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# OPTIMIZING PREHOSPITAL HEMORRHAGE CONTROL: A REVIEW OF TRANEXAMIC ACID USE IN EMERGENCY MEDICAL SERVICES

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**Abstract:**

*Uncontrolled hemorrhage remains one of the leading causes of preventable death in trauma patients, particularly in the critical prehospital phase of care. Tranexamic acid (TXA), an antifibrinolytic agent, has emerged as a simple, cost-effective intervention to improve survival by reducing trauma-related bleeding. Landmark studies such as the CRASH-2 trial demonstrated significant reductions in mortality when TXA was administered early, with subsequent trials including MATTERs, STAAMP, and PATCH-Trauma expanding the evidence base to both military and civilian prehospital settings. The rationale for prehospital TXA administration lies in its time-sensitive mechanism, where early inhibition of fibrinolysis during the "golden hour" is most effective. Despite promising outcomes, implementation in emergency medical services (EMS) faces challenges, including variable protocols, dosing uncertainties, logistic barriers, and concerns regarding thromboembolic events. This review critically examines the current evidence, clinical outcomes, and barriers associated with prehospital TXA use, while exploring strategies for optimizing its role in EMS. By integrating TXA into standardized prehospital trauma protocols, supported by provider training and technological decision-support systems, EMS can further reduce hemorrhage-related mortality and enhance patient survival outcomes worldwide.*

***Keywords:*** *Tranexamic Acid; Prehospital Care; Trauma; Hemorrhage Control; Emergency Medical Services; Patient Outcomes; CRASH-2; MATTERs; EMS Protocols*

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## 1. INTRODUCTION:

Trauma remains one of the leading causes of mortality and disability worldwide, particularly among individuals under the age of 45 years (World Health Organization [WHO], 2018). Uncontrolled hemorrhage accounts for a substantial proportion of trauma-related deaths, often occurring in the prehospital setting before patients reach definitive care (Beekley, 2015). The concept of the "golden hour" underscores the importance of early interventions in trauma management, as survival outcomes are significantly influenced by the speed and quality of care delivered during this critical time frame (Ryb et al., 2017). Within this context, pharmacological agents that can be safely and effectively administered by emergency medical services (EMS) have attracted growing attention, with tranexamic acid (TXA) emerging as a pivotal therapeutic option.

TXA is a synthetic derivative of the amino acid lysine that functions as an antifibrinolytic by inhibiting the activation of plasminogen to plasmin, thereby stabilizing blood clots and reducing bleeding (Roberts & Shakur-Still, 2017). Its affordability, ease of administration, and proven effectiveness have led to widespread interest in its integration into trauma care protocols. The landmark CRASH-2 trial, which enrolled over 20,000 patients across 40 countries, demonstrated a significant reduction in all-cause mortality when TXA was administered within three hours of injury, with the greatest benefit observed when given within the first hour (CRASH-2 Collaborators, 2010). Following this, the MATTERs study conducted in military settings provided further evidence of TXA's survival benefit among combat casualties with severe hemorrhage (Morrison et al., 2012).

While the hospital-based use of TXA is now well established, its prehospital administration remains an evolving area of research and practice. Early administration has been consistently linked with improved outcomes, reinforcing the rationale for EMS personnel to initiate treatment at the scene of injury or during transport (Cole et al., 2020). Recent trials such as STAAMP and PATCH-Trauma have specifically examined prehospital TXA use, highlighting both potential survival benefits and areas of ongoing debate, including patient selection, optimal dosing, and risks of thromboembolic complications (Rowell et al., 2020; Gruen et al., 2023).

Despite the encouraging evidence, the integration of TXA into EMS practice is not without challenges. Variability in national and regional protocols, differences in EMS training, logistical issues related to drug storage and administration, and lingering safety concerns have limited universal adoption (Lau et al., 2017). Moreover, questions remain regarding its effectiveness in different trauma subgroups, including blunt versus penetrating injuries, pediatric and elderly populations, and patients with traumatic brain injury (Myburgh & Myles, 2019). These gaps underscore the need for ongoing investigation and refinement of guidelines.

This review seeks to provide a comprehensive overview of TXA's role in prehospital trauma care, with a focus on its pharmacological rationale, evidence base, clinical outcomes, and implementation in EMS systems. By critically appraising current research and identifying barriers and opportunities, the review aims to inform policy, practice, and future directions for optimizing prehospital hemorrhage control. Ultimately, integrating TXA into standardized EMS protocols has the potential to enhance trauma survival outcomes and reduce preventable deaths globally.

