endotype (81), and those who were transferred directly from the scene of the accident to the hospital (20). Interestingly, another secondary analysis of PAMPer found that compared to those who received saline alone, injured patients who received both RBCs and plasma had the highest 30-day survival (13). Further, a study that combined data from PAMPer and the randomized Study of Tranexamic Acid during Air and ground Medical Prehospital transport (STAAMP) trial found that for every minute that the provision of prehospital RBC, plasma, or tranexamic acid was delayed, there was a 2% increase in the adjusted odds ratio of 30-day mortality (adjusted odds ratio [aOR] 1.020; 95% CI: 1.006–1.033, $p < 0.01$) (10).

Not all randomized trials have found mortality benefits to prehospital transfusion. A single center randomized trial Control of Major Bleeding After Trauma (COMBAT) that randomized injured patients to receive up to two units of plasma or saline did not find a significant difference in 28-day mortality (15% in the plasma group vs 10% in the saline group, $p = 0.37$). However, there were important differences in the study design and the demographics of the enrolled patients in PAMPer and COMBAT (82) Prehospital time differed between the studies, with PAMPer having a median of 40–42 min and COMBAT a median of 16–19 min, while only 32% of the patients in COMBAT received both plasma units prehospital whereas in PAMPer 84.4% of patients received both plasma units prehospital likely owing to the longer transport times in the latter study. A secondary analysis of both of these studies combined found that when transport times exceeded 20 min, plasma transfusion conferred a survival advantage compared to usual care (crystalloid with or without packed red blood cells) alone (83).

In terms of in-hospital transfusion requirements, none of the RCTs evaluated the number or volume of blood products transfused after the patients arrived at the hospital as a primary outcome. However, when evaluated as secondary outcomes, receipt of prehospital transfusions did not reduce the number of blood products transfused once the patient was in the hospital.

Importantly, none of these studies found an increased risk of adverse clinical events amongst those who received prehospital blood products compared to the patients in the control arm. These studies transfused conventional components, LTOWB was not included in these trials.

Several observational studies have also found improved vital sign and laboratory parameters (11,15), reduced transfusion requirements once hospitalized (7,15,28), shock (7), coagulopathy (6), and prehospital (27) and in-hospital mortality (6,7) following prehospital blood component transfusion. Conversely, not all observational studies found differences in various outcomes including mortality (22,26) and shock (26).

Given the potential for benefit from prehospital transfusion and the absence of a harm signal, we suggest the use of blood components over crystalloids for the first-line treatment of patients with life-threatening bleeding in the prehospital phase of resuscitation, when it is available.

Prehospital Whole Blood versus Component Therapy

We Recommend the Use of Low Titer Group O Whole Blood (LTOWB) as the First-Choice Blood Product for Treatment of Patients with Traumatic Life-Threatening Bleeding in the Prehospital Phase of Resuscitation

Low titer group O whole blood (LTOWB) is collected from type O donors with low titers of anti-A and-B antibodies. Low titer group O whole blood transfusion provides red blood cells, plasma, and platelets in a balanced ratio, which may be more advantageous compared to the use of individual blood components. Additional potential advantages of LTOWB compared to balanced component therapy (e.g., 1:1:1 RBCs to plasma to platelets as described in the PROPPR trial (84), which is unlikely to be available in the prehospital setting) include having a more concentrated product with higher hemoglobin, platelet count, and coagulation factors concentrations due to reduced use of anticoagulant and additive solution. In addition, the platelets in LTOWB may have higher *in vitro* hemostatic function due to cold storage compared to room temperature stored platelets commonly used in component therapy. There is also increased safety due to lower risk of fatal ABO-incompatible hemolytic reactions since the red cells in LTOWB are universally ABO-compatible. Low titer group O whole blood is logistically simpler to allocate and administer than component therapy, reducing the time to effective resuscitation (85). These potential benefits are magnified for prehospital resuscitation of life-threatening bleeding where it is not logistically feasible to provide all blood components. Early data suggest providing LTOWB in a civilian setting is feasible (40).

Several retrospective studies support the use of prehospital LTOWB. Prehospital LTOWB is associated with improved survival to hospital arrival (38), overall 6-h survival upon adjusted analyses, and reduced in-patient transfusion requirement (39). Data suggest that a larger dose of LTOWB relative to the total amount of blood transfused is associated with increased survival, further supporting the hypothesis that LTOWB may be optimal compared to component therapy (42). Data indicate that the association between LTOWB and survival is strengthened in trauma patients with elevated

probability of mortality (86). There are no reports of increased adverse events or safety outcomes with the use of prehospital LTOWB compared to component therapy. One retrospective study that used a leukoreduction filter that removes almost all platelets reported no association with improved survival, which may emphasize the importance of the cold stored platelets within LTOWB units (41). It is important to note that there are no data supporting the use of blood components compared to LTOWB for prehospital treatment of severe bleeding. Ongoing randomized controlled trials will determine the efficacy and safety of LTOWB compared to individual blood components in the prehospital setting. Until these trials are complete, based on biologic rationale, safety, and logistic benefits for LTOWB compared to component therapy, we suggest that LTOWB should be the blood product of choice for life-threatening bleeding in the prehospital phase of resuscitation.

