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CLINICAL PREHOSPITAL INTERVENTIONS IN TRAUMA CARE: A SYSTEMATIC LITERATURE REVIEW

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ABSTRACT

Trauma remains a leading cause of mortality and disability worldwide, particularly among working-age individuals. A significant proportion of trauma deaths occur during the early post-injury period, underscoring the critical need for effective prehospital interventions. Various strategies including airway management, hemorrhage control, blood product resuscitation, oxygen therapy, and pharmacological treatments have been implemented, though their efficacy varies across studies. This study aims to identify and classify prehospital clinical interventions for trauma patients, assess the quality and strength of the evidence, and determine evidence gaps and their implications for clinical practice and trauma system policy. This systematic review adhered to PRISMA 2020 guidelines, searching in database Scopus (2020-2026) for studies on trauma patients receiving prehospital interventions (RCTs/cohort studies) reporting outcomes such as mortality, survival to discharge, hemodynamic stability, complications, or length of hospital stay. Methodological quality was assessed using Joanna Briggs Institute tools, with narrative synthesis due to study heterogeneity. Of 1,877 records, seven studies met inclusion criteria, primarily RCTs from high-income countries. Tranexamic acid (TXA) was most frequently studied, demonstrating reduced 28-day mortality and transfusion requirements without increased thromboembolic risk. Prehospital blood product resuscitation and oxygen therapy strategies yielded mixed or neutral findings. Prehospital TXA administration provides the most consistent survival benefit for bleeding trauma patients. Further high-quality research is needed to optimize other prehospital interventions and strengthen evidence-based trauma systems.

Keywords: emergency medical services; life-saving interventions; prehospital trauma care; systematic literature review; trauma guidelines

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INTRODUCTION

Trauma represents a leading cause of mortality and disability worldwide, particularly among individuals of working age, and constitutes a substantial contributor to the global burden of disease. Globally, injuries account for over five million deaths annually, representing a significant proportion of years of life lost (YLL) and years lived with disability (YLD) (World Health Organization (Vos et al., 2020; WHO, 2018). Beyond mortality, trauma imposes long-term social and economic consequences, especially in low- and middle-income countries (LMICs), where healthcare systems and emergency infrastructure remain (Vos et al., 2020)

Trauma-related deaths often follow a trimodal distribution, with a substantial proportion occurring during the early post-injury phase, including the "golden hour" within the first hour (Søreide, 2009). This pattern underscores the critical role of the prehospital phase the period from injury occurrence to definitive hospital care in determining clinical outcomes. Prehospital clinical interventions aim to prevent secondary injury, maintain vital organ perfusion, and stabilize life-threatening conditions prior to hospital-based definitive management (Lockey et al., 2015)

Physiologically, early trauma mortality primarily results from airway obstruction, hypoxia, and uncontrolled massive hemorrhage—conditions that are largely preventable through rapid, targeted interventions (Kauvar et al., 2006). Accordingly, various prehospital strategies have been developed, including advanced airway management, hemorrhage control via direct pressure or tourniquets, fluid resuscitation, tranexamic acid (TXA) administration, and spinal immobilization (collaborators, 2010; Morrison et al., 2012) The landmark CRASH-2 trial demonstrated that TXA administration within three hours of injury significantly reduced mortality among patients with substantial bleeding (collaborators, 2010) providing compelling evidence that evidence-based early interventions can improve trauma survival.

Nevertheless, evidence regarding the effectiveness of diverse prehospital clinical interventions for trauma patients remains substantially heterogeneous. Randomized controlled trials (RCTs) in the prehospital setting are relatively scarce due to ethical, logistical, and operational challenges (Björklund et al., n.d.) Much of the available literature comprises observational studies characterized by variable designs, populations, and outcome measures, complicating consistent interpretation and generalizability across healthcare systems.

Moreover, significant disparities exist in emergency medical services (EMS) structure and capacity across countries. High-income countries typically feature structured EMS systems with trained personnel and standardized protocols, whereas many LMICs face limitations in training, referral integration, and medical resources (Joshipura et al., 2004; WHO, 2018) These contextual variations likely influence both the implementation and effectiveness of prehospital interventions, limiting the direct applicability of findings from one setting to another. Although several reviews have addressed specific aspects of trauma management, a comprehensive synthesis systematically evaluating the full spectrum of prehospital clinical interventions across study designs and healthcare contexts remains lacking. This evidence integration gap contributes to clinical practice variability, inconsistent trauma system policies, and potential overuse of interventions lacking robust high-quality support.

