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Prehospital Blood Transfusion: Systematic Review

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Abstract

Background:
Severe traumatic hemorrhage is a major cause of preventable mortality in the prehospital setting, where delays in resuscitation can rapidly lead to hemodynamic collapse and early coagulopathy. Prehospital blood transfusion (PBT) has emerged as a potential life-saving intervention aimed at stabilizing patients before arrival at definitive care. This systematic review examines the impact of PBT on mortality and key clinical outcomes among trauma patients with suspected or confirmed severe hemorrhage.

Methods:
A systematic search of PubMed, Embase, Web of Science, Scopus, and CENTRAL was conducted following PRISMA 2020 guidelines. Eligible studies included randomized trials, quasi-experimental studies, and observational cohort and case–control studies comparing PBT with standard prehospital care. Data extraction was performed independently by two reviewers, and risk of bias was assessed using Joanna Briggs Institute (JBI) tools. Outcomes included prehospital, 24-hour, in-hospital, and 30-day mortality, as well as physiological and transfusion-related secondary outcomes.

Results:
Eight studies met the inclusion criteria, representing military and civilian EMS systems, including ground EMS and HEMS services. Across most studies, PBT was associated with reduced early mortality—particularly within the first 24 hours—and improved hemodynamic stability on arrival, including higher systolic blood pressure and improved metabolic markers. Evidence regarding in-hospital and 30-day mortality was mixed, with some studies demonstrating benefit and others showing no significant difference. PBT was also associated with reduced crystalloid use, decreased activation of massive transfusion protocols, and a low incidence of transfusion-related complications.

Conclusion:
Prehospital blood transfusion appears to be a safe and effective intervention that can improve early survival and physiological outcomes among severely hemorrhaging trauma patients. While long-term mortality benefits remain inconsistent, the evidence supports expanding PBT programs—particularly in systems with prolonged transport times or high trauma burden. Further randomized trials and standardized reporting are required to determine optimal transfusion strategies and strengthen the evidence for widespread implementation.

Keywords: Prehospital blood transfusion; trauma; hemorrhagic shock; EMS; HEMS; early mortality; whole blood; PRBC; emergency medical services.

Introduction

Severe traumatic hemorrhage remains one of the leading causes of preventable death in prehospital care, accounting for a large proportion of mortality during the first "golden hour" after injury (Kauvar et al., 2021). Patients with uncontrolled bleeding experience rapid hemodynamic collapse, impaired oxygen delivery, and early coagulopathy, making timely resuscitation essential for survival (Spahn et al., 2023). Traditionally, emergency medical services (EMS) have focused on rapid transport to definitive hospital care; however, many patients deteriorate significantly before arrival, prompting interest in prehospital blood transfusion (PBT) as an advanced intervention to stabilize critically injured patients (Gurney et al., 2022).

Prehospital blood transfusion involves administering packed red blood cells, whole blood, or blood components at the scene or during transport. Growing evidence suggests that early transfusion may improve oxygen delivery, reduce shock severity, and prevent trauma-induced coagulopathy (Howard et al., 2022). In military medicine, early blood product administration has been associated with improved outcomes, influencing civilian EMS and helicopter emergency medical services (HEMS) to explore similar protocols (Morrison et al., 2020). Despite promising results, the effectiveness of PBT in reducing mortality remains a subject of debate. Some observational studies have shown survival benefits with early transfusion (Pham et al., 2022), while others report no significant reduction in 24-hour or 30-day mortality (Heschl et al., 2023).

Variability in study designs, patient selection, trauma mechanisms, and transfusion protocols contributes to inconsistent findings across the literature (Rogers et al., 2024). Additionally, logistical challenges—including cold-chain maintenance, training, cost, and storage—shape the feasibility of implementing PBT in different EMS settings (Harper et al., 2023). Therefore, a systematic synthesis of available evidence is needed to determine whether prehospital blood transfusion truly reduces mortality among severely bleeding patients.

This systematic review aims to evaluate the impact of PBT on mortality outcomes, compare findings across civilian and military EMS systems, and identify gaps to guide future research and policy development. Understanding the role of early transfusion in hemorrhage control will support evidence-based decision-making and improve the management of trauma patients in prehospital care.

Literature Review

Severe traumatic hemorrhage remains a major contributor to early trauma-related death, particularly in the prehospital phase where delays in resuscitation significantly worsen outcomes (Spahn et al., 2023). Over the past decade, the concept of damage control resuscitation has shifted toward earlier delivery of blood products to counteract shock, oxygen debt, and trauma-induced coagulopathy. This movement has catalyzed the expansion of prehospital blood transfusion (PBT) programs across civilian EMS and military settings (Gurney et al., 2022).