Prehospital Blood Program Best Practices

We Recommend Use of a Combination or Composite of Prehospital Transfusion Indications, Focused on Physiologic Abnormalities and/or Injury Patterns with Obvious Significant Blood Loss

The indications for prehospital transfusion are a key part of any transfusion program; however, there is significant heterogeneity among criteria in the published literature (12,19, 35,45,50,55,57,68,70), with a paucity of robust literature supporting any one single or set of transfusion criteria for field use. Nearly all published transfusion criteria include a systolic blood pressure (SBP) threshold, ranging from <70mmHg to <100mmHg, with most using a typical triage threshold of <90mmHg. Heart rate (HR) thresholds indicating significant tachycardia with thresholds ranging between >110 and >130 beats per minute were also common but often required additional criteria present to trigger transfusion. Shock index criteria are also common with thresholds ranging from 0.9 to 1.3.

Other common criteria included major amputations, largely from military experience, elevated point-of-care lactate with thresholds between >4 and >5mmol/L, positive Focused Assessment with Sonography for Trauma (FAST) ultrasound, as well as penetrating injury. There is evidence that significant hypotension (SBP < 70mmHg), hypotension with tachycardia (SBP < 90 + HR > 108 />130; shock index >0.9), and tourniquet application are associated with trauma-induced coagulopathy, massive transfusion, or the need for ongoing blood product transfusion at the trauma center (45,50). Evaluation of saturation has been undertaking primarily in military settings. One report found an peripheral oxygen saturation (SpO2)<90% as a potential criterion was not predictive of the need for prehospital transfusion (57). Only one article found it useful as part of a prehospital transfusion scoring system as the lowest point value (45), suggesting the evidence is weak for using SpO2 as a transfusion criterion and its role in civilian settings remains uncertain. Table 1 includes a selection of suggested indications for prehospital transfusion to consider in the context of the resources and setting of an individual program.

We Recommend the Use of Active Monitoring for Transfusion Complications or Adverse Events

Monitoring and treating transfusion reactions and other potential adverse events associated with prehospital blood product transfusion is an essential component of robust quality assurance with detailed documentation. Emergency medical service agencies should have protocols in place to manage potential adverse events, clear guidelines directing when to halt transfusions for serious reactions, and follow-up procedures with the blood supplier and receiving hospital.

The literature documents a very low adverse event rate over thousands of cumulative prehospital transfusions across several blood products including red blood cells, plasma, freeze dried plasma, and LTOWB, suggesting prehospital transfusion programs are safe (11,28, 35,42, 48,61, 62,64,66).

We Recommend Developing a Mechanism to Recycle Unused Blood Product Units Nearing Their Expiration Date to a High-Use Hospital Facility to Minimize Wastage

Minimizing wastage of precious and limited blood supply is essential to a prehospital transfusion program. Most successful programs developed procedures to return blood products as they near the end of their life cycle to a hospital blood bank for immediate use in operating rooms, intensive car e units (ICU), or other transfusion needs. Identifying a high-use facility such as the regional trauma center increases the chance the blood product will be used prior to expiration, but having multiple options to locally recycle units may be desirable for more rural programs that are farther from a tertiary trauma center.

Integrating these procedures with restock locations is also important to ensure a stable supply for the prehospital program. Using products with a longer shelf life, such as liquid plasma over thawed plasma, can reduce wastage and minimize logistic burden of recycling as well as costs (43). Developing a reliable protocol for recycling or exchanging units can lead to low wastage rates of 1–2% annually or even lower in some programs (11,15, 28,53, 60,62–64, 66,70). This is on par with in-hospital wastage rates between 1 and 1.6% at trauma centers for red blood cells and plasma (87).

We Recommend Engaging in a Comprehensive Longitudinal Active Collaboration between EMS Agencies, Trauma Centers, and Blood Suppliers to Ensure the Success of a Prehospital Transfusion Program

Several successful prehospital transfusion programs have been described in the literature (53,56, 63,68,70). A common thread among these was a strong and ongoing collaboration between the EMS agency and blood supplier with buy-in from all stakeholders to make the program successful. Essential considerations in the relationship are the type(s) of blood products that will be available for use in the prehospital environment, how the blood will be supplied to the field, the model of deployment (carried by EMS units versus picked up from a depot), resupply/re-stock logistics when units are transfused, supply sustainability considerations, health equity, recycle options for expiring units, and storage/transport consideration.

Commercially available thermal insulation transport coolers can maintain blood products at safe temperatures across a variety of ambient temperatures in the field with minimal impact on blood product quality and biochemistry (46,47, 59,65,67). A robust quality assurance program engaging multiple stakeholders is essential to monitor appropriate use, storage, monitor wastage, adverse events, temperature audits, and ongoing competency based training for EMS clinicians providing transfusion (51,53). A collaborative model can result in an economically feasible prehospital transfusion program (44,54, 58,63), translating to a highly cost-effective intervention (52).

Considerations for Implementation

Implementation of these recommendations must consider the clinical, logistical, regulatory, and financial burdens of initiating and maintaining a prehospital blood program. Deploying blood products over crystalloid is dependent on identifying a population of trauma patients that will consistently benefit from the intervention. Which EMS units will carry blood will vary between and within EMS agencies in most cases, particularly for ground-based programs, due to limitations in supply and challenges in storing blood products. Since these blood carrying units cannot be dispatched to every potential trauma call, the role dispatch plays in the success of a prehospital transfusion program is essential and must depend on appropriate dispatch evaluation and response-code determination in patients most likely to require blood transfusion on scene. Working with national standard-setting dispatch organizations to incorporate reliable, protocol-based evaluation and response coding processes for the most accurate identification of cases likely needing blood-carrying emergency units for initial response will be important for successful scaling of prehospital transfusion programs.