Research Question: What prehospital clinical interventions are employed in trauma patient management, and what is the strength and consistency of evidence regarding their effectiveness on key clinical outcomes, including mortality, hemodynamic stability, complications, time to definitive care, and functional outcomes?. This systematic review aims to systematically identify and classify prehospital clinical interventions for trauma patients, evaluate methodological quality and evidence strength, and synthesize findings to identify evidence gaps and implications for clinical practice and trauma system policy development. Through a rigorous, transparent approach, this review seeks to provide a stronger scientific foundation for global optimization of prehospital trauma care.

METHOD

Study Design

This systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency and reproducibility in reporting (Page et al., 2021) PRISMA 2020 emphasizes comprehensive documentation from search strategy to result synthesis, enhancing the quality and credibility of systematic reviews (Cumpston et al., 2019)

Eligibility Criteria (PICOS Framework)

Inclusion criteria were defined using the PICOS framework (Population, Intervention, Comparator, Outcome, Study Design) (Page et al., 2021) The population comprised trauma patients receiving prehospital management, without restriction on trauma mechanism, provided interventions occurred prior to arrival at definitive care facilities.

Interventions included prehospital clinical procedures such as advanced airway management, oxygen therapy, hemorrhage control (e.g., tourniquets or hemostatic dressings), fluid resuscitation, tranexamic acid (TXA) administration, spinal immobilization, needle thoracostomy, prehospital analgesia, and other Advanced Life Support (ALS) measures. Comparators encompassed standard care or alternatives, including Basic Life Support (BLS), no specific intervention, delayed in-hospital interventions, or comparisons between prehospital strategies.

Primary outcomes were mortality (prehospital, 24-hour, or 30-day) and survival to hospital discharge. Secondary outcomes included neurological function, hemodynamic stability, complications, and length of hospital stay. Eligible designs were randomized controlled trials (RCTs) and analytical cohort studies reporting at least one relevant clinical outcome. Editorials, reviews, and studies lacking clear clinical outcomes were excluded. Publications were limited to January 2020–October 2026, with only peer-reviewed full-text articles included.

Literature Search Strategy

A systematic search was performed across international electronic databases, specifically Scopus, targeting articles published from 2020 to 2026 to ensure evidence currency. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords using Boolean operators (Rethlefsen et al., 2021) Key terms included: "prehospital care," "prehospital intervention," "trauma," "trauma care," "emergency medical services," "clinical intervention," "hemorrhage control," "airway management," and "tranexamic acid." Strategies were adapted to each database's syntax.

Inclusion and Exclusion Criteria

Inclusion criteria were: (1) studies evaluating prehospital clinical interventions in trauma patients; (2) RCTs, cohort studies, or analytical cross-sectional designs; (3) English-language articles; and (4) accessible full-text publications. Exclusions comprised: (1) editorials, commentaries, letters, or reviews; (2) studies not specifically addressing prehospital interventions; (3) non-trauma populations; or (4) unclear clinical outcome data. (Moola, 2017)

Study Selection Process

Study selection proceeded in stages. Initial search results were exported to reference management software for deduplication, followed by title/abstract screening against inclusion/exclusion criteria. Potentially eligible full texts underwent detailed evaluation.(Stoll et al., 2019). Selection was conducted independently by two reviewers, with discrepancies resolved through discussion to achieve consensus. The selection flowchart was reported per PRISMA guidelines.

Data Extraction

Data from eligible studies were systematically extracted using a pre-developed form, capturing: author/year, study country, design, sample size, population characteristics, prehospital intervention type, comparator (if applicable), primary outcomes, and key findings. Extraction was performed independently by two reviewers to ensure accuracy and consistency.

Methodological Quality Assessment and Risk of Bias

Methodological quality was appraised using Joanna Briggs Institute (JBI) critical appraisal tools. RCTs were assessed with the JBI Checklist for Randomized Controlled Trials; cohort and analytical cross-sectional studies used corresponding JBI checklists(Moola, 2017). JBI tools evaluate domains including randomization method, allocation concealment, baseline comparability, blinding, outcome measurement validity, confounder control, follow-up completeness, and statistical analysis appropriateness. Items were scored as "Yes," "No," "Unclear," or "Not Applicable." Assessments were conducted independently by two reviewers, with discrepancies resolved via discussion. Studies with high risk of bias were included but interpreted cautiously in synthesis.

