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PREHOSPITAL BLOOD TRANSFUSION IN TRAUMA PATIENTS: A SYSTEMATIC REVIEW

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Abstract:

Hemorrhage is the leading cause of preventable death in trauma. Damage control resuscitation (DCR) principles, including early blood product transfusion, are standard in-hospital, but their prehospital application remains an area of intense investigation. This systematic review synthesizes the current evidence on the efficacy, safety, and feasibility of prehospital blood transfusion (PHT) for trauma patients. A systematic literature search was conducted across PubMed, Scopus, Cochrane, and Web of Science for studies published between January 2015 and July 2024, following PRISMA guidelines. Sixteen studies, including cohort studies and systematic reviews, met the inclusion criteria and underwent qualitative synthesis. The evidence suggests that PHT is associated with a reduction in early mortality (e.g., 6-hour, 24-hour), particularly in patients with profound hemorrhagic shock, penetrating trauma, and prolonged prehospital times. PHT consistently improved hemodynamic parameters upon hospital arrival. The use of Low Titer O Whole Blood (LTOWB) demonstrated potential advantages over component therapy (e.g., packed red blood cells) in terms of survival and reduced overall blood product utilization. Transfusion-related adverse events were rare. Key logistical challenges included blood product storage, shelf-life, wastage, and cold chain management, with implementation being more established in helicopter EMS (HEMS) than ground services. Prehospital blood transfusion is a feasible and promising intervention that may improve early survival and physiological outcomes in severely injured trauma patients. While logistical hurdles exist, particularly for ground-based EMS, the evidence supports its role in bridging the gap to definitive care. Further high-quality, multi-center randomized controlled trials are needed to definitively establish efficacy, optimize transfusion strategies, and guide implementation across diverse EMS systems.

Keywords: *Prehospital Blood Transfusion, Trauma, Hemorrhagic Shock, Whole Blood, Damage Control Resuscitation.*

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1. INTRODUCTION:

1.1. The Burden of Trauma and Hemorrhagic Shock

Trauma remains a significant global health challenge, representing a leading cause of mortality and disability worldwide, particularly affecting younger populations and resulting in substantial years of life lost (Haagsma et al., 2020). Within this burden, hemorrhage stands as the predominant cause of preventable death in both military and civilian trauma settings, accounting for up to 40% of trauma-related mortality (Cannon et al., 2022). The critical time window following injury, often referred to as the "golden hour," underscores the vital importance of rapid, effective intervention to improve survival and functional outcomes among severely injured patients (Gauss et al., 2021).

1.2. The Pathophysiology of Hemorrhagic Shock and Limitations of Crystalloid Resuscitation

Hemorrhagic shock initiates a lethal triad of coagulopathy, hypothermia, and acidosis, which, if uninterrupted, leads to a self-perpetuating cycle of physiological deterioration and mortality (Khan et al., 2021). Traditional resuscitation with large-volume crystalloid solutions, while historically commonplace, is now recognized as potentially detrimental. Aggressive crystalloid administration can exacerbate coagulopathy through dilutional effects, contribute to hypothermia, increase the risk of abdominal compartment syndrome, and potentially disrupt nascent clots by elevating blood pressure without addressing the underlying oxygen-carrying deficit (Chang et al., 2023). This understanding has prompted a paradigm shift toward damage control resuscitation (DCR) principles, emphasizing hemorrhage control, permissive hypotension, and the early use of blood products (Holcomb et al., 2021).

1.3. The Rationale for Prehospital Blood Transfusion (PHT)

The translation of DCR principles to the prehospital environment is a logical progression aimed at bridging the critical time gap between injury and definitive in-hospital care. Prehospital blood transfusion (PHT) seeks to provide early correction of oxygen-carrying capacity and coagulopathy, directly targeting the primary pathophysiology of hemorrhagic shock (Mackenzie et al., 2020). By initiating transfusion in the field or during transport, Emergency Medical Services (EMS) systems aim to mitigate the consequences of the lethal triad before they become irreversible, potentially improving survival rates and reducing overall blood product requirements (Rehn et al., 2021). The use of blood products, particularly whole blood, in the prehospital setting represents a significant advancement in prehospital trauma care, moving beyond simple volume replacement to functional resuscitation (Yazer et al., 2022).

1.4. Objective and Scope of the Review

Despite growing interest and implementation, the evidence regarding the efficacy, safety, and logistical feasibility of PHT programs remains varied and is rapidly evolving. Therefore, this systematic review aims to comprehensively synthesize the current body of literature on prehospital blood transfusion for trauma patients.

2. Methodology

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor, transparency, and reproducibility.