Best practices for sourcing, cold-chain maintenance, and delivering blood in the field are necessary for practical and safe administration at scale. Maintaining adequate blood supply given the necessarily increased demand is also critical and may be facilitated through novel blood donation recruitment strategies such as "Brothers in Arms" (70). Recycling programs are critical for the sustainability of blood resources. Financial incentives for EMS agencies to administer blood products must also be aligned to remunerate agencies for the additional costs of product, equipment for administration, cold-chain maintenance, and ongoing training. The commitment must also consider health equity, ensuring that communities with more disadvantaged socioeconomic circumstances have access to prehospital transfusion when indicated as well. Community engagement is also an important consideration for faith based groups that may not accept blood product transfusion such as Jehovah's Witnesses, as well as addressing concerns about the risk of hemolytic disease of the fetus and newborn (HDFN), which is generally considered a low-risk event (88,89).

An individual EMS agency that is considering implementing a prehospital transfusion program must consider several potential facilitators and barriers. Important facilitators include strong buy-in from EMS clinicians and from regional trauma system stakeholders such as trauma centers and blood banking/supply organizations. Management of clinician perceptions and facilitation of EMS clinician buy-in might be enabled by providing targeted education about the potential benefits and rationale of prehospital transfusion for trauma patients, with focus on the relative advantages of transfusion over IV-crystalloid-centered therapies. It is also necessary to achieve buy-in from local or regional blood supply organizations, so they are willing to invest the resources to establish and maintain a steady supply of blood products. This can be a particularly difficult barrier in some locales and providing education on the benefits to patients as well as example cost and supply models from other blood banking systems as potential solutions may help overcome these. Emergency medical service agencies will need to enlist local trauma system leadership to develop allies and sponsorship of EMS transfusion programs. Further, a committed EMS medical director with active and direct involvement in all aspects of program monitoring is also key to implementing and maintaining a successful prehospital transfusion program.

Barriers to implementation may include costs, particularly startup cost to obtain fixed equipment. Enlisting allies in the larger EMS and trauma system and seeking out potential grant programs may help defray startup costs. Legislation or other local rule of government that prohibits or does not expressly allow for prehospital transfusion may also be a barrier in some locations. Partnering with trauma system allies through advocacy at state, regional, or local levels may be necessary to help launch a prehospital transfusion program.

Each EMS agency and system will certainly face unique facilitators and barriers to prehospital transfusion programs; however, many of these elements have been encountered by other EMS agencies that have led the innovation of prehospital blood transfusion programs. Active communication and knowledge sharing with successful programs can be invaluable to gain insight regarding how other programs overcame initial challenges and how they sustained their program over time. Finally, EMS agencies that do choose to employ a prehospital blood transfusion program should be actively engaged in well-designed prospective research to rigorously evaluate the outcomes of blood transfusion in the prehospital environment in conjunction with the local institutional review board and other potential research partners.

Limitations

There are several limitations to this document. We performed a structured review of two medical literature databases with limitations on the time period and language that may not capture the entire breadth of relevant literature. Literature on this topic is rapidly evolving at a high rate. However, this document is as up to date as is possible.

We performed single screening and full-text extraction with only limited double screening sampling which may produce different inclusions or exclusions of articles if double screening and extraction was employed. We also did not

perform formal risk of bias assessment nor grading of the strength of literature in developing our recommendations.

Conclusion

Among trauma patients with hemorrhagic shock, there is evidence in support of the shift of prehospital resuscitation strategies toward blood product use when such resources are available. While much of the literature supporting this change in practice is retrospective with limitations, the existing evidence suggests there is an early mortality benefit with a reduction in total transfusion requirements when prehospital blood product resuscitation is employed. Importantly, these benefits are realized without risk of increased adverse events. For these reasons we recommend use of blood components over crystalloids and suggest LTOWB as the preferred transfusion product for the first-line prehospital treatment of patients with life-threatening bleeding and/or hemorrhagic shock. A multidisciplinary approach involving multiple trauma system stakeholders, with well-defined indications, active monitoring/quality assurance, and planned recycling of products to reduce wastage are essential components of a robust and sustainable prehospital transfusion program.

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Authorship Statement

JBB, CMG, FXG conceived of the project with the oversight of the NAEMSP Trauma Compendium editorial board. JBB, CMG, FXG developed the plan for literature review and evidence extraction. All authors assume full responsibility for the collection and integrity of the data. All authors participated in the evidence extraction, data analysis, and development of the clinical practice guideline. JBB, CMG, FXG, MHY, and PCS wrote the initial draft of the manuscript. All authors participated in editing the manuscript for critical intellectual content. All authors assume full responsibility for the entire content of the manuscript.

Declaration of Generative AI in Scientific Writing

The authors did not use a generative artificial intelligence (AI) tool or service to assist with preparation or editing of this work. The author(s) take full responsibility for the content of this publication.

External Review

This document was created solely by NAEMSP and was not subject to review by external parties.

Updating Procedure

Pursuant to NAEMSP Standards & Clinical Practices Committee procedures and practices, this position statement and resource document will be reviewed and updated five years after its publication. Applicable NAEMSP review and revision practices that are current at the time of the review will be followed. At a minimum the review process should include a search and synthesis of any new and relevant evidence that is published since the printing of this document.

Disclosure Statement

The authors report there are no competing interests to declare.