1. Evolution of Prehospital Blood Transfusion

Early international experiences—primarily from military operations—demonstrated that administering blood products before hospital arrival could improve survival among severely bleeding combat casualties. These findings encouraged civilian helicopter emergency medical services (HEMS) in Europe, North America, and Australia to adopt early transfusion protocols. Whole blood and packed red blood cells (pRBCs) emerged as the most commonly used products, while some systems also incorporated plasma and low-titer O-positive whole blood (Howard et al., 2022). The concept of prehospital blood transfusion originated from military experience, where

early use of blood products on the battlefield was shown to improve survival in severely bleeding casualties. These findings encouraged civilian emergency medical systems—especially helicopter emergency medical services to adopt early transfusion protocols. Whole blood and packed red blood cells became the most commonly used products, while some systems also implemented plasma or low-titer O-positive whole blood. Advances such as portable blood warmers and improved storage technologies further enhanced the safety and feasibility of administering blood before hospital arrival. Overall, these developments transformed trauma care by emphasizing early, targeted resuscitation for patients with life-threatening

2. Effectiveness in Reducing Mortality

Recent research presents mixed but encouraging evidence regarding the mortality benefits of PBT. Several observational studies and meta-analyses have reported that early transfusion—especially within minutes of patient contact—is associated with improved 24-hour and 30-day survival (Pham et al., 2022). A multicenter study across European HEMS programs found that PBT reduced early mortality, particularly in patients presenting with systolic blood pressure below 90 mmHg (Heschl et al., 2023).

However, other studies highlight variable outcomes depending on injury mechanism, transfusion timing, and prehospital infrastructure (Rogers et al., 2024). For example, some EMS systems showed no statistically significant survival advantage when PBT was administered late during transport or in cases of non-hemorrhagic trauma. These inconsistencies underscore the need for better patient-selection criteria and standardized PBT protocols.

The effectiveness of prehospital blood transfusion (PBT) in reducing mortality has been the focus of considerable investigation, and although findings remain mixed, the overall trend in the literature is cautiously optimistic. Multiple observational studies and meta-analyses indicate that early initiation of transfusion—particularly within minutes of patient contact—can significantly improve both 24-hour and 30-day survival outcomes. This survival benefit is largely attributed to the rapid correction of hemorrhagic shock, prevention of coagulopathy progression, and stabilization of hemodynamics before irreversible physiological deterioration occurs.

Further supporting this evidence, a multicenter study conducted across various European Helicopter Emergency Medical Service (HEMS) systems demonstrated that PBT was associated with a notable reduction in early mortality, especially among severely hypotensive patients presenting with systolic blood pressure below 90 mmHg. These findings suggest that the benefits of PBT may be most pronounced in patients who are critically unstable and at high risk of exsanguination.Despite these encouraging results, the literature also reveals considerable variability in outcomes. Several studies highlight that the effect of PBT is influenced by a range of contextual factors, including injury mechanism, timing and volume of transfusion, and the availability of robust prehospital infrastructure. For instance, some Emergency Medical Services (EMS) systems report no statistically significant survival advantage when PBT is administered later during transport or when used for patients who do not exhibit clear signs of hemorrhagic shock. These discrepancies underscore the need for improved patient-selection criteria, as inappropriate or delayed transfusion may dilute the measurable benefits observed in higher-risk subgroups.Collectively, these findings illustrate that while PBT holds substantial promise for improving trauma survival, its effectiveness is not uniform across all scenarios. Standardized protocols, optimized logistics, and evidence-based inclusion criteria are essential to ensure that PBT is delivered efficiently and to the patients who stand to benefit the most.

3. Physiological Rationale and Clinical Benefits

The theoretical benefits of PBT stem from its ability to immediately restore circulating volume and improve oxygen-carrying capacity, thereby limiting tissue hypoxia and preventing the progression to irreversible shock (Kauvar et al., 2021). Early transfusion may also delay or reduce the development of coagulopathy, a major determinant of trauma mortality (Spahn et al., 2023). The combination of blood products with hemostatic agents—such as tranexamic acid (TXA)—has shown synergistic survival effects in some settings.

Prehospital blood transfusion helps save a patient's life for several key reasons:

1. Quickly restoring lost blood

Giving blood early replaces the blood the patient has lost and improves the amount of oxygen delivered to the tissues. This helps prevent tissue damage and stops the patient from going into irreversible shock.

2. Reducing clotting problems

After major trauma, the body may lose its ability to form blood clots, which increases the risk of severe bleeding and death. Early transfusion can delay or reduce this problem.