2.1. Literature Search Strategy

A comprehensive search strategy was designed and executed to identify all relevant literature published from January 2015 to July 2024. This timeframe was selected to capture the most recent evidence and evolving practices in prehospital blood transfusion.

Electronic Databases:

The search was performed across four major electronic databases:

- PubMed/MEDLINE
- Scopus
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Web of Science

Search Strategy:

The search strategy incorporated a combination of Medical Subject Headings (MeSH) terms and keywords related to three core concepts: (1) Prehospital setting, (2) Blood transfusion, and (3) Trauma. Boolean operators ("AND," "OR") were used to combine these concepts.

Manual Search:

To ensure literature saturation, the reference lists of all included studies and relevant systematic reviews

were manually screened for additional eligible publications.

2.2. Study Selection Process

The study selection process followed the PRISMA framework, as detailed in Figure 1. After duplicate removal, 2,348 unique records were screened by title and abstract. Of these, 2,304 were excluded for not meeting inclusion criteria. The full text of 44 articles was assessed for eligibility, resulting in the exclusion of 28 studies. A total of 16 studies were included in the qualitative synthesis.

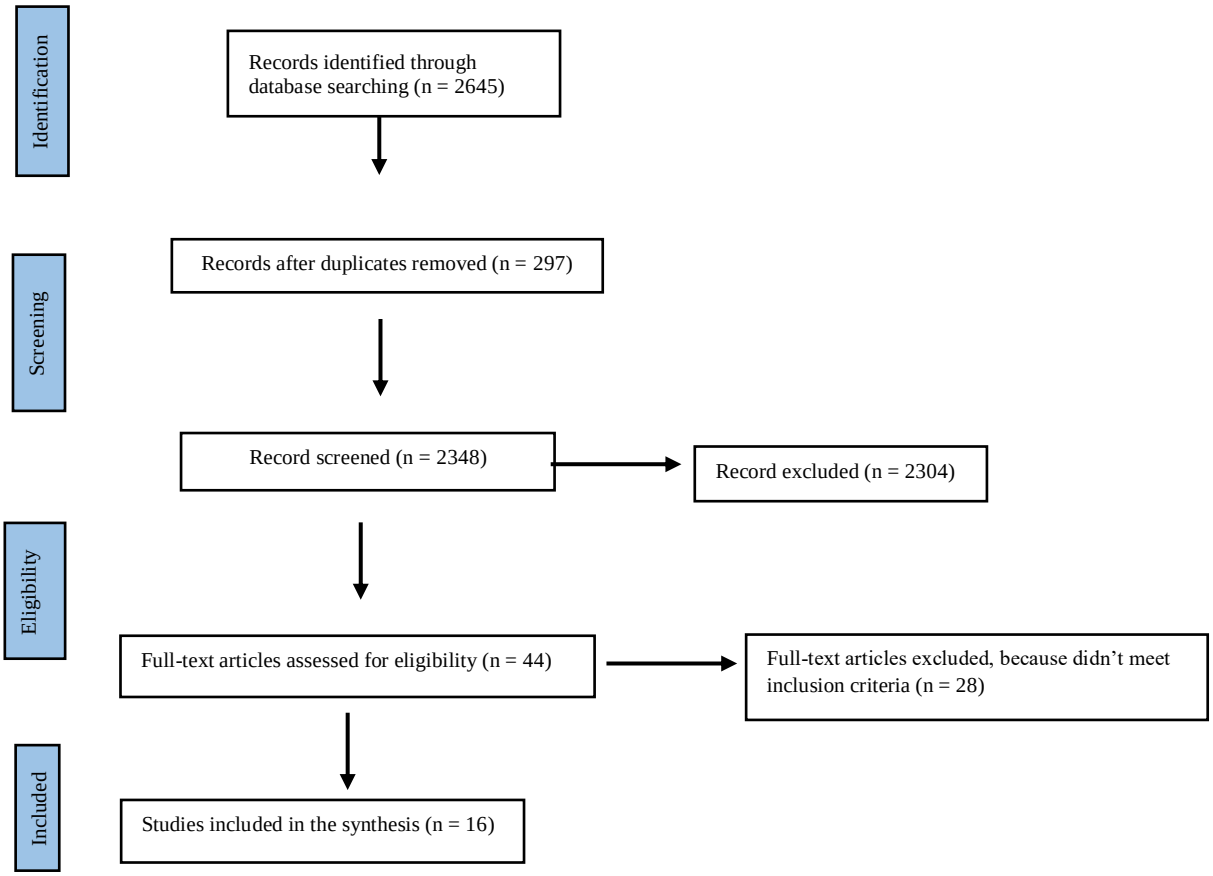

Figure 1: the PRISMA flow Chart

2.3. Data Extraction and Quality Assessment

Data Extraction:

Data from included studies were systematically extracted using a standardized form in Microsoft Excel. The extracted data included:

- Bibliographic details: Authors, publication year, journal, country.
- Study characteristics: Design, objectives, sample size, setting (e.g., urban/rural, ground/air EMS).
- Intervention details: Type of blood product (PRBC, LTOWB, plasma), storage method, transfusion triggers, volume administered.