## 2. Mechanism and Rationale for Prehospital TXA Use

Hemorrhage following traumatic injury is characterized not only by blood loss but also by the development of trauma-induced coagulopathy (TIC), a condition that significantly worsens outcomes and increases mortality. TIC is driven by a complex interplay of hypoperfusion, endothelial damage, fibrinolytic activation, and inflammatory responses (Brohi et al., 2017). One of the hallmarks of TIC is hyperfibrinolysis, where excessive breakdown of fibrin clots leads to uncontrolled bleeding. This pathophysiological cascade provides the foundation for the use of tranexamic acid (TXA) in trauma management, particularly in the prehospital phase where rapid intervention can alter the trajectory of patient survival.

TXA is a synthetic derivative of lysine that acts as an antifibrinolytic by competitively inhibiting the binding of plasminogen to fibrin. This inhibition prevents plasmin formation, thereby stabilizing existing clots and reducing ongoing bleeding (Ker et al., 2012). Unlike procoagulant drugs that may heighten the risk of disseminated intravascular coagulation, TXA exerts its effect by preserving the patient's natural hemostatic mechanisms rather than promoting new clot formation. This pharmacological profile makes it particularly suitable for use in trauma, where coagulopathy rather than simple blood loss is the primary driver of mortality.

The rationale for prehospital administration of TXA is strongly tied to timing. Evidence from the CRASH-2 trial showed that administration within the first hour of injury resulted in the greatest reduction in mortality, with diminishing returns and potential harm when given beyond three hours (CRASH-2 Collaborators, 2010). This finding

underscores the importance of rapid delivery in the prehospital setting, where delays in transport or in-hospital initiation may compromise patient outcomes. EMS providers are uniquely positioned to deliver TXA at the scene or during transport, effectively extending the therapeutic window and maximizing survival benefits.

Hemorrhage control is one of the cornerstones of trauma management, alongside airway stabilization and fluid resuscitation. Traditional prehospital hemorrhage control strategies include tourniquets, hemostatic dressings, and fluid therapy, but these measures alone may not adequately address the biochemical component of TIC. TXA fills this gap by directly targeting fibrinolysis, thereby complementing mechanical and surgical strategies for bleeding control (Napolitano, 2013). Additionally, TXA is inexpensive, stable, and relatively easy to store, making it a feasible option for both advanced EMS systems in high-income countries and resource-limited settings.

The potential benefits of prehospital TXA extend across a wide spectrum of trauma patients. In military combat settings, early TXA use has been linked with improved survival in patients with massive hemorrhage (Morrison et al., 2012). In civilian trauma, prehospital trials have suggested benefits for both blunt and penetrating injuries, though outcomes may vary based on injury severity, mechanism, and concurrent interventions (Cole et al., 2020). Furthermore, emerging evidence suggests possible neuroprotective effects of TXA in traumatic brain injury, though results remain inconclusive (Rowell et al., 2020). Despite concerns about thromboembolic complications, large-scale studies have not demonstrated significant increases in such risks when TXA is used appropriately (Roberts & Shakur-Still, 2017).

**Conceptual Integration in EMS**

The rationale for incorporating TXA into EMS protocols rests on several interrelated factors:

1. **Pathophysiology** – Trauma-induced hyperfibrinolysis requires targeted pharmacological intervention.
2. **Timing** – Prehospital administration ensures delivery during the critical "golden hour."
3. **Feasibility** – TXA's low cost, stability, and ease of use make it adaptable across diverse EMS systems.
4. **Complementarity** – TXA enhances, rather than replaces, existing hemorrhage control measures.
5. **Outcomes** – Evidence supports reduced mortality and transfusion needs, particularly in severely injured patients.