Data Synthesis

Data were analyzed descriptively and synthesized narratively by prehospital intervention type. Interventions were categorized (e.g., airway management, hemorrhage control, pharmacological agents like TXA, initial stabilization). Synthesis compared intervention effectiveness against clinical outcomes such as mortality, hemodynamic stability, time to definitive care, and complications. Heterogeneity in study design, interventions, and outcomes precluded meta-analysis.

RESULT

Study Selection

The literature search in Scopus yielded 1,877 unique records. Following initial screening by publication year, language, full-text availability, and document type, 24 articles met preliminary criteria as randomized controlled trials (RCTs). Full-text evaluation using the PICOS framework then excluded 17 articles due to misalignment with intervention or outcome criteria. (Cohen, 1960) Ultimately, seven studies satisfied all inclusion criteria and were included in the qualitative synthesis (Figure 1, PRISMA Flow Diagram).

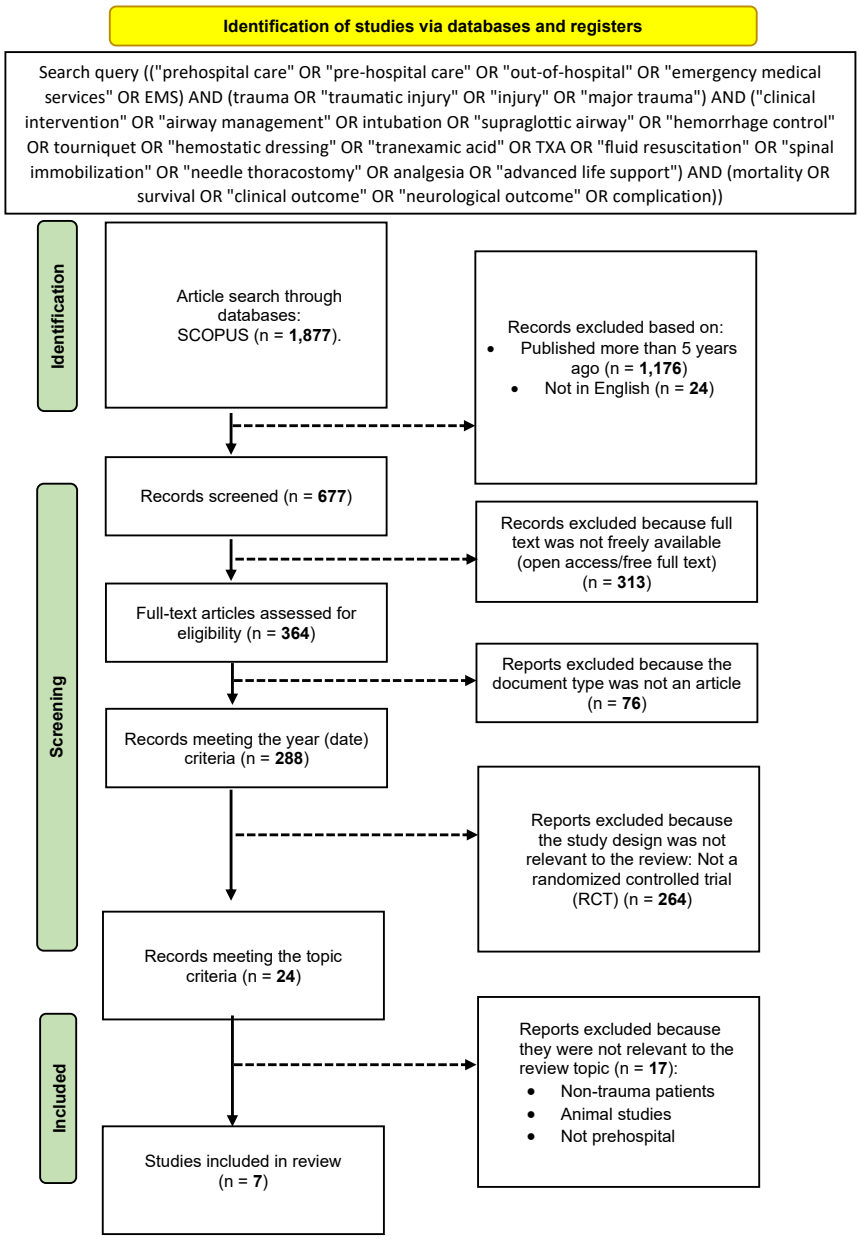

Figure 1. PRISMA Flow Diagram

Table 1.
Characteristics of Included Studies

Author & Year	Country/ Setting	Population	Intervention	Comparison	Outcomes	Study Design	Key Findings	Limitations
(Doughty et al., 2022)	United Kingdom	Adults ≥16 years with trauma-related hemorrhagic shock (SBP ≤90 mmHg or absent radial pulse), assessed by prehospital critical care teams	Prehospital PRBC + lyophilized plasma (≤2 units each) IV/IO via fluid warmer	0.9% sodium chloride (up to 1 L; 250 mL boluses)	Primary: Composite episode mortality or impaired lactate clearance (≤20%/h at 2 h). Secondary: 3/30-day mortality, ARDS, VTE, transfusion	Multicentre, allocation-concealed, open-label, parallel-group phase 3 RCT	No significant difference in primary outcome; 30-day mortality comparable	Early termination (COVID-19); open-label; composite primary outcome criticized
(Tamura et al., 2023)	Japan	Ages 20–80 years, comatose post-cardiogenic OHCA (trauma-OHCA excluded)	2% inhaled hydrogen (H_2) + titrated O_2 for 18 h	O_2 alone (placebo-controlled)	Primary: CPC 1–2 at 90 days. Secondary: mRS, 90-day survival, GCS, MMSE, AE/SAE	Multicentre, double-blind, placebo-controlled RCT	CPC 1–2 nonsignificant; improved mRS and 90-day survival in H_2 group	Not trauma-specific; early termination; limited generalizability
(Mitra et al., 2021)	Australia, New Zealand, Germany	Adults with severe trauma at risk of acute traumatic coagulopathy (COAST ≥3), ≤3 h post-injury	TXA 1 g IV bolus prehospital + 1 g over 8 h	Placebo (0.9% NaCl)	Primary: GOSE at 6 months. Secondary: Mortality, VTE, ventilator-free days	International multicentre, double-blind RCT protocol	Strong design for mid-term functional outcomes	Protocol only; no efficacy results available