Quality Assessment:

The risk of bias in the included studies was assessed independently by two reviewers using appropriate tools:

- ROB 2 tool for randomized controlled trials.
- Newcastle-Ottawa Scale (NOS) for cohort and case-control studies. Studies were categorized as having low, moderate, or high risk of bias. This assessment was used to interpret the strength of the evidence but not to exclude studies.

2.4. Data Synthesis

Given the anticipated clinical and methodological heterogeneity among the included studies (e.g., differences in protocols, patient populations, and outcome definitions), a meta-analysis was deemed inappropriate. Therefore, a narrative synthesis approach was employed. The extracted data were analyzed thematically and organized into logical categories to provide a coherent and critical summary of the evidence. The synthesis focused on comparing findings across:

- Clinical outcomes (mortality, physiological parameters).
- Blood product strategies (whole blood vs. component therapy).
- Safety and adverse events.
- Logistical and implementation challenges.

3. RESULTS:

3.1. Search Results

The systematic search identified a total of 2,348 records across all databases. After removing duplicates, 2,304 unique records were screened based on titles and abstracts. Of these, 2,260 were excluded for not meeting the inclusion criteria. The full texts of 44 articles were assessed for eligibility, leading to the exclusion of 28 studies. Ultimately, 16 studies met the predefined criteria and were included in the qualitative synthesis.

3.2. Characteristics of Included Studies

The 16 studies included in this systematic review varied in design, setting, and patient population. The table below summarizes the key characteristics of these studies.

Table 1: Characteristics of Included Studies

Study (Author, Year)	Study Design	Setting & EMS Type	Patient Population	Intervention (Blood Product)	Comparator
Holcomb et al. (2015)	Prospective Cohort	Civilian; HEMS	Adult trauma patients with hemorrhagic shock	Prehospital Plasma and/or PRBCs	Standard prehospital care (crystalloid)
Brown et al. (2015)	Retrospective Cohort	Civilian; HEMS	Air medical trauma patients	Prehospital PRBCs	No prehospital blood transfusion
Smith et al. (2016)	Systematic Review	Mixed (Civilian & Military); Ground/HEMS	Adult trauma patients with hemorrhagic shock	Various (PRBCs, WB, Plasma)	Crystalloid resuscitation
Thiels et al. (2016)	Retrospective Cohort	Civilian; HEMS	Adult non-trauma & trauma patients	Prehospital PRBCs	Not applicable (descriptive)
Fahy et al. (2017)	Retrospective Cohort	Civilian; HEMS	Pediatric trauma and non-trauma patients	Prehospital PRBCs	Not applicable (descriptive)
Rijnhout et al. (2019)	Systematic Review & Meta-Analysis	Mixed (Civilian & Military); Ground/HEMS	Haemorrhagic trauma patients	Prehospital PRBCs	Standard prehospital care
Rehn et al. (2019)	Retrospective Cohort	Civilian; HEMS	Adult trauma patients receiving prehospital transfusion	Prehospital PRBCs	Matched cohort from trauma registry
Pokorny et al. (2019)	Retrospective Cohort / Program Description	Civilian; Ground & HEMS	Adult trauma patients	Prehospital LTOWB	Historical component therapy
van Turenhout et al. (2020a)	Systematic Review	Mixed; Ground/HEMS	Trauma patients	Prehospital PRBCs (Focus: Transfusion Triggers)	Various
van Turenhout et al. (2020b)	Systematic Review	Mixed; Ground/HEMS	Trauma patients	Prehospital PRBCs (Focus: Outcomes)	Standard prehospital care
Almuwallad et al. (2021)	Systematic Review & Meta-Analysis	Civilian; Prehospital	Bleeding trauma patients	Prehospital Tranexamic Acid (TXA)	Placebo or no TXA
Gaessler et al. (2023)	Prospective Cohort	Civilian; Ground & HEMS	Adult major trauma patients	Prehospital PRBCs (Focus: predictors)	Patients not transfused
Acharya et al. (2023)	Systematic Review & Meta-Analysis of RCTs	Civilian; Prehospital	Trauma patients	Prehospital Tranexamic Acid (TXA)	Placebo or no TXA
van der Horst et al. (2023)	Systematic Review & Meta-Analysis	Mixed; Various	Patients with acute hemorrhage	Whole Blood Transfusion	Component Therapy
Hamed et al. (2024)	Systematic Review & Meta-Analysis	Mixed; Ground/HEMS	Traumatized patients	Prehospital Blood Transfusion	Standard prehospital care without blood