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References

1. Davis JS, Satahoo SS, Butler FK, Dermer H, Naranjo D, Julien K, Van Haren RM, Namias N, Blackbourne LH, Schulman CI. An analysis of prehospital deaths: Who can we save? J Trauma Acute Care Surg. 2014;77(2):213–8. doi:10.1097/TA.0000000000000292.
2. Eastridge BJ, Hardin M, Cantrell J, Oetjen-Gerdes L, Zubko T, Mallak C, Wade CE, Simmons J, Mace J, Mabry R, et al. Died of wounds on the battlefield: causation and implications for improving combat casualty care. J Trauma. 2011;71(1 Suppl):S4–S8. doi:10.1097/TA.0b013e318221147b.
3. Berry C, Gallagher JM, Goodloe JM, Dorlac WC, Dodd J, Fischer PE. Prehospital hemorrhage control and treatment by Clinicians: a joint position statement. Prehosp Emerg Care. 2023;27(5):544–51. doi:10.1080/10903127.2023.2195487.
4. Martin-Gill C, Lyng JW. Methodology for evidence evaluation and reporting of the NAEMSP trauma compendium position statements. Prehosp Emerg Care. 2024;28(4):660–5. doi:10.1080/10903127.2024.2329217.
5. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan – a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):210. doi:10.1186/s13643-016-0384-4.
6. Brown JB, Cohen MJ, Minei JP, Maier RV, West MA, Billiar TR, Peitzman AB, Moore EE, Cuschieri J, Sperry JL. Pretrauma center red blood cell transfusion is associated with reduced mortality and coagulopathy in severely injured patients with blunt trauma. Ann Surg. 2015;261(5):997–1005. doi:10.1097/SLA.0000000000000674.
7. Brown JB, Sperry JL, Fombona A, Billiar TR, Peitzman AB, Guyette FX. Pre-trauma center red blood cell transfusion is associated with improved early outcomes in air medical trauma patients. J Am Coll Surg. 2015;220(5):797–808. doi:10.1016/j.jamcollsurg.2015.01.006.
8. Clements T, McCoy C, Assen S, Cardenas J, Wade C, Meyer D, Cotton BA. The prehospital use of younger age whole blood is associated with an improved arrival coagulation profile. J Trauma Acute Care Surg. 2021;90(4):607–14. doi:10.1097/TA.0000000000003058.
9. Crombie N, Doughty HA, Bishop JRB, Desai A, Dixon EF, Hancox JM, Herbert MJ, Leech C, Lewis SJ, Nash MR, et al. Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial. Lancet Haematol. 2022;9(4):e250–e61. doi:10.1016/S2352-3026(22)00040-0.
10. Deeb AP, Guyette FX, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Eastridge BJ, Joseph B, Nirula R, et al. Time to early resuscitative intervention association with mortality in trauma patients at risk for hemorrhage. J Trauma Acute Care Surg. 2023;94(4):504–12. doi:10.1097/TA.0000000000003820.
11. Greene A, Vu EN, Archer T, Norman S, Trojanowski J, Shih AW. A service evaluation of prehospital blood transfusion by critical