(Hinson et al., 2024)	Multicentre (U.S./Canada)	TBI subset with initial positive CT and follow-up CT	Predictive model for PICH/IPPICH using admission variables + biomarkers	N/A (no intervention comparator)	PICH/IPPICH; associations with GOSE, mortality, DRS	Secondary predictive analysis (machine learning)	IPPICH strongly linked to mortality/disability	No clinical intervention evaluation; requires external validation
(Steinmetz et al., 2025)	Denmark, Netherlands, Switzerland	Trauma patients triggering full trauma team activation	Restrictive oxygen strategy	Liberal oxygen strategy	Primary: Composite death/major respiratory complications at 30 days	Multicentre RCT	No significant primary outcome difference (OR ≈1.01)	Detailed outcomes in primary article; some exploratory results unreported
(Gruen et al., 2023)	USA	Trauma at hemorrhage risk (SBP ≤90 or HR ≥110)	Prehospital TXA 1 g; total doses 1–3 g	Placebo	Endothelial biomarkers; 30-day survival	Secondary analysis of RCT	TXA reduced syndecan-1; dose-response; lower biomarkers tied to survival	Biomarker primary endpoint; potential survival bias
(Mazzei et al., 2024)	USA	1,744 trauma patients (harmonized STAAMP & ROC-TXA)	Prehospital TXA (dose-response analysis)	Placebo	Primary: 28-day mortality. Secondary: 24-h RBC transfusion, VTE, seizure, stroke	Secondary analysis of 2 double-blind RCTs	TXA associated with lower 28-day mortality (HR 0.72); significant dose-response	Post hoc analysis; trial heterogeneity; possible VTE under-detection

Characteristics of Included Studies

The seven included studies encompassed trauma patients with diverse clinical profiles across varied emergency medical services (EMS) systems. Cumulatively, they involved over 2,500 participants, with the largest contribution from a harmonized analysis of two major U.S. trials (n = 1,744). All studies were conducted in high-income countries (United Kingdom, United States, Australia, New Zealand, Germany, Denmark, Netherlands, Switzerland), featuring structured trauma and EMS systems. Study designs primarily comprised randomized controlled trials (RCTs) and secondary RCT analyses, including one phase 3 RCT on prehospital blood products (RePHILL), one RCT on oxygen strategies, one international TXA RCT protocol (PATCH-Trauma), and secondary analyses from large trials (e.g., STAAMP; STAAMP–ROC TXA harmonization). Tranexamic acid (TXA) administration dominated evaluations, alongside prehospital blood product resuscitation and oxygen therapy.