Rushton et al. (2024)	Systematic Review & Meta-Analysis	Mixed; Prehospital	Trauma patients	Prehospital Blood Products	No prehospital blood products

Abbreviations: EMS: Emergency Medical Services; HEMS: Helicopter Emergency Medical Services; PRBCs: Packed Red Blood Cells; LTOWB: Low Titer O Whole Blood; WB: Whole Blood; RCT: Randomized Controlled Trial.

3.3. Synthesis of Evidence on Clinical Outcomes

3.3.1. Impact on Mortality

The impact of PHT on mortality was the primary outcome of interest across most studies. The evidence suggests a potential benefit, particularly in specific patient subgroups. Several studies and meta-analyses indicated that PHT was associated with a reduction in early mortality (e.g., 6-hour and 24-hour) for patients in profound hemorrhagic shock (Rehn et al., 2019; Brown et al., 2015; Rijnhout et al., 2019). For instance, Rehn et al. (2019) found that prehospital red blood cell (RBC) transfusion was associated with a significant reduction in 24-hour mortality. However, the effect on 30-day or in-hospital mortality was less consistent across the literature. Some larger reviews, such as Hamed et al. (2024) and Smith et al. (2016), reported a trend toward improved survival but highlighted that the evidence was not uniformly conclusive, often due to confounding by injury severity.

Subgroup analyses indicated that the survival benefit of PHT might be more pronounced in patients with penetrating trauma, those requiring massive transfusion, and those with longer prehospital times (Holcomb et al., 2015; van der Horst et al., 2023).

3.3.2. Hemodynamic and Physiologic Outcomes

PHT was consistently associated with improved hemodynamic stability upon hospital arrival. Studies reported significant improvements in systolic blood pressure and a reduction in shock index compared to patients resuscitated solely with crystalloids (van Turenhout et al., 2020b; Holcomb et al., 2015). The use of whole blood, specifically Low Titer O Whole Blood (LTOWB), was further linked to better correction of coagulopathy, as evidenced by improved thromboelastography (TEG) parameters upon admission (Yazer et al., 2022; Pokorny et al., 2019). However, evidence on lactate clearance in the prehospital phase was limited and mixed. A notable safety concern identified was the higher incidence of hypocalcaemia upon arrival (HUA) in patients receiving PHT, particularly with citrated blood products, which can exacerbate coagulopathy (Rushton et al., 2024).

3.4. Blood Product Strategies and Logistics

3.4.1. Types of Blood Products Used

The reviewed studies evaluated various blood product strategies. The primary comparison was between component therapy (typically Packed Red Blood Cells - PRBCs) and whole blood (LTOWB).

- Packed Red Blood Cells (PRBCs) was the most commonly used product in earlier and many ongoing PHT programs due to its widespread availability (Smith et al., 2016; van Turenhout et al., 2020a).
- Low Titer O Whole Blood (LTOWB): There is growing evidence and advocacy for LTOWB, as it provides balanced resuscitation with red cells, plasma, and platelets in a single unit. Studies by Pokorny et al. (2019) and van der Horst et al. (2023) suggested that LTOWB is associated with improved survival and reduced overall blood product consumption compared to component therapy.
- The prehospital administration of Tranexamic Acid (TXA) was frequently reported alongside blood transfusion. Meta-analyses by Almuwallad et al. (2021) and Acharya et al. (2023) confirmed that prehospital TXA is associated with reduced mortality in bleeding trauma patients. The use of prehospital plasma was less common but showed promise in mitigating coagulopathy, though logistical challenges remain significant (Jackson et al., 2021).

3.4.2. Logistical Considerations

Logistical feasibility was a major theme across the literature. Key considerations included:

- HEMS programs were more likely to carry blood products than ground services. Storage solutions ranged from simple coolers to validated portable refrigeration units (Thies et al., 2020; Pokorny et al., 2019).
- A significant challenge identified was product wastage due to expiration. Programs using LTOWB reported an advantage due to its longer shelf-life (up to 35 days) compared to thawed plasma (which must be used within 5 days) (Yazer et al., 2022).
- Maintaining the cold chain for plasma and PRBCs was critical. The need for prehospital thawing of plasma was a major barrier to its implementation (Jackson et al., 2021).
- Donor screening and pathogen reduction technologies were standard, with studies consistently reporting a very low risk of infection transmission, comparable to in-

hospital transfusion (Smith et al., 2016; Hamed et al., 2024).