care paramedics in British Columbia, Canada. Air Med J. 2021;40(6):441–5. doi:10.1016/j.amj.2021.07.004.
12. Griggs JE, Jeyanathan J, Joy M, Russell MQ, Durge N, Bootland D, Dunn S, Sausmarez ED, Wareham G, Weaver A, et al. Mortality of civilian patients with suspected traumatic haemorrhage receiving pre-hospital transfusion of packed red blood cells compared to pre-hospital crystalloid. Scand J Trauma Resusc Emerg Med. 2018;26(1):100. doi:10.1186/s13049-018-0567-1.
13. Guyette FX, Sperry JL, Peitzman AB, Billiar TR, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Putnam T, Duane TM, et al. Prehospital blood product and crystalloid resuscitation in the severely injured patient: a secondary analysis of the prehospital air medical plasma trial. Ann of Surg. 2021;273(2):358–64.
14. Henriksen HH, Rahbar E, Baer LA, Holcomb JB, Cotton BA, Steinmetz J, Ostrowski SR, Stensballe J, Johansson PI, Wade CE. Pre-hospital transfusion of plasma in hemorrhaging trauma patients independently improves hemostatic competence and acidosis. Scand J Trauma Resusc Emerg Med. 2016;24(1):145. doi:10.1186/s13049-016-0327-z.
15. Holcomb JB, Donathan DP, Cotton BA, Del Junco DJ, Brown G, Wenckstern TV, Podbielski JM, Camp EA, Hobbs R, Bai Y, et al. Prehospital transfusion of plasma and red blood cells in trauma patients. Prehosp Emerg Care. 2015;19(1):1–9. doi:10.3109/10903127.2014.923077.
16. Holcomb JB, Swartz MD, DeSantis SM, Greene TJ, Fox EE, Stein DM, Bulger EM, Kerby JD, Goodman M, Schreiber MA, et al. Multicenter observational prehospital resuscitation on helicopter study. J Trauma Acute Care Surg. 2017;83(1 Suppl 1):S83–S91. doi:10.1097/TA.0000000000001484.
17. Howard JT, Kotwal RS, Santos-Lazada AR, Martin MJ, Stockinger ZT. Reexamination of a battlefield trauma golden hour policy. J Trauma Acute Care Surg. 2018;84(1):11–8. doi:10.1097/TA.0000000000001727.
18. Huang GS, Dunham CM. Mortality outcomes in trauma patients undergoing prehospital red blood cell transfusion: a systematic literature review. Int J Burn Trauma. 2017;7(2):17–26.
19. Kim BD, Zielinski MD, Jenkins DH, Schiller HJ, Berns KS, Zietlow SP. The effects of prehospital plasma on patients with injury: a prehospital plasma resuscitation. J Trauma Acute Care Surg. 2012;73(2 Suppl 1):S49–S53. doi:10.1097/TA.0b013e31826060ff.
20. Lewis RE, Muluk SL, Reitz KM, Guyette FX, Brown JB, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Yazer MH, et al. Prehospital plasma is associated with survival principally in patients transferred from the scene of injury: a secondary analysis of the PAMPer trial. Surgery. 2022;172(4):1278–84. doi:10.1016/j.surg.2022.04.039.
21. Mena-Munoz J, Srivastava U, Martin-Gill C, Suffoletto B, Callaway CW, Guyette FX. Characteristics and outcomes of blood product transfusion during critical care transport. Prehosp Emerg Care. 2016;20(5):586–93. doi:10.3109/10903127.2016.1163447.
22. Miller BT, Du L, Krzyzaniak MJ, Gunter OL, Nunez TC. Blood transfusion: in the air tonight? J Trauma Acute Care Surg. 2016;81(1):15–20. doi:10.1097/TA.0000000000001045.
23. Moore HB, Moore EE, Chapman MP, McVaney K, Bryskiewicz G, Blechar R, Chin T, Burlew CC, Pieracci F, West FB, et al. Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial. Lancet. 2018;392(10144):283–91. doi:10.1016/S0140-6736(18)31553-8.
24. O'Reilly DJ, Morrison JJ, Jansen JO, Apodaca AN, Rasmussen TE, Midwinter MJ. Prehospital blood transfusion in the en route management of severe combat trauma: a matched cohort study. J Trauma Acute Care Surg. 2014;77(3 Suppl 2):S114–S20. doi:10.1097/TA.0000000000000328.
25. Oakeshott JE, Griggs JE, Wareham GM, Lyon RM. Feasibility of prehospital freeze-dried plasma administration in a UK Helicopter Emergency Medical Service. Eur J Emerg Med. 2019;26(5):373–8. doi:10.1097/MEJ.0000000000000585.
26. Peters JH, Smulders PSH, Moors XRJ, Bouman SJM, Meijs C, Hoogerwerf N, Edwards MJR. Are on-scene blood transfusions by a helicopter emergency medical service useful and safe? A multicentre case-control study. Eur J Emerg Med. 2019;26(2):128–32. doi:10.1097/MEJ.0000000000000516.
27. Rehn M, Weaver A, Brohi K, Eshelby S, Green L, Røislien J, Lockey DJ. Effect of prehospital red blood cell transfusion on mortality and time of death in civilian trauma patients. Shock. 2019;51(3):284–8. doi:10.1097/SHK.0000000000001166.
28. Rehn M, Weaver AE, Eshelby S, Røislien J, Lockey DJ. Pre-hospital transfusion of red blood cells in civilian trauma patients. Transfus Med. 2018;28(4):277–83. doi:10.1111/tme.12483.
29. Reitz KM, Gruen DS, Guyette F, Brown JB, Yazer MH, Vodovotz Y, Johanssen PI, Stensballe J, Daley B, Miller RS, et al. Age of thawed plasma does not affect clinical outcomes or biomarker expression in patients receiving prehospital thawed plasma: a PAMPer secondary analysis. Trauma Surg Acute Care Open. 2021;6(1):e000648. doi:10.1136/tsaco-2020-000648.
30. Reitz KM, Moore HB, Guyette FX, Sauaia A, Pusateri AE, Moore EE, Hassoune A, Chapman MP, Daley BJ, Miller RS, et al. Prehospital plasma in injured patients is associated with survival principally in blunt injury: results from two randomized prehospital plasma trials. J Trauma Acute Care Surg. 2020;88(1):33–41. doi:10.1097/TA.0000000000002485.
31. Rijnhout TWH, Wever KE, Marinus R, Hoogerwerf N, Geeraedts LMG, Jr., Tan E. Is prehospital blood transfusion effective and safe in haemorrhagic trauma patients? A systematic review and meta-analysis. Injury. 2019;50(5):1017–27. doi:10.1016/j.injury.2019.03.033.
32. Shackelford SA, Del Junco DJ, Powell-Dunford N, Mazuchowski EL, Howard JT, Kotwal RS, Gurney J, Butler FK, Jr., Gross K, Stockinger ZT. Association of prehospital blood product transfusion during medical evacuation of combat casualties in Afghanistan with acute and 30-day survival. Jama. 2017;318(16):1581–91. doi:10.1001/jama.2017.15097.
33. Shirek G, Phillips R, Shahi N, Pickett K, Meier M, Recicar J, Moulton SL. To give or not to give? Blood for pediatric trauma patients prior to pediatric trauma center arrival. Pediatr Surg Int. 2022;38(2):285–93. doi:10.1007/s00383-021-05015-9.
34. Smith IM, James RH, Dretzke J, Midwinter MJ. Prehospital blood product resuscitation for trauma: a systematic review. Shock. 2016;46(1):3–16. doi:10.1097/SHK.0000000000000569.
35. Sperry JL, Guyette FX, Brown JB, Yazer MH, Triulzi DJ, Early-Young BJ, Adams PW, Daley BJ, Miller RS, Harbrecht BG, et al. Prehospital plasma during air medical transport in trauma patients at risk for hemorrhagic shock. N Engl J Med. 2018;379(4):315–26. doi:10.1056/NEJMoa1802345.
36. Strauss R, Menchetti I, Perrier L, Blondal E, Peng H, Sullivan-Kwantes W, Tien H, Nathens A, Beckett A, Callum J, et al. Evaluating the Tactical Combat Casualty Care principles in civilian and military settings: systematic review, knowledge gap analysis and recommendations for future research. Trauma Surg Acute Care Open. 2021;6(1):e000773. doi:10.1136/tsaco-2021-000773.
37. Van Dijck CP, Stansbury LG, Latimer AJ, Butler EK, Nathwani R, Wall J, Utarnachitt RB, Vavilala MS, Hess JR. Hemostatic resuscitation of pediatric trauma patients during air medical transport: a retrospective matched cohort study. Air Med J. 2021;40(5):344–9. doi:10.1016/j.amj.2021.04.004.
38. Braverman MA, Smith A, Pokorny D, Axtman B, Shahan CP, Barry L, Corral H, Jonas RB, Shiels M, Schaefer R, et al. Prehospital whole blood reduces early mortality in patients with hemorrhagic shock. Transfusion. 2021;61(Suppl 1):S15–S21. doi:10.1111/trf.16528.
39. Gurney JM, Staudt AM, Del Junco DJ, Shackelford SA, Mann-Salinas EA, Cap AP, Spinella PC, Martin MJ. Whole blood at the tip of the spear: a retrospective cohort analysis of warm fresh whole blood resuscitation versus component therapy in severely injured combat casualties. Surgery. 2022;171(2):518–25. doi:10.1016/j.surg.2021.05.051.
40. Guyette FX, Zenati M, Triulzi DJ, Yazer MH, Skroczky H, Early BJ, Adams PW, Brown JB, Alarcon L, Neal MD, et al. Prehospital low titer group O whole blood is feasible and safe: results of a prospective randomized pilot trial. J Trauma Acute Care Surg. 2022;92(5):839–47. doi:10.1097/TA.0000000000003551.
41. Tucker H, Brohi K, Tan J, Aylwin C, Bloomer R, Cardigan R, Davenport R, Davies ED, Godfrey P, Hawes R, et al. Association of red blood cells and plasma transfusion versus red blood cell