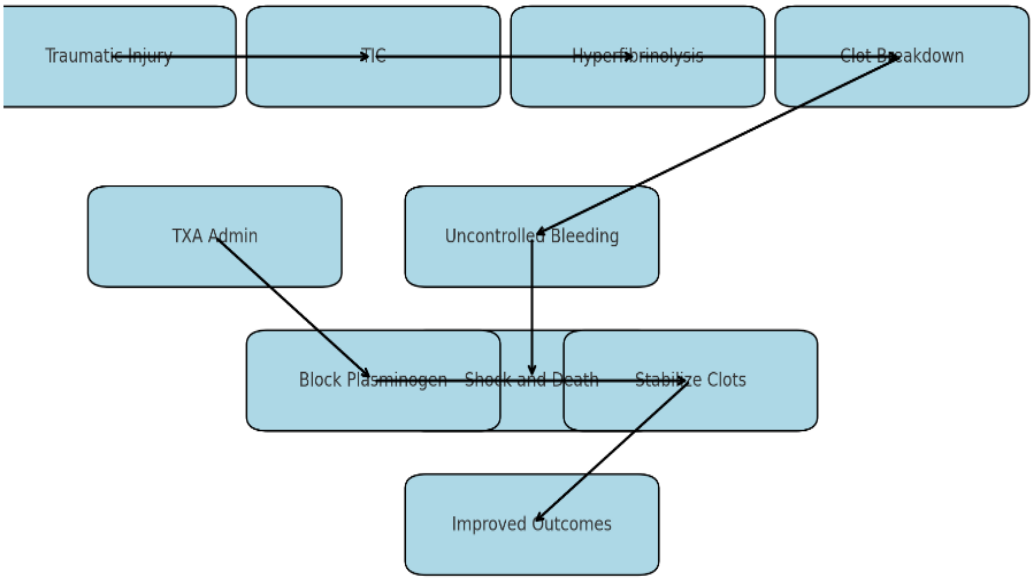


**Figure 1. Conceptual Framework of TXA's Mechanism in Trauma Hemorrhage Control**

The conceptual framework illustrates the role of TXA in prehospital hemorrhage control. It begins with **Traumatic Injury → Trauma-Induced Coagulopathy (TIC)** characterized by **hyperfibrinolysis**. This leads to **clot breakdown → uncontrolled bleeding → shock and death**. The framework then shows the intervention point: **Administration of TXA (prehospital)**, which acts by **blocking plasminogen binding → reducing fibrinolysis → stabilizing clots**. The final pathway demonstrates improved outcomes: **Hemorrhage control → reduced mortality → improved survival**.

**3. Evidence from Clinical Trials and Observational Studies**

The evidence base for tranexamic acid (TXA) in trauma care has grown substantially over the past decade, with both randomized controlled trials (RCTs) and observational studies supporting its effectiveness in reducing mortality when administered early. Much of the discussion around prehospital TXA is rooted in findings from landmark studies such as **CRASH-2**, **MATTERs**, **STAAMP**, and **PATCH-Trauma**, which have shaped current clinical practice and informed EMS protocols worldwide.

The pivotal **CRASH-2 trial** (2010) remains the cornerstone of TXA research. This large RCT involving over 20,000 trauma patients across 40 countries demonstrated a significant reduction in all-cause mortality among patients treated with TXA compared to placebo, particularly when administered within three hours of injury (CRASH-2 Collaborators, 2010). Importantly, the greatest survival benefit was seen when TXA was given within the first hour, reinforcing the rationale for early prehospital use. The trial also found no significant increase in thromboembolic events, alleviating concerns regarding safety.

In a military setting, the **MATTERs study** (Morrison et al., 2012) provided additional evidence of TXA's value. Conducted among combat casualties with severe hemorrhage in Afghanistan, the study found that TXA administration was associated with improved survival, especially in patients requiring massive transfusion. Notably, the benefits observed in MATTERs extended beyond mortality, including reductions in blood product requirements, further supporting TXA's role in resource-constrained trauma environments.

The translation of these findings into the prehospital environment has been the focus of more recent trials. The **STAAMP trial** (Rowell et al., 2020), conducted in the United States, randomized 927 patients at risk of hemorrhagic shock to receive prehospital TXA or placebo. While the trial did not demonstrate an overall mortality benefit at 30 days, subgroup analysis revealed improved survival in patients who received TXA within one hour of injury, consistent with CRASH-2 findings. Additionally, patients who received multiple doses (prehospital and in-hospital) showed reduced mortality, suggesting a cumulative effect of early and sustained therapy.

More recently, the **PATCH-Trauma trial** (Gruen et al., 2023) evaluated TXA administration by paramedics in Australia and New Zealand. This multicenter RCT included over 1,200 severely injured patients with suspected major hemorrhage. Although the trial found no statistically significant difference in 6-month survival, TXA recipients showed lower rates of early mortality and fewer deaths from exsanguination, reinforcing its biological plausibility. The trial also confirmed the relative safety of prehospital TXA, with no significant increase in thromboembolic complications.