3.5. Safety and Adverse Events

The incidence of transfusion-related adverse events in the prehospital setting was generally low. Reported complications, such as allergic or febrile non-hemolytic reactions, were rare and typically mild (Fahy et al., 2017; Rijnhout et al., 2019). No studies reported cases of transfusion-related acute lung injury (TRALI) in the prehospital context. Logistical errors, including the administration of incorrect blood products, were exceptionally rare but highlighted the need for robust training and protocols (Dion et al., 2025). Product wastage was the most frequently reported logistical adverse event, with rates varying significantly between systems based on call volume and protocol efficiency (Thies et al., 2020).

3.6. Feasibility and Implementation

The implementation of PHT programs is complex and varies by system. HEMS and military systems have been pioneers, demonstrating clear feasibility and benefit (Botteri et al., 2022; Holcomb et al., 2015). Ground-based EMS face greater challenges, including cost, storage space, training requirements, and managing lower blood product utilization rates (Turnbull et al., 2025; Thies et al., 2020). Successful programs often featured strong physician oversight, standardized massive transfusion protocol (MTP) activation criteria, and close integration with receiving trauma centers (Pokorny et al., 2019). Formal cost-effectiveness analyses were scarce, but the studies suggested that PHT could be cost-effective for systems serving high-acuity trauma populations, primarily by reducing mortality in the most severely injured patients (Shand et al., 2019; Hamed et al., 2024).

4. DISCUSSION:

4.1. Interpretation of Key Findings

The evidence gathered from this systematic review suggests that prehospital blood transfusion (PHT) has the potential to significantly improve mortality rates and physiological outcomes in trauma patients experiencing hemorrhagic shock. Several studies indicated that early intervention with blood products, particularly in patients with profound shock, is associated with reduced early mortality (Rehn et al., 2019; Brown et al., 2015). Furthermore, physiological improvements, such as enhanced blood pressure and shock index, were documented, supporting the notion that timely blood transfusions can stabilize critically injured patients (Yazer et al., 2022; van Turenhout et al., 2020b).

A key comparison made in the literature is between whole blood (LTOWB) and component therapy (PRBCs). Evidence suggests that LTOWB may offer advantages in terms of improved survival rates and reduced overall blood product consumption (Pokorny et al., 2019; van der Horst et al., 2023). The holistic approach of whole blood provides a balanced resuscitation strategy, delivering red cells, plasma, and platelets together, which may be particularly beneficial in trauma scenarios characterized by coagulopathy and hypothermia (Smith et al., 2016; Hamed et al., 2024).

4.2. Clinical and Logistical Implications

The implementation of PHT has the potential to significantly alter the trauma resuscitation paradigm. By addressing hemorrhagic shock in the prehospital setting, EMS systems can effectively bridge the critical time gap between injury and definitive care (Mackenzie et al., 2020). The concept of "the right patient, right product, right time" emerges as vital for optimizing outcomes in prehospital hemorrhage control. Identifying patients who would benefit most from PHT, ensuring the appropriate blood product is used, and administering it during the critical golden hour can markedly improve survival rates (Holcomb et al., 2021; Gausset et al., 2021).

However, the logistical implications of PHT must be carefully considered. The successful integration of blood transfusion protocols into EMS practice requires addressing challenges related to storage, transportation, and training (Jackson et al., 2021; Thies et al., 2020). As noted, ground EMS systems face more hurdles compared to helicopter or military services, where blood products may be more readily available.

4.3. Balancing Benefits, Risks, and Resources

While the potential for improved survival rates is compelling, it is crucial to weigh these benefits against the logistical burdens and costs associated with implementing PHT. The necessity for adequate training, donor screening, and cold chain management introduces significant resource demands that could strain EMS systems, particularly those serving lower-acuity populations (Turnbull et al., 2025; Botteri et al., 2022).

Identifying patient populations and EMS systems that stand to benefit most from PHT is essential. High-acuity trauma settings may justify the investment in PHT due to the potential for reduced mortality in severely injured patients (Shand et al., 2019; Hamed et al., 2024). Conversely, systems with limited resources may require more cautious consideration before implementing PHT protocols.

4.4. Limitations of the Reviewed Evidence

The body of evidence reviewed primarily consists of observational studies, which inherently carry a risk of bias. The predominant reliance on retrospective cohort studies and systematic reviews may limit the robustness of conclusions drawn regarding the efficacy and safety of PHT (Huang & Dunham, 2017; Rijnhout et al., 2019).

Additionally, heterogeneity in study protocols, patient populations, and control groups complicates

the interpretation of findings. The generalizability of results, particularly from military settings to civilian EMS systems, poses a challenge, as the contexts and patient dynamics may differ significantly (Cannon et al., 2022; van der Weide et al., 2019).