3. Better survival when combined with other treatments

Using blood products together with medications that help control bleeding—such as tranexamic acid (TXA)—has been shown to improve survival in some situations.

Very Simple Summary

Prehospital blood transfusion can save lives because it:

- Quickly replaces lost blood
- Prevents shock
- Reduces clotting problems
- Works even better when combined with TXA

4. Operational and Logistical Considerations

Despite growing interest, PBT faces significant logistical challenges. These include:

- Maintaining cold-chain storage during field operations
- Ensuring blood type compatibility or using universal/low-titer whole blood
- Training paramedics and flight crews to handle transfusion reactions
- Implementing rapid documentation and monitoring protocols
- Addressing costs and blood-unit wastage (Harper et al., 2023)

The paragraph emphasizes that these logistical issues remain the primary reason PBT is not widely adopted in some EMS systems. Operational feasibility varies significantly depending on whether the service is ground-based, aeromedical, or military.

5. Gaps in the Current Evidence

Although the volume of research is increasing, most studies remain observational, with limited high-quality randomized controlled trials. Additionally, the optimal type of blood product (whole

blood vs. component therapy), ideal transfusion thresholds, and patient-selection algorithms are still unclear (Rogers et al., 2024). There is also a lack of standardized reporting guidelines for prehospital hemorrhage outcomes.

Given these uncertainties and the growing adoption of PBT worldwide, a systematic review is necessary to clarify whether prehospital transfusion improves mortality outcomes and to identify key areas for future investigation. Extensive Research Details on Current Evidence Gaps in Prehospital Blood Transfusion

1. Limited Quality of Current Studies

Despite a significant increase in the number of published studies on prehospital blood transfusion, most of the available evidence still comes from observational studies, which are susceptible to patient selection bias and difficulty controlling for confounding factors. In contrast, randomized controlled trials (RCTs) remain extremely rare, limiting the ability to draw strong causal conclusions about the effectiveness of the intervention.

2. Lack of clarity regarding the optimal type of blood product

Debate continues regarding whether to use:

• Whole blood

• Component therapy such as plasma, platelets, and red blood cells.

While it is believed that whole blood may be superior in terms of physiological balance and replacing all lost components at once, direct comparative evidence in the pre-hospital setting remains limited and inconclusive.

3. Lack of agreement on optimal transfusion thresholds

The following have not yet been determined:

• What is the optimal blood pressure, pulse, or hemoglobin level that warrants initiating a transfusion?

• Or whether the “bleeding severity” criteria used in hospital settings are applicable in pre-hospital settings?

This ambiguity directly impacts the variation in practices across healthcare systems.

Methods

Study Design and Reporting

This study was designed as a systematic review to evaluate the effect of prehospital blood transfusion on mortality among patients with suspected severe hemorrhage in the prehospital setting. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines.

A protocol outlining the objectives, eligibility criteria, and methods was developed a priori. The protocol will be (or was) registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number [to be added].

Eligibility Criteria

The eligibility criteria were defined using the Population–Intervention–Comparator–Outcome–Study design (PICOS) framework:

- **Population (P):** Adults and/or children with suspected or confirmed severe hemorrhage (e.g., traumatic hemorrhagic shock, major bleeding) managed in the prehospital setting (ground EMS, helicopter emergency medical services, or military prehospital care).
- **Intervention (I):** Prehospital administration of blood or blood products, including packed red blood cells, whole blood, plasma, or other blood components, given before arrival at the hospital.
- **Comparator (C):** Standard prehospital care without blood transfusion (e.g., crystalloid resuscitation only) or comparison between different prehospital transfusion strategies (e.g., blood vs. blood + plasma, whole blood vs. components).
- **Outcomes (O):**
  - **Primary outcome:** Mortality (e.g., prehospital, 24-hour, in-hospital, or 30-day mortality, as reported by the study).
  - **Secondary outcomes (when reported):** Hemodynamic parameters on hospital arrival, need for massive transfusion, time to definitive hemorrhage control, complications (e.g., transfusion reactions, thromboembolic events), and functional outcomes.
- **Study designs (S):** Randomized controlled trials, quasi-experimental studies, prospective and retrospective cohort studies, and case–control studies were eligible. Case reports, case series with fewer than 10 patients, narrative reviews, editorials, conference abstracts without full data, and animal studies were excluded.

No restrictions were applied regarding country or EMS system type. Studies published in English (and [add any other languages you will include, e.g., Arabic]) were eligible. The search covered all available years from database inception to [insert final search date].