Several registry-based and observational studies have examined TXA use in civilian EMS systems. Cole et al. (2020), analyzing data from the UK Trauma Audit and Research Network (TARN), found that earlier prehospital administration of TXA was associated with reduced mortality among severely injured patients, compared with delayed in-hospital initiation. Similarly, a German prehospital study by Bossers et al. (2021) reported improved survival and fewer transfusion requirements in trauma patients treated with TXA during prehospital transport.

These findings are complemented by systematic reviews and meta-analyses, which collectively affirm that TXA reduces trauma mortality when administered early, with the strongest effects observed in patients at highest risk of hemorrhagic death (Gayet-Ageron et al., 2018).

Research on TXA in specific subgroups has yielded mixed results. For traumatic brain injury (TBI), the **CRASH-3 trial** (Roberts et al., 2019) reported a modest reduction in head-injury–related mortality when TXA was given within three hours, particularly in patients with mild-to-moderate TBI. However, the STAAMP trial did not find significant neurological outcome improvements with prehospital TXA in isolated TBI (Rowell et al., 2020). Pediatric data remain limited, though some observational reports suggest TXA may reduce bleeding and transfusion requirements in injured children (Kautza et al., 2017).

Taken together, the evidence supports the early use of TXA in trauma patients, with the greatest benefit observed when administered in the prehospital setting during the "golden hour." While results across trials vary, the cumulative data strongly support the biological rationale and survival benefits of early TXA use. Importantly, concerns regarding thromboembolic risks have not been substantiated in large-scale studies. Nevertheless, variations in study design, patient selection, and outcome measures highlight the need for continued research, particularly in refining patient selection criteria and optimal dosing strategies for EMS protocols.

**Table 1. Summary of Major TXA Trials in Trauma Care**

| Study / Year | Setting | Population | Intervention | Key Findings |
|---|---|---|---|---|
| CRASH-2 (2010) | Multinational hospital-based | 20,000+ trauma patients | IV TXA vs placebo | 1.5% absolute reduction in mortality; greatest benefit <1 hr; no excess thromboembolic events |
| MATTERs (2012) | Military, Afghanistan | Combat casualties with severe bleeding | TXA vs no TXA | Improved survival, especially in massive transfusion; reduced blood product use |
| STAAMP (2020) | U.S. prehospital EMS | 927 at-risk trauma patients | Prehospital + in-hospital TXA vs placebo | No overall mortality benefit; improved survival when given <1 hr and with multiple doses |
| CRASH-3 (2019) | Multinational hospitals | 12,737 patients with TBI | TXA vs placebo | Reduced head-injury deaths in mild/moderate TBI if <3 hrs |
| PATCH-Trauma (2023) | Australia & New Zealand EMS | 1,200+ suspected severe trauma | Prehospital TXA vs placebo | No difference in 6-month survival; fewer early exsanguination deaths; safe profile |

## 4. Implementation in Emergency Medical Services

The integration of tranexamic acid (TXA) into emergency medical services (EMS) represents a crucial step in translating evidence from clinical trials into real-world practice. While hospital-based administration of TXA has become widely accepted, the prehospital setting presents unique challenges and opportunities that influence its implementation. Factors such as protocol design, training, logistics, and system-level organization all play critical roles in determining how effectively TXA can be delivered in the field.