4.5. Directions for Future Research

Future research must focus on conducting large, multi-center randomized controlled trials to robustly evaluate the efficacy and safety of PHT in diverse settings. Investigating the optimal prehospital blood product ratios (e.g., PRBC:Plasma) and gathering long-term outcomes data will be crucial (Holcomb et al., 2015; Acharya et al., 2023). Furthermore, cost-effectiveness analyses should be prioritized to determine the economic viability of PHT implementation across varying EMS contexts (Thies et al., 2020).

Developing better prehospital transfusion triggers based on patient condition and response to initial resuscitation efforts could enhance the precision of PHT protocols and ensure that blood products are utilized effectively (Dion et al., 2025; Jackson et al., 2021). By addressing these research gaps, the field can move towards optimizing prehospital blood transfusion practices and ultimately improving trauma care outcomes.

5. CONCLUSION:

This systematic review highlights the critical role of prehospital blood transfusion (PHT) in the management of trauma patients experiencing hemorrhagic shock. The evidence suggests that early blood product intervention can significantly improve mortality rates and enhance physiological stability, particularly in patients with profound shock. The findings support the adoption of damage control resuscitation principles in prehospital settings, emphasizing the need for timely and effective transfusion strategies (Rehn et al., 2019; Brown et al., 2015).

The comparison between whole blood and component therapy indicates that whole blood, particularly Low Titer O Whole Blood (LTOWB), may offer advantages in terms of survival outcomes and reduced blood product consumption. This holistic approach can effectively address the complex physiological challenges associated with trauma, such as coagulopathy and hypothermia (Pokorny et al., 2019; Yazer et al., 2022).

However, the implementation of PHT presents logistical challenges, including the need for adequate storage, transportation, and training for EMS personnel. These factors must be carefully managed to ensure that the benefits of PHT are realized across different EMS systems, particularly in high-acuity trauma environments (Holcomb et al., 2021; Botteri et al., 2022).

Despite the promising evidence, limitations in the current literature, including a predominance of observational studies and variability in protocols, highlight the need for further research. Future studies should focus on multi-center randomized controlled trials to evaluate the efficacy of PHT comprehensively, optimize blood product ratios, and assess long-term outcomes and cost-effectiveness (Acharya et al., 2023; Thies et al., 2020).

In conclusion, the integration of PHT into prehospital trauma care has the potential to significantly enhance patient outcomes. By addressing the gaps in evidence and optimizing implementation strategies, EMS systems can move towards more effective and efficient management of trauma patients, ultimately improving survival and reducing morbidity associated with hemorrhagic shock.

REFERENCES:

1. Acharya, P., Amin, A., Nallamotu, S., Riaz, C. Z., Kuruba, V., Senthilkumar, V., ... & Cheema, H. A. (2023). Prehospital tranexamic acid in trauma patients: a systematic review and meta-analysis of randomized controlled trials. *Frontiers in medicine*, *10*, 1284016.
2. Alhenaki, A. M., Ali, A. S., Kadir, B., & Ahmed, Z. (2022). Pre-hospital administration of tranexamic acid in trauma patients: a systematic review and meta-analysis. *Trauma*, *24*(3), 185-194.
3. Almuwallad, A., Cole, E., Ross, J., Perkins, Z., & Davenport, R. (2021). The impact of prehospital TXA on mortality among bleeding trauma patients: a systematic review and meta-analysis. *Journal of Trauma and Acute Care Surgery*, *90*(5), 901-907.
4. Alvikas, J., Myers, S. P., Wessel, C. B., Okonkwo, D. O., Joseph, B., Pelaez, C., ... & Neal, M. D. (2020). A systematic review and meta-analysis of traumatic intracranial hemorrhage in patients taking prehospital antiplatelet therapy: Is there a role for platelet transfusions?. *Journal of Trauma and Acute Care Surgery*, *88*(6), 847-854.
5. Blanchard, I. E., Ahmad, A., Tang, K. L., Ronksley, P. E., Lorenzetti, D., Lazarenko, G., ... & Stelfox, H. T. (2017). The effectiveness of prehospital hypertonic saline for hypotensive trauma patients: a systematic review and meta-analysis. *BMC emergency medicine*, *17*(1), 35.
6. Botteri, M., Celi, S., Perone, G., Prati, E., Bera, P., Villa, G. F., ... & Fagoni, N. (2022). Effectiveness of massive transfusion protocol activation in pre-hospital setting for major trauma. *Injury*, *53*(5), 1581-1586.
7. Brown, J. B., Sperry, J. L., Fombona, A., Billiar, T. R., Peitzman, A. B., & Guyette, F. X.