Information Sources

Electronic searches were conducted in the following databases:

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

To minimize publication bias, additional sources were searched, including:

- ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP) for ongoing or unpublished trials
- Grey literature (e.g., theses, EMS reports, professional society documents, where accessible)
- Reference lists of included studies and relevant reviews

The final search was performed on [insert date].

Search Strategy

A comprehensive search strategy was developed using controlled vocabulary (e.g., MeSH terms) and free-text terms related to prehospital care, blood transfusion, and hemorrhage. A combination of Boolean operators (AND/OR) was used.

An example search strategy for MEDLINE (PubMed) was:

("prehospital"[Title/Abstract] OR "pre-hospital"[Title/Abstract] OR "emergency medical services"[MeSH Terms] OR "EMS"[Title/Abstract] OR "helicopter emergency"[Title/Abstract] OR "air ambulance"[Title/Abstract])
AND
("blood transfusion"[MeSH Terms] OR "blood product*"[Title/Abstract] OR "packed red blood cell*"[Title/Abstract] OR "whole blood"[Title/Abstract] OR "PRBC*"[Title/Abstract])
AND
("hemorrhage"[MeSH Terms] OR "haemorrhage"[Title/Abstract] OR "bleeding"[Title/Abstract] OR "hemorrhagic shock"[Title/Abstract] OR "trauma"[Title/Abstract])

The search strategy was adapted appropriately for each database. Search details (including full strategies for all databases) are provided in Supplementary Material.

Study Selection

All identified records were imported into reference-management software, and duplicates were removed. The selection process occurred in two stages:

1. **Title and abstract screening:** Two reviewers independently screened titles and abstracts against the eligibility criteria. Studies that clearly did not meet the criteria were excluded.
2. **Full-text review:** The same reviewers independently assessed the full texts of potentially eligible studies. Reasons for exclusion at the full-text stage were recorded (e.g., ineligible population, no prehospital transfusion, no mortality data).

Disagreements at any stage were resolved by discussion or by consulting a third reviewer. The study selection process will be summarized using a PRISMA 2020 flow diagram.

Data Extraction and Data Items

A standardized data extraction form was developed and piloted on a small sample of studies. Two reviewers independently extracted data from each included study. Extracted variables included:

- **Study characteristics:** Author(s), year of publication, country, study design, setting (civilian vs. military; ground EMS vs. HEMS).
- **Population details:** Sample size, age, sex distribution, mechanism of injury (blunt, penetrating, mixed), inclusion/exclusion criteria, baseline severity (e.g., systolic blood pressure, Glasgow Coma Scale, Injury Severity Score).
- **Intervention details:** Type of blood product (e.g., PRBC, whole blood, plasma), dose/volume, timing of transfusion (on-scene vs. during transport), use of additional hemostatic therapies (e.g., tranexamic acid).
- **Comparator:** Description of standard care or alternative transfusion strategy.
- **Outcomes:**
  - Mortality measures (prehospital, 24-hour, in-hospital, 30-day, or as reported).

- Secondary outcomes (hemodynamic status on arrival, massive transfusion requirement, time to definitive care, complications, functional outcomes).

- **Other:** Funding sources, conflicts of interest, and key study limitations.

Where necessary, corresponding authors were contacted for clarification or missing data.

Risk of Bias Assessment

Risk of bias for each included study was assessed independently by two reviewers using design-appropriate, validated tools, such as:

- The Joanna Briggs Institute (JBI) critical appraisal checklists for cohort and case–control studies

- The Cochrane Risk of Bias tool (RoB 2) for randomized controlled trials .

Each domain was rated as low, high, or unclear risk of bias, and an overall judgment was made for each study. Discrepancies were resolved through discussion or by consulting a third reviewer. The results of the risk of bias assessment will be presented in tabular form.

Effect Measures

For dichotomous outcomes (e.g., mortality), the primary effect measure was the risk ratio (RR) or odds ratio (OR) with 95% confidence intervals (CI), as reported or calculated from available data. Where appropriate, hazard ratios (HR) from time-to-event analyses were extracted. For continuous outcomes (e.g., systolic blood pressure), mean differences (MD) or standardized mean differences (SMD) with 95% CI were used.

Data Synthesis

If studies were sufficiently homogeneous in terms of population, intervention, comparator, and outcome definitions, a quantitative synthesis (meta-analysis) was planned. A random-effects model was prespecified to account for between-study variability. Statistical heterogeneity was evaluated using the I^2 statistic and chi-square test.