transfusion only with survival for treatment of major traumatic hemorrhage in prehospital setting in England: a multicenter study. Crit Care. 2023;27(1):25. doi:10.1186/s13054-022-04279-4.
42. Williams J, Merutka N, Meyer D, Bai Y, Prater S, Cabrera R, Holcomb JB, Wade CE, Love JD, Cotton BA. Safety profile and impact of low-titer group O whole blood for emergency use in trauma. J Trauma Acute Care Surg. 2020;88(1):87–93. doi:10.1097/TA.0000000000002498.
43. Adams PW, Warren KA, Guyette FX, Yazer MH, Brown JB, Daily BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, et al. Implementation of a prehospital air medical thawed plasma program: Is it even feasible? J Trauma Acute Care Surg. 2019;87(5):1077–81. doi:10.1097/TA.0000000000002406.
44. Addams J, Arbabi S, Bulger EM, Stansbury LG, Tuott EE, Hess JR. How we built a hospital-based community whole blood program. Transfusion. 2022;62(9):1699–705. doi:10.1111/trf.17018.
45. Avital G, Gelikas S, Radomislensky I, Tsur AM, Sorkin A, Shinar E, Bodas M, Yazer MH, Cap AP, Chen J, et al. A prehospital scoring system for predicting the need for emergent blood product transfusion. Transfusion. 2021;61(Suppl 1):S195–S205. doi:10.1111/trf.16529.
46. Bjerkvig C, Sivertsen J, Braathen H, Lunde THF, Strandenes G, Assmus J, Hervig T, Cap A, Kristoffersen EK, Fosse T, et al. Cold-stored whole blood in a Norwegian emergency helicopter service: an observational study on storage conditions and product quality. Transfusion. 2020;60(7):1544–51. doi:10.1111/trf.15802.
47. Boecker C, Sitzmann N, Halblaub Miranda JL, Suhr H, Wiedemann P, Bieback K, Rudolph M, Klüter H. Noninferior red cell concentrate quality after repeated air rescue mission transport for prehospital transfusion. Transfus Med Hemother. 2022;49(3):172–9. doi:10.1159/000520650.
48. Brill JB, Mueck KM, Tang B, Sandoval M, Cotton ME, Cameron McCoy C, Cotton BA. Is Low-Titer Group O whole blood truly a universal blood product? J Am Coll Surg. 2023;236(3):506–13.
49. Chen J, Benov A, Nadler R, Darlington DN, Cap AP, Lipsky AM, Glassberg E. Prehospital Blood transfusion during aeromedical evacuation of trauma patients in Israel: the IDF CSAR experience. Mil Med. 2017;182(S1):47–52. doi:10.7205/MILMED-D-16-00081.
50. David JS, Voiglio EJ, Cesareo E, Vassal O, Decullier E, Gueugniaud PY, Peyrefitte S, Tazarourte K. Prehospital parameters can help to predict coagulopathy and massive transfusion in trauma patients. Vox Sang. 2017;112(6):557–66. doi:10.1111/vox.12545.
51. Gehrie EA, Szklarski PC, Nooner K, Booth GS. Storage age of RBCs transfused by a prehospital patient transport program vs the hospital emergency department. Am J Clin Pathol. 2019;152(4):537–41. doi:10.1093/ajcp/aqz071.
52. Hrebinko KA, Sperry JL, Guyette FX, Brown JB, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Neal MD, et al. Evaluating the cost-effectiveness of prehospital plasma transfusion in unstable trauma patients: a secondary analysis of the PAMPer Trial. JAMA Surg. 2021;156(12):1131–9. doi:10.1001/jamasurg.2021.4529.
53. Krook C, O'Dochartaigh D, Martin D, Piggott Z, Deedo R, Painter S, van Werkhoven G, McKay D, Nesdoly D, Armstrong JN. Blood on board: the development of a prehospital blood transfusion program in a Canadian helicopter emergency medical service. CJEM. 2019;21(3):365–73. doi:10.1017/cem.2018.457.
54. Latimer A, Utarnachitt RB, Tuott EE, Hess JR. Economical provision of blood components for critical patient transport across a large geographic area. Transfusion. 2021;61(5):1435–8. doi:10.1111/trf.16315.
55. Le Clerc S, McLennan J, Kyle A, Mann-Salinas EA, Russell RJ. Predicting when to administer blood products during tactical aeromedical evacuation: evaluation of a US Model. J Spec Oper Med. 2014;14(4):48–52. doi:10.55460/HSMR-SMBF.
56. Levin D, Zur M, Shinar E, Moshe T, Tsur AM, Nadler R, Yazer MH, Epstein D, Avital G, Gelikas S, et al. Low-Titer Group O whole-blood resuscitation in the prehospital setting in Israel: review of the First 2.5 years' experience. Transfus Med Hemother. 2021;48(6):342–9. doi:10.1159/000519623.
57. Malsby RF, 3rd, Quesada J, Powell-Dunford N, Kinoshita R, Kurtz J, Gehlen W, Adams C, Martin D, Shackelford S. Prehospital blood product transfusion by U.S. army MEDEVAC during combat operations in Afghanistan: a process improvement initiative. Mil Med. 2013;178(7):785–91. doi:10.7205/MILMED-D-13-00047.