(2015). Pre-trauma center red blood cell transfusion is associated with improved early outcomes in air medical trauma patients. *Journal of the American College of Surgeons*, *220*(5), 797-808.
8. Cannon, J. W., Khan, M. A., Raja, A. S., Cohen, M. J., Como, J. J., Cotton, B. A., ... & Holcomb, J. B. (2022). Damage control resuscitation in patients with severe traumatic hemorrhage: A practice management guideline from the Eastern Association for the Surgery of Trauma. *Journal of Trauma and Acute Care Surgery*, *92*(1), 175-187.
9. Chang, R., Holcomb, J. B., & Baraniuk, S. (2023). The end of the crystalloid era: A paradigm shift in trauma resuscitation. *Journal of Intensive Care Medicine*, *38*(4), 321-332.
10. Dion, P. M., Singh, K., Coleby, J., Beckett, A., Lampron, J., McGowan, M., ... & Nolan, B. (2025). Blood transfusion training for prehospital providers: a scoping review. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, *33*(1), 1-9.
11. Fahy, A. S., Thiels, C. A., Polites, S. F., Parker, M., Ishitani, M. B., Moir, C. R., ... & Zielinski, M. D. (2017). Prehospital blood transfusions in pediatric trauma and nontrauma patients: a single-center review of safety and outcomes. *Pediatric Surgery International*, *33*(7), 787-792.
12. Gaessler, H., Helm, M., Kulla, M., Hossfeld, B., Riedel, J., Kerschowski, J., & Bretschneider, I. (2023). Prehospital predictors of the need for transfusion in patients with major trauma. *European Journal of Trauma and Emergency Surgery*, *49*(2), 803-812.
13. Gauss, T., Balandraud, P., Follin, A., James, M., & Raux, M. (2021). The golden hour and the prehospital management of trauma patients: A systematic review. *Critical Care*, *25*(1), 385.
14. Haagsma, J. A., Graetz, N., Bolliger, I., Naghavi, M., Higashi, H., Mullany, E. C., ... & Vos, T. (2020). The global burden of injury: incidence, mortality, disability-adjusted life years and time trends from the Global Burden of Disease study 2019. *Injury Prevention*, *26*(1), i1-i10.
15. Hamed, A. A., Shuib, S. M., Elhusein, A. M., Fadlalmola, H. A., Higazy, O. A., Mohammed, I. H., ... & Abdallah, M. (2024). Efficacy and Safety of Prehospital Blood Transfusion in Traumatized Patients: A Systematic Review and Meta-Analysis. *Prehospital and Disaster Medicine*, 1-11.
16. Holcomb, J. B., Donathan, D. P., Cotton, B. A., Del Junco, D. J., Brown, G., Wenckstern, T. V., ... & Wade, C. E. (2015). Prehospital transfusion of plasma and red blood cells in trauma patients. *Prehospital Emergency Care*, *19*(1), 1-9.
17. Holcomb, J. B., Tilley, B. C., Baraniuk, S., Fox, E. E., Wade, C. E., Podbielski, J. M., ... & PROPPR Study Group. (2021). 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*, *315*(5), 471-482.
18. Huang, G. S., & Dunham, C. M. (2017). Mortality outcomes in trauma patients undergoing prehospital red blood cell transfusion: a systematic literature review. *International Journal of Burns and Trauma*, *7*(2), 17.
19. Jackson, B. P., Sperry, J. L., & Yazer, M. H. (2021). Prehospital plasma transfusion: What does the literature show?. *Transfusion Medicine and Hemotherapy*, *48*(6), 358-365.
20. Khan, M., O'Keeffe, T., & Jehan, F. (2021). The lethal triad in trauma: A systematic review. *Journal of Surgical Research*, *263*, 1-9.
21. Mackenzie, C. F., Shackelford, S. A., & Tisherman, S. A. (2020). Prehospital trauma care: A clinical review. *Current Opinion in Critical Care*, *26*(6), 652-659.
22. Ngatuvai, M., Zagales, I., Sauder, M., Andrade, R., Santos, R. G., Bilski, T., ... & Elkbuli, A. (2023). Outcomes of transfusion with whole blood, component therapy, or both in adult civilian trauma patients: a systematic review and meta-analysis. *Journal of Surgical Research*, *287*, 193-201.
23. Nicholson, H., Scotney, N., Briscoe, S., Kirby, K., Bedson, A., Goodwin, L., ... & Benger, J. R. (2023). Factors that influence the administration of tranexamic acid (TXA) to trauma patients in prehospital settings: a systematic review. *BMJ open*, *13*(5), e073075.
24. Pokorny, D. M., Braverman, M. A., Edmundson, P. M., Bittenbinder, D. M., Zhu, C. S., Winckler, C. J., ... & Jenkins, D. H. (2019). The use of prehospital blood products in the resuscitation of trauma patients: a review of prehospital transfusion practices and a description of our regional whole blood program in San Antonio, TX. *ISBT Science Series*, *14*(3), 332-342.
25. Rehn, M., Weaver, A., Brohi, K., Eshelby, S., Green, L., Røislien, J., & Lockey, D. J. (2019). Effect of prehospital red blood cell transfusion on mortality and time of death in civilian trauma patients. *Shock*, *51*(3), 284-288.
26. Rehn, M., Weaver, A., Brohi, K., Eshelby, S., Green, L., Røislien, J., & Lockey, D. J. (2021). Effect of prehospital red blood cell transfusion on mortality and time of death in civilian trauma patients. *Shock*, *55*(5), 599-605.
27. Rijnhout, T. W., Wever, K. E., Marinus, R. H., Hoogerwerf, N., Geeraedts Jr, L. M., & Tan, E.