Quality Assessment of Included Studies

Table 2.
Critical Appraisal JBI – RCT

Item	RePHILL	TRAUMOX2	PATCH-Trauma (Protocol)	HYBRID II
Brief design	RCT open-label; allocation concealed; ITT	Pragmatic RCT open-label; assessor-blinded; modified ITT (secondary exclusions)	Double blind RCT protocol (no results yet)	Double-blind RCT; early termination
Item 1	Y	Y	Y	Y
Item 2	Y	Y	Y	Y
Item 3	Y	Y	U	U
Item 4	N	N	Y	Y
Item 5	N	N	Y	Y
Item 6	Y	Y	Y	Y
Item 7	U	U	U	U
Item 8	Y	U	U	U
Item 9	Y	U	Y	Y
Item 10	Y	Y	Y	Y
Item 11	Y	Y	Y	Y
Item 12	Y	Y	Y	Y
Y (dari 12)	10	7	9	9
Persentase	83.3%	58.3%	75.0%	75.0%

Keterangan: Y=Yes, N=No, U=Unclear.

Table 3.
Critical Appraisal JBI – Cohort

Item	STAAMP biomarker secondary analysis	Harmonized TXA trials secondary analysis	Predicting progression of ICH
Tipe observasional yang dipakai untuk appraisal	Secondary analysis RCT untuk hubungan TXA–biomarker (Cohort-analytic)	Harmonized secondary analysis (gabungan 2 RCT; dianalisis sebagai cohort-analytic)	Cohort prediksi/prognostik (modeling)
Item 1	Y	U	Y
Item 2	Y	Y	U
Item 3	Y	Y	Y
Item 4	Y	Y	U
Item 5	Y	Y	NA
Item 6	NA	NA	Y
Item 7	Y	Y	Y
Item 8	Y	Y	Y
Item 9	U	U	Y
Item 10	U	U	Y
Item 11	Y	Y	Y
Y (dari 11)	7	6	8
Persentase	63.6%	54.5%	72.7%

Keterangan: Y=Yes, N=No, U=Unclear, NA=Not applicable

Methodological quality was evaluated using Joanna Briggs Institute (JBI) Critical Appraisal Tools tailored to each study's design. Four RCTs were appraised with the JBI Checklist for Randomized Controlled Trials; three secondary/observational analyses used the JBI Checklist for Cohort Studies. Items were scored as Yes (Y), No (N), Unclear (U), or Not Applicable (NA), with total scores reflecting overall quality) (Munn et al., 2019; Sterne et al., 2016)

Interpretation of Study Quality

RCTs generally demonstrated good methodological quality. The RePHILL trial achieved the highest score (10/12 items; 83.3%), despite limitations in blinding due to its open-label design. The PATCH-Trauma protocol and HYBRID II trials scored 75.0%, though PATCH-Trauma interpretation is constrained as it remains a protocol. TRAUMOX2 scored lower (58.3%) owing to unclear reporting in several domains and blinding limitations. Observational studies ranged from 54.5% to 72.7%. The study on predicting intracranial hemorrhage progression exhibited the highest quality (72.7%), while the two TXA secondary analyses scored lower due to unclear domains. Overall, RCTs provided primary causal evidence on prehospital intervention efficacy, with observational and secondary analyses offering supportive insights into biological mechanisms, clinical associations, and predictive modeling

Thematic Synthesis of Findings

Prehospital Blood Product Effectiveness

The RePHILL trial (Doughty et al., 2022) compared packed red blood cells (PRBCs) plus lyophilized plasma versus 0.9% sodium chloride resuscitation in hemorrhagic shock patients. No significant differences emerged in the composite primary outcome (mortality or lactate clearance) or 30-day mortality, indicating prehospital blood products were not superior to crystalloids in this context.

Tranexamic Acid (TXA) Effectiveness

TXA dominated the evidence base. Harmonized analysis of two large RCTs (Mazzei et al., 2024) linked prehospital TXA to reduced 28-day mortality (HR 0.72) and a dose-response relationship, alongside lower 24-hour red blood cell transfusion needs without independent increases in venous thromboembolism, seizures, or stroke. A secondary STAAMP analysis (Gruen et al., 2023) associated TXA with reduced endothelial biomarker levels (syndecan-1), supporting biological improvements in endothelial integrity and 30-day survival. The PATCH-Trauma protocol (Mitra et al., 2021) evaluates TXA's impact on 6-month functional outcomes (GOSE), though final results were unavailable.