58. Mapp JG, Bank EA, Osborn LA, Stringfellow ML, Reininger DW, Winckler CJ, Prehospital R. Epidemiological and accounting analysis of ground ambulance whole blood transfusion. Prehosp Disaster Med. 2020;35(1):98–103. doi:10.1017/S1049023X1900517X.
59. Martin SM, Fisher AD, Meledeo MA, Wampler D, Nicholson SE, Raczek K, April MD, Weymouth WL, Bynum J, Schauer SG. More sophisticated than a drink cooler or an old sphygmomanometer but still not adequate for prehospital blood: a market review of commercially available equipment for prehospital blood transport and administration. Transfusion. 2021;61(Suppl 1):S286–S293. doi:10.1111/trf.16461.
60. McCullagh J, Proudlove N, Tucker H, Davies J, Edmondson D, Lancut J, Maddison A, Weaver A, Davenport R, Green L. Making every drop count: reducing wastage of a novel blood component for transfusion of trauma patients. BMJ Open Qual. 2021;10(3):e001396. doi:10.1136/bmjoq-2021-001396.
61. Nadler R, Mozer-Glassberg Y, Gaines B, Glassberg E, Chen J. The Israel Defense Forces experience with freeze-dried plasma for the resuscitation of traumatized pediatric patients. J Trauma Acute Care Surg. 2019;87(6):1315–20. doi:10.1097/TA.0000000000002477.
62. Raitt J, Curry N, Lewis P, Dearman J, Poole K, Surendra Kumar D. Developing clinical performance indicators for pre-hospital blood transfusion: the Thames Valley Air Ambulance approach. Transfus Med. 2020;30(2):134–40. doi:10.1111/tme.12668.
63. Sayre MR, Yang BY, Murphy DL, Counts CR, Dang M, Ubaldi P, Tuott EE, Hess JR. Providing whole blood for an urban paramedical ambulance system. Transfusion. 2022;62(1):82–6. doi:10.1111/trf.16749.
64. Schaefer R, Long T, Wampler D, Summers R, Epley E, Waltman E, Eastridge B, Jenkins D. Operationalizing the deployment of low-titer o-positive whole blood within a regional trauma system. Mil Med. 2021;186(Suppl 1):391–9. doi:10.1093/milmed/usaa283.
65. Selleng K, Baschin M, Henkel B, Jenichen G, Thies KC, Rudolph M, Reifferscheid F, Braun J, Hannich M, Winter T, et al. Blood product supply for a helicopter emergency medical service. Transfus Med Hemother. 2021;48(6):332–41. doi:10.1159/000519825.
66. Shand S, Curtis K, Dinh M, Burns B. Prehospital blood transfusion in New South Wales, Australia: a retrospective cohort study. Prehosp Emerg Care. 2021;25(3):404–11. doi:10.1080/10903127.2020.1769781.
67. Smith H, Doughty H, Bishop J, Herbert M, Nash M. Temperature mapping in an air ambulance helicopter: implications for the delivery of pre-hospital transfusion. Transfusion. 2021;61(Suppl 1):S206–S213. doi:10.1111/trf.16517.
68. Weymouth W, Long B, Koyfman A, Winckler C. Whole Blood in trauma: a review for emergency clinicians. J Emerg Med. 2019;56(5):491–8. doi:10.1016/j.jemermed.2019.01.024.
69. Wheeler R, von Recklinghausen FM, Brozen R. Blood administration in helicopter emergency medical services patients associated with hypothermia. Air Med J. 2013;32(1):47–51. doi:10.1016/j.amj.2012.02.001.
70. Zhu CS, Pokorny DM, Eastridge BJ, Nicholson SE, Epley E, Forcum J, Long T, Miramontes D, Schaefer R, Shiels M, et al. Give the trauma patient what they bleed, when and where they need it: establishing a comprehensive regional system of resuscitation based on patient need utilizing cold-stored, low-titer O+whole blood. Transfusion. 2019;59(S2):1429–38. doi:10.1111/trf.15264.
71. Blumberg N, Cholette JM, Pietropaoli AP, Phipps R, Spinelli SL, Eaton MP, Noronha SA, Seghatchian J, Heal JM, Refaai MA. 0.9% NaCl (Normal Saline) - Perhaps not so normal after all? Transfus Apher Sci. 2018;57(1):127–31. doi:10.1016/j.transci.2018.02.021.
72. Feinman M, Cotton BA, Haut ER. Optimal fluid resuscitation in trauma: type, timing, and total. Curr Opin Crit Care. 2014;20(4):366–72. doi:10.1097/MCC.0000000000000104.
73. Edwards MJ, Lustik MB, Clark ME, Creamer KM, Tuggle D. The effects of balanced blood component resuscitation and crystalloid administration in pediatric trauma patients requiring transfusion in Afghanistan and Iraq 2002 to 2012. J Trauma Acute Care Surg. 2015;78(2):330–5. doi:10.1097/TA.0000000000000469.
74. Young JB, Utter GH, Schermer CR, Galante JM, Phan HH, Yang Y, Anderson BA, Scherer LA. Saline versus Plasma-Lyte A in initial