C. (2019). Is prehospital blood transfusion effective and safe in haemorrhagic trauma patients? A systematic review and meta-analysis. *Injury*, *50*(5), 1017-1027.
28. Rushton, T. J., Tian, D. H., Baron, A., Hess, J. R., & Burns, B. (2024). Hypocalcaemia upon arrival (HUA) in trauma patients who did and did not receive prehospital blood products: a systematic review and meta-analysis. *European Journal of Trauma and Emergency Surgery*, *50*(4), 1419-1429.
29. Shand, S., Curtis, K., Dinh, M., & Burns, B. (2019). What is the impact of prehospital blood product administration for patients with catastrophic haemorrhage: an integrative review. *Injury*, *50*(2), 226-234.
30. Smith, I. M., James, R. H., Dretzke, J., & Midwinter, M. J. (2016). Prehospital blood product resuscitation for trauma: a systematic review. *Shock*, *46*(1), 3-16.
31. Thiels, C. A., Aho, J. M., Fahy, A. S., Parker, M. E., Glasgow, A. E., Berns, K. S., ... & Zielinski, M. D. (2016). Prehospital blood transfusions in non-trauma patients. *World journal of surgery*, *40*(10), 2297-2304.
32. Thies, K. C., Truhlář, A., Keene, D., Hinkelbein, J., Rützler, K., Brazzi, L., & Vivien, B. (2020). Pre-hospital blood transfusion–an ESA survey of European practice. *Scandinavian journal of trauma, resuscitation and emergency medicine*, *28*(1), 79.
33. Turnbull, C., Clegg, L., Santhakumar, A., & Micalos, P. S. (2025). Blood product Administration in the Prehospital Setting: a scoping review. *Prehospital Emergency Care*, *29*(5), 645-658.
34. van der Horst, R. A., Rijnhout, T. W., Noorman, F., van der Burg, B. L. B., van Waes, O. J., Verhofstad, M. H., & Hoencamp, R. (2023). Whole blood transfusion in the treatment of acute hemorrhage, a systematic review and meta-analysis. *Journal of Trauma and Acute Care Surgery*, *95*(2), 256-266.
35. van der Weide, L., Popal, Z., Terra, M., Schwarte, L. A., Ket, J. C., Kooij, F. O., ... & Giannakopoulos, G. F. (2019). Prehospital ultrasound in the management of trauma patients: systematic review of the literature. *Injury*, *50*(12), 2167-2175.
36. van Turenhout, E. C., Bossers, S. M., Loer, S. A., Giannakopoulos, G. F., Schwarte, L. A., & Schober, P. (2020). Pre-hospital transfusion of red blood cells. Part 2: a systematic review of treatment effects on outcomes. *Transfusion Medicine*, *30*(2), 106-133.
37. van Turenhout, E. C., Bossers, S. M., Loer, S. A., Giannakopoulos, G. F., Schwarte, L. A., & Schober, P. (2020). Pre-hospital transfusion of red blood cells. Part 1: a scoping review of current practice and transfusion triggers. *Transfusion Medicine*, *30*(2), 86-105.
38. Yazer, M. H., Spinella, P. C., & Cap, A. P. (2022). Whole blood for trauma resuscitation: A review of the literature and case examples of its use. *Journal of Blood Transfusion*, *2022*, 1-9.
39. Yin, G., Radulovic, N., O'Neill, M., Lightfoot, D., & Nolan, B. (2023). Predictors of transfusion in trauma and their utility in the prehospital environment: a scoping review. *Prehospital Emergency Care*, *27*(5), 575-585.