Prehospital Oxygen Strategies

(Steinmetz et al., 2025) found no significant difference in the 30-day composite primary outcome (death or major respiratory complications; OR ≈1.0) or mortality between restrictive and liberal oxygen strategies, suggesting no clear clinical advantage for restrictive approaches in the studied population.

Mechanistic Evidence and Secondary Analyses

Secondary RCT analyses explored biological mechanisms and predictive associations. STAAMP biomarker findings reinforced TXA's endothelial benefits, indirectly supporting mortality reductions. A predictive study on intracranial hemorrhage progression highlighted early high-risk identification, though it did not directly assess interventions. Overall, thematic synthesis reveals consistent, replicated evidence for prehospital TXA benefits, whereas blood products and oxygen strategies yield neutral or inconclusive results.

DISCUSSION

This systematic review identified contemporary evidence on prehospital interventions for trauma patients. The seven included studies (predominantly randomized controlled trials) reflect the growing emphasis on high-quality evidence in prehospital trauma research (Björklund et al., n.d.). Tranexamic acid (TXA) emerged as the most consistently effective intervention, demonstrating reductions in mortality and transfusion requirements. Other interventions, such as blood product resuscitation and oxygen therapy, yielded heterogeneous results. The synthesis was conducted following established systematic review methodologies (Page et al., 2021; Cumpston et al., 2019).

TXA exhibited the strongest efficacy, with harmonized RCT analyses showing decreased 28-day mortality and dose-response relationships (Mazzei et al., 2024). Mechanistically, TXA inhibits fibrinolysis and ameliorates endothelial dysfunction (Gruen et al., 2023). Optimal benefits occur when administered within <3 hours post-injury, consistent with findings from the CRASH-2 trial (CRASH-2 collaborators, 2010) and supported by earlier trauma studies (Morrison et al., 2012). Integration into emergency medical services (EMS) protocols is therefore strongly recommended. The RePHILL trial found no significant differences in primary outcomes (mortality and lactate clearance) compared with crystalloid resuscitation (Doughty et al., 2022). However, results remain inconclusive due to temporal variations and limited sample size, partly influenced by early trial termination during the COVID-19 pandemic. Further large-scale RCTs are required to clarify the effectiveness of prehospital blood product administration.

Comparisons between restrictive and liberal oxygen strategies demonstrated no significant differences in mortality or major respiratory complications (Steinmetz et al., 2025). These findings suggest that individualized, physiology-guided oxygen therapy is preferable to avoid both hypoxia and hyperoxia-related complications. Prehospital TXA administration should be prioritized in EMS protocols for patients with suspected hemorrhagic trauma. Other interventions should be adapted based on local resources, system capacity, and contextual needs to optimize trauma care delivery globally (Joshipura et al., 2004). Several limitations warrant consideration. First, the limited number of eligible studies restricted the synthesis to selected interventions. Second, reliance on secondary analyses of RCTs necessitates cautious interpretation of causal relationships. Third, most included studies were conducted in high-income countries, limiting generalizability to low- and middle-income countries (LMICs), where trauma burden is disproportionately high (Vos et al., 2020; WHO, 2018).

Additionally, heterogeneity in study design, populations, and outcomes precluded meta-analysis, necessitating a narrative synthesis approach. Risk of bias and methodological variability were considered using established appraisal frameworks (Sterne et al., 2016; Munn et al., 2019). Despite promising findings, significant evidence gaps remain. Future large-scale RCTs should evaluate a broader range of prehospital interventions and assess long-term outcomes, including mortality, complications, and functional recovery. Implementation research in LMIC settings is essential, particularly focusing on resource constraints and system adaptability. Furthermore, translational research is needed to bridge the gap between evidence generation and integration into EMS practice. Strengthening the global trauma evidence base will support the development of more effective policies and standardized protocols for prehospital trauma management.

CONCLUSION

This systematic review synthesized contemporary evidence on prehospital clinical interventions for trauma management. Tranexamic acid (TXA) administration emerged as the most consistently supported intervention, reducing mortality in patients at risk of significant hemorrhage, particularly when delivered early in the prehospital phase. In contrast, prehospital blood product resuscitation and oxygen therapy strategies demonstrated heterogeneous results, warranting further investigation.

Overall, these findings underscore the pivotal role of rapid, evidence-based prehospital interventions in improving trauma outcomes. Integrating proven strategies into emergency medical services protocols holds substantial potential to reduce global trauma mortality and morbidity.

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