resuscitation of trauma patients: a randomized trial. Ann Surg. 2014;259(2):255–62. doi:10.1097/SLA.0b013e318295feba.
75. Ley EJ, Clond MA, Srour MK, Barnajian M, Mirocha J, Margulies DR, Salim A. Emergency department crystalloid resuscitation of 1.5 L or more is associated with increased mortality in elderly and nonelderly trauma patients. J Trauma. 2011;70(2):398–400. doi:10.1097/TA.0b013e318208f99b.
76. Harada MY, Ko A, Barmparas G, Smith EJ, Patel BK, Dhillon NK, Thomsen GM, Ley EJ. 10-Year trend in crystalloid resuscitation: reduced volume and lower mortality. Int J Surg. 2017;38:78–82. doi:10.1016/j.ijsu.2016.12.073.
77. Neal MD, Hoffman MK, Cuschieri J, Minei JP, Maier RV, Harbrecht BG, Billiar TR, Peitzman AB, Moore EE, Cohen MJ, et al. Crystalloid to packed red blood cell transfusion ratio in the massively transfused patient: when a little goes a long way. J Trauma Acute Care Surg. 2012;72(4):892–8. doi:10.1097/TA.0b013e31823d84a7.
78. Bickell WH, Wall MJ, Jr., Pepe PE, Martin RR, Ginger VF, Allen MK, Mattox KL. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med. 1994;331(17):1105–9. doi:10.1056/NEJM199410273311701.
79. Yazer MH, Cap AP, Glassberg E, Green L, Holcomb JB, Khan MA, Moore EE, Neal MD, Perkins GD, Sperry JL, et al. Toward a more complete understanding of who will benefit from prehospital transfusion. Transfusion. 2022;62(8):1671–9. doi:10.1111/trf.17012.
80. Holcomb JB, Moore EE, Sperry JL, Jansen JO, Schreiber MA, Del Junco DJ, Spinella PC, Sauaia A, Brohi K, Bulger EM, et al. Evidence-based and clinically relevant outcomes for hemorrhage control trauma trials. Ann Surg. 2021;273(3):395–401. doi:10.1097/SLA.0000000000004563.
81. Wu J, Cyr A, Gruen DS, Lovelace TC, Benos PV, Das J, Kar UK, Chen T, Guyette FX, Yazer MH, et al. Lipidomic signatures align with inflammatory patterns and outcomes in critical illness. Nat Commun. 2022;13(1):6789. doi:10.1038/s41467-022-34420-4.
82. Jackson BP, Sperry JL, Yazer MH. Prehospital plasma transfusion: What does the literature show? Transfus Med Hemother. 2021;48(6):358–65. doi:10.1159/000519627.
83. Pusateri AE, Moore EE, Moore HB, Le TD, Guyette FX, Chapman MP, Sauaia A, Ghasabyan A, Chandler J, McVaney K, et al. Association of prehospital plasma transfusion with survival in trauma patients with hemorrhagic shock when transport times are longer than 20 minutes: a post hoc analysis of the PAMPer and COMBAT clinical trials. JAMA Surg. 2020;155(2):e195085. doi:10.1001/jamasurg.2019.5085.
84. Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, del Junco DJ, Brasel KJ, Bulger EM, Callcut RA, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. Jama. 2015;313(5):471–82. doi:10.1001/jama.2015.12.
85. Yazer MH, Cap AP, Spinella PC. Raising the standards on whole blood. J Trauma Acute Care Surg. 2018;84(6S Suppl 1):S14–S17. doi:10.1097/TA.0000000000001778.
86. Sperry JL, Cotton BA, Luther JF, Cannon JW, Schreiber MA, Moore EE, Namias N, Minei JP, Wisniewski SR, Guyette FX. Whole blood resuscitation and association with survival in injured patients with an elevated probability of mortality. J Am Coll Surg. 2023;237(2):206–19. doi:10.1097/XCS.0000000000000708.
87. Dunbar NM, Olson NJ, Szczepiorkowski ZM, Martin ED, Tysarcyk RM, Triulzi DJ, Alarcon LH, Yazer MH. Blood component transfusion and wastage rates in the setting of massive transfusion in three regional trauma centers. Transfusion. 2017;57(1):45–52. doi:10.1111/trf.13880.
88. Cardigan R, Latham T, Weaver A, Yazer M, Green L. Estimating the risks of prehospital transfusion of D-positive whole blood to trauma patients who are bleeding in England. Vox Sang. 2022;117(5):701–7. doi:10.1111/vox.13249.
89. Yazer MH, Leeper C, Spinella PC, Emery SP, Horvath S, Seheult JN. Maternal and child life years gained by transfusing low titer group O whole blood in trauma: a computer simulation. Transfusion. 2024;64(S2):S93–S99. doi:10.1111/trf.17767.