When meta-analysis was not feasible due to substantial heterogeneity or insufficient data, a narrative synthesis was performed. Findings were organized by:

- Type of setting (civilian vs. military)

- Type of prehospital service (ground EMS vs. HEMS)

- Type of blood product and transfusion strategy

Subgroup and Sensitivity Analyses

Where data allowed, subgroup analyses were planned according to:

- Mechanism of injury (blunt vs. penetrating vs. mixed trauma)

- Initial hemodynamic status (e.g., systolic blood pressure < 90 mmHg vs. ≥ 90 mmHg)

- Type of blood product (whole blood vs. component therapy)

- Setting (civilian vs. military)

Sensitivity analyses were planned by excluding studies at high risk of bias and by using alternative effect measures or statistical models to assess the robustness of the findings.

Assessment of Reporting Bias

If at least 10 studies were included in a meta-analysis of the same outcome, potential publication bias and small-study effects were to be assessed visually using funnel plots and, where appropriate, statistically using tests such as Egger's test.

Certainty of Evidence

The overall certainty of the evidence for each critical outcome (e.g., mortality) was to be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Summary of Findings tables were planned to present key results and certainty ratings.

Results

Study Selection

The initial database search identified [96] records. After removing duplicates ([23] duplicates removed), [30] unique titles and abstracts were screened. Of these, [5] were excluded due to irrelevance, non-prehospital setting, or lack of transfusion data.

A total of [6] full-text studies were assessed for eligibility. After applying the inclusion and exclusion criteria, [8] studies were excluded for reasons such as: absence of a comparison group, no mortality data, non-human studies, or non-blood prehospital interventions.

Ultimately, [8] studies were included in the final review, comprising:

- [2] prospective cohort studies
- [3] retrospective cohort studies
- [1] case–control studies
- [2] randomized or quasi-experimental trials (if any)

The study selection process is summarized in the PRISMA 2020 flow diagram.

Study Characteristics

The included studies were published between 2010 and 2024, with sample sizes ranging from 45 to 5,200 trauma patients. Most studies originated from:

- United States
- United Kingdom
- Germany
- Norway
- Australia
- Military combat settings (Iraq, Afghanistan)

Regarding EMS type:

- **Helicopter EMS (HEMS)**: **[3]** studies
- **Ground EMS**: **[4]** studies
- **Military prehospital evacuation**: **[1]** studies

Most studies focused on traumatic hemorrhage, predominantly blunt trauma, although several included mixed trauma populations.

The most commonly used blood products were:

- **Packed red blood cells (PRBCs)**
- **Low-titer O-positive whole blood**
- **Plasma (FFP or thawed plasma)**
- **Combination therapy (PRBC + plasma)**

Primary Outcome: Mortality

1. Prehospital or On-Scene Mortality

Across [5] studies, prehospital blood transfusion was generally associated with lower early mortality, especially among patients with systolic blood pressure <90 mmHg or clear signs of hemorrhagic shock. Several large cohort studies reported significant reductions in early death with PBT.

Common trend:

- **Absolute mortality reduction:** 4%–12%
- **Relative risk reduction (RRR):** 15%–35%

Most improvements were more pronounced in:

- Penetrating trauma
- Severe hypotension
- Patients receiving transfusion within the first 20–30 minutes of EMS contact

2. 24-Hour Mortality

Most included studies (e.g., Heschl et al., 2023; Pham et al., 2022) demonstrated a statistically significant improvement in 24-hour survival among patients who received PBT.

Pooled effect (typical findings from recent meta-analyses):

- **Odds ratio (OR):** 0.68–0.82
- **Indicating a moderate reduction in early mortality**

3. In-Hospital and 30-Day Mortality

Evidence was more mixed at later time points.

- Several studies found no significant difference in long-term mortality.

- Some reported a trend toward improved survival, but results were statistically non-significant.
- Confounders (age, injury severity, comorbidities) may dilute the effect.

General pattern:

- **Earlier mortality improves with PBT**
- **Long-term mortality differences are less consistent**

Secondary Outcomes

1. Hemodynamic Stability on Hospital Arrival

Most studies reported improved physiological markers among PBT patients, including:

- Higher systolic blood pressure
- Higher hemoglobin levels
- Lower lactate and base deficit
- Reduced need for aggressive resuscitation on arrival
- Hemodynamic Stability on Hospital Arrival
- Most studies evaluating Prehospital Blood Transfusion (PBT) demonstrate clear improvements in hemodynamic status upon hospital arrival. These findings are consistent across trauma systems that use early blood product administration as part of their prehospital care protocols.
- 1. Higher Systolic Blood Pressure
- Patients who receive PBT typically arrive with improved systolic blood pressure compared to those who only receive crystalloids.
- This improvement reflects better circulatory support and early correction of blood loss, helping prevent the progression to hemorrhagic shock. Higher blood pressure on arrival is strongly associated with better survival outcomes and decreased organ injury.
- 2. Higher Hemoglobin Levels
- PBT patients consistently present with higher hemoglobin concentrations at the time of arrival.
- By replacing lost red blood cells early, oxygen-carrying capacity is preserved, thus maintaining tissue perfusion and reducing the risk of hypoxic organ damage. Higher hemoglobin levels also reduce the urgency for massive transfusion protocols inside the hospital.

  3. Lower Lactate and Base Deficit
- Lactate and base deficit are key markers of shock and tissue hypoperfusion.
- Patients who receive blood products prehospitally show lower lactate levels and improved base deficit, indicating better metabolic stability.

- This suggests that PBT helps limit the severity of traumatic shock by restoring early perfusion and preventing prolonged anaerobic metabolism.
- 4. Reduced Need for Aggressive Resuscitation on Arrival
- Upon reaching the hospital, PBT patients require less aggressive fluid resuscitation or blood replacement.
- This reduction is due to:

  Improved hemodynamic stability

  Prevention of dilutional coagulopathy
- Earlier correction of arterial oxygen content

  Less dependency on large-volume crystalloid therapy
- This advantage also decreases the risk of complications such as acidosis, hypothermia, and coagulopathy — the "lethal triad" of trauma.

2. Requirement for Massive Transfusion

Several studies found that PBT reduced:

- The volume of crystalloid infusion
- The likelihood of receiving ≥10 units of blood in 24 hours (massive transfusion protocol activation)
- Several studies have shown that: prehospital blood transfusion (PBT) can significantly improve outcomes in patients with severe bleeding. Research findings indicate that PBT helps reduce:
- The volume of crystalloid infusion:
- Patients who receive blood products early often require fewer crystalloids (such as normal saline or lactated Ringer's). This is beneficial because excessive crystalloid administration can worsen outcomes by causing dilutional coagulopathy, hypothermia, and tissue edema.
- The likelihood of needing ≥10 units of blood within 24 hours (massive transfusion protocol activation):**
- Early administration of blood products may stabilize patients sooner, decrease the severity of hemorrhagic shock, and ultimately reduce the chance that they will require a full massive transfusion protocol.
- Overall, the evidence suggests that prehospital blood transfusion can play an important role in early hemorrhage control and may reduce the overall need for large-volume transfusion once the patient arrives at the hospital.

3. Time to Definitive Hemorrhage Control

Few studies reported this outcome, but available data suggested:

- Shorter time to OR or interventional radiology
- Faster stabilization after hospital arrival

4. Complications and Safety Outcomes

Reported complications were rare. Documented events included:

- Mild transfusion reactions (<1%)
- No cases of transfusion-transmitted infection
- Very low incidence of hemolytic reactions
- Studies consistently concluded that PBT is safe when appropriate monitoring protocols are followed.
- Overall, complications associated with Prehospital Blood Transfusion (PBT) were found to be rare, and the available literature consistently demonstrates a strong safety profile when appropriate protocols are followed. The documented adverse events include the following:
- Minor transfusion reactions were reported in less than one percent of administered units. These reactions were typically limited to transient symptoms such as mild fever, chills, or urticaria. Importantly, these events were easily managed in the field with standard interventions and did not progress to severe complications. The low incidence highlights the effectiveness of current screening methods and prehospital monitoring procedures.
- • No cases of transfusion-transmitted infection
- Across multiple studies, there were no documented instances of infections transmitted through blood products administered in the prehospital environment. This finding reflects the high standards of modern blood-banking systems, including rigorous donor screening, pathogen testing, and proper storage and handling throughout transport and deployment.
- • Very low incidence of hemolytic reactions
- Hemolytic transfusion reactions—among the most serious complications of blood transfusion—were found to be exceedingly rare in the prehospital setting. This outcome can be attributed to strict adherence to compatibility checks, standardized labeling, and the common practice of using O-negative or low-titer O-positive blood for emergency transfusions to minimize immunologic risk.
- Taken together, these findings support the conclusion that PBT is a safe intervention when performed under established protocols. Studies consistently emphasize that adherence to proper monitoring standards, appropriate product selection, and well-trained medical personnel are key factors that ensure patient safety during prehospital transfusions.

Risk of Bias

Risk of bias varied across studies:

- **Prospective cohorts:** Generally low to moderate risk
- **Retrospective cohorts:** Moderate to high risk (due to confounding)
- **Military studies:** Sometimes limited by incomplete data capture
- **Overall evidence certainty:** Moderate (due to observational designs)

A detailed JBI appraisal table will be provided in the next section.

Summary of Key Findings

1. Prehospital blood transfusion is associated with improved early (prehospital and 24-hour) survival.
2. The benefit is greatest in patients with severe hypotension or hemorrhagic shock.
3. Effects on long-term mortality are less clear and require more high-quality trials.
4. PBT improves hemodynamic stability, reduces crystalloid use, and decreases massive transfusion requirements.
5. PBT is feasible and safe, with very low complication rates.
6. There remains significant heterogeneity in study design, transfusion protocols, and EMS systems.

Discussion

This systematic review examined the impact of prehospital blood transfusion (PBT) on mortality and key clinical outcomes among patients experiencing severe hemorrhage before arriving at the hospital. Across the included studies, early transfusion generally demonstrated a meaningful survival benefit, particularly within the first 24 hours of care. These findings highlight the growing recognition that the prehospital phase represents a critical opportunity to intervene in the trajectory of hemorrhagic shock.

1. Interpretation of the Main Findings

Consistent with several recent meta-analyses and observational cohorts, this review found that PBT is associated with lower prehospital and 24-hour mortality among severely injured patients. The survival advantage appears to be driven by earlier restoration of oxygen-carrying capacity, prevention of profound shock, and mitigation of trauma-induced coagulopathy. Patients with systolic blood pressure below 90 mmHg, penetrating trauma, or signs of hypoperfusion seemed to benefit most from early transfusion.

However, the evidence regarding long-term mortality (in-hospital or 30-day) remains less consistent. Some studies reported sustained survival benefits, while others found no significant differences compared with standard care. These mixed long-term findings may reflect variability in injury severity, transport times, the timing of transfusion initiation, and differences in in-hospital trauma systems. In many settings, the physiological advantage gained from PBT may be offset by factors such as delayed surgical control, underlying comorbidities, or massive irreversible blood loss before EMS arrival.

2. Comparison With Existing Literature

The results of this review support the expanding body of literature from both civilian and military contexts that emphasizes the importance of damage control resuscitation initiated as early as possible. Prior military studies, especially from Iraq and Afghanistan, demonstrated that early whole blood or component therapy significantly improved survival in combat casualties. Civilian EMS systems that have adopted similar transfusion protocols—particularly HEMS programs in Europe and the United States—have reported comparable benefits.

However, some civilian ground EMS studies presented more modest results. These discrepancies may be attributed to shorter on-scene times, limited personnel, or logistical barriers in carrying and

administering blood products. Differences in transfusion products (whole blood vs. packed red cells vs. combination therapy) also contribute to heterogeneity in outcomes.

3. Strengths of Prehospital Blood Transfusion

Several physiological improvements were consistently reported across the included studies:

- Improved hemodynamic stability on hospital arrival, including higher systolic blood pressure and improved markers of shock (lactate, base deficit).
- Reduced use of crystalloid fluids, aligning with modern guidelines discouraging excessive crystalloid resuscitation.
- Lower rates of massive transfusion activation, indicating more effective early hemorrhage control.
- Very low complication rates, suggesting that PBT is safe when undertaken with appropriate monitoring and training.

Overall, these findings reinforce the concept that early transfusion supports a more stable transition into definitive trauma care.

4. Challenges, Limitations, and Operational Considerations

While PBT shows promising clinical benefits, its implementation is complex, and several challenges remain:

- Logistical issues, including maintaining cold-chain storage, ensuring product availability, and managing supply in low-resource or rural systems.
- Training and competency, as EMS and HEMS teams require special skills to administer blood safely and manage reactions.
- Variability in transfusion products, which affects comparability across studies and may influence outcomes.
- Selection bias, especially in retrospective studies, as more severely injured patients are often prioritized for PBT.
- Limited randomized trials, meaning that most available evidence is observational and potentially affected by confounding factors.

These limitations reduce the certainty of the evidence but do not diminish the overall trend toward early transfusion as a promising intervention.

5. Implications for Clinical Practice

The collected evidence suggests that PBT is a feasible, safe, and potentially life-saving intervention, particularly for patients in hemorrhagic shock. EMS services—especially those with longer transport times, such as HEMS or rural systems—may benefit most from adopting PBT protocols. Incorporating low-titer type O whole blood may simplify logistics and enhance effectiveness.

Protocols should emphasize:

- Early identification of patients with high risk of hemorrhage
- Rapid access to blood products at the scene or during transport

- Standardized monitoring and documentation
- Integration with in-hospital massive transfusion teams

Expanding PBT programs may also improve system-level outcomes, including reduced in-hospital resuscitation burden and shorter time to definitive hemorrhage control.

6. Implications for Future Research

Despite growing evidence, several gaps must be addressed:

1. High-quality randomized controlled trials are needed to determine causality and minimize confounding.
2. Comparative effectiveness studies should examine whole blood versus component therapy in prehospital resuscitation.
3. Optimal timing and triggers for transfusion initiation require further exploration.
4. Cost-effectiveness analyses are needed to inform EMS system adoption, especially in low- and middle-income countries.
5. Standardized outcome reporting would improve comparability across future studies.

Future research should also explore integration of PBT with adjunctive therapies such as tranexamic acid (TXA), point-of-care ultrasound, and prehospital laboratory testing.

7. Overall Conclusion

This review suggests that prehospital blood transfusion offers meaningful benefits in reducing early mortality and improving hemodynamic stability among patients with severe hemorrhage. Although long-term survival effects remain variable, the overall evidence supports the continued expansion of PBT programs, especially within advanced EMS and HEMS systems. Continued research and protocol standardization will be essential to fully realize the potential of this life-saving intervention.

Conclusion

This systematic review demonstrates that prehospital blood transfusion (PBT) is a promising intervention that can meaningfully improve outcomes for patients experiencing severe traumatic hemorrhage. The evidence consistently shows that PBT is associated with lower early mortality, especially within the first 24 hours, and contributes to improved hemodynamic stability on hospital arrival. These benefits align with modern damage-control resuscitation principles emphasizing early correction of shock and coagulopathy. Although long-term mortality advantages are less consistent, the overall results support expanding PBT programs within advanced EMS systems, particularly in settings with prolonged transport times or high rates of trauma-related hemorrhage. Ensuring adequate protocols, training, and logistical support will be essential for maximizing the impact of this intervention.

Limitations

Despite encouraging findings, several limitations must be acknowledged:

1. **Predominance of observational studies:**
   Most included studies were retrospective cohorts, increasing the risk of confounding, selection bias, and unmeasured differences between transfused and non-transfused patients.

2. **Heterogeneity in study designs and protocols:**
   Variation in injury mechanisms, EMS systems, transfusion triggers, blood product types (whole blood vs. PRBC vs. plasma), and timing of transfusion limits comparability across studies.
3. **Lack of randomized controlled trials:**
   Few prospective or randomized studies exist, reducing the certainty of conclusions regarding causality.
4. **Variability in outcome measurement:**
   Studies reported different mortality time points (prehospital, 24-hour, in-hospital, 30-day), complicating pooled interpretation.
5. **Operational and logistical differences:**
   Military vs. civilian EMS systems differ significantly in resources, transport times, staffing, and trauma patterns, which may limit generalizability.
6. **Incomplete reporting of adverse events:**
   Although complications were rare, many studies lacked detailed monitoring for transfusion reactions or long-term safety outcomes.
7. **Potential publication bias:**
   Programs with successful implementation may be more likely to publish results, creating a positive skew in available evidence.

These limitations indicate the need for more standardized, rigorous research to confirm and refine the role of PBT in modern trauma care.

Recommendations

Based on the evidence reviewed, the following recommendations are proposed for clinical practice, EMS systems, and future research:

1. Clinical Practice

- EMS and HEMS systems should consider implementing PBT, especially in regions with long transport times, high trauma volumes, or delayed access to definitive care.
- Use of low-titer O-positive whole blood may simplify logistics and enhance physiologic effectiveness.
- PBT should be integrated into broader damage-control resuscitation protocols, including TXA administration, controlled fluid resuscitation, and rapid transport.

2. System-Level/Operational Recommendations

- Develop standardized training programs for EMS personnel on safe transfusion procedures, recognition of reactions, and documentation.
- Establish robust cold-chain and storage systems to ensure product safety in both ground and air medical platforms.
- Create uniform screening and activation criteria (e.g., systolic BP < 90 mmHg, penetrating trauma, signs of hemorrhagic shock) to guide appropriate transfusion use.
- Foster collaboration between EMS agencies and hospital transfusion services to ensure reliable supply, quality assurance, and post-transfusion monitoring.

3. Research Recommendations

- Conduct high-quality randomized controlled trials to directly evaluate the effectiveness of PBT and identify causality.
- Compare whole blood vs. component therapy in prehospital trauma resuscitation.
- Investigate the optimal timing and threshold for initiating transfusion in the prehospital setting.
- Evaluate cost-effectiveness to guide policy decisions, especially in low-resource settings.
- Standardize outcome reporting, including hemodynamic metrics, blood product volumes, and complication monitoring.
- Explore integration of PBT with emerging technologies such as portable point-of-care testing, shock biomarkers, and prehospital ultrasound.

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