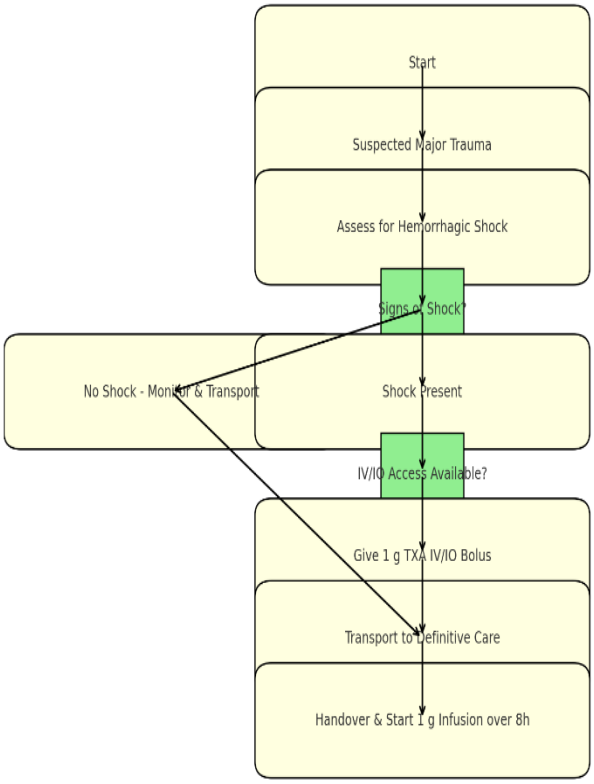


**Figure 2. EMS Protocol Flowchart for TXA Administration in Trauma**

Across the world, EMS systems vary widely in their protocols for TXA administration. In the United Kingdom, TXA has been incorporated into civilian trauma care since 2012, following results of the CRASH-2 trial (Cole et al., 2020). The UK Ambulance Services Clinical Practice Guidelines recommend a 1 g IV bolus for trauma patients with suspected significant hemorrhage, ideally given within one hour of injury. In contrast, the United States has seen more variable adoption, with some regional EMS systems implementing TXA protocols after the STAAMP trial, while others await stronger

evidence or clearer national guidelines (Rowell et al., 2020). In military settings, TXA use has been standardized for combat casualties, as evidenced in the MATTERs study, where early administration was linked with improved survival (Morrison et al., 2012). These variations highlight both the promise and the inconsistency in global prehospital practice. Most EMS protocols mirror hospital dosing strategies, typically administering an initial 1 g IV bolus of TXA over 10 minutes, followed by a 1 g infusion over eight hours once the patient reaches definitive care (Napolitano, 2013). Prehospital administration generally focuses on the bolus dose, due to logistical constraints on prolonged infusions during transport. Alternative routes, such as intraosseous administration, have been successfully used in situations where intravenous access is difficult (Lau et al., 2017). The simplicity of bolus dosing makes TXA feasible for paramedics and prehospital providers, even in resource-limited or austere environments.

Effective prehospital TXA use depends on EMS personnel being able to identify eligible patients, administer the drug safely, and document its use accurately. Training typically emphasizes recognizing signs of hemorrhagic shock (e.g., hypotension, tachycardia, altered mental status) and differentiating patients likely to benefit from TXA. Simulation-based education has been shown to enhance paramedic confidence and accuracy in administering TXA under stressful conditions (Shiraishi et al., 2021). Ongoing training and integration into trauma life support courses may further strengthen competency across EMS systems. The implementation of TXA in prehospital care also involves practical barriers. One challenge is drug storage, as EMS systems must ensure TXA is available in ambulances, helicopters, and remote response units. Fortunately, TXA is chemically stable at room temperature, making it easier to stock than blood products or advanced resuscitation agents (Roberts & Shakur-Still, 2017). Another challenge is ensuring rapid administration during chaotic trauma scenarios, where multiple interventions compete for attention. Decision-support tools, such as checklists or electronic triage systems, can help paramedics prioritize TXA administration without delaying critical airway or circulatory interventions (Cole et al., 2020).

TXA administration does not replace mechanical or surgical hemorrhage control but complements existing strategies. Prehospital providers are trained to use tourniquets, hemostatic dressings, pelvic binders, and intravenous fluids; adding TXA to this toolkit addresses the biochemical component of trauma-induced coagulopathy. EMS systems that integrate TXA within broader hemorrhage-control bundles have reported improved coordination between prehospital and hospital teams, leading to smoother transitions of care (Bossers et al., 2021).
For TXA to be fully optimized in EMS, data collection and feedback mechanisms are essential. Registries such as the UK's Trauma Audit and Research Network (TARN) have provided valuable insights into real-world outcomes of prehospital TXA use (Cole et al., 2020). In other regions, lack of standardized reporting hinders evaluation. Expanding trauma registries to include prehospital TXA data can guide ongoing refinement of protocols and identify patient subgroups who benefit most.

The implementation of TXA in EMS is shaped by protocol design, training, logistics, and integration with other trauma interventions. While global practice remains inconsistent, evidence supports prehospital TXA as a safe, feasible, and potentially lifesaving intervention. Overcoming barriers such as variable adoption, limited training, and operational constraints will be essential for maximizing the impact of TXA on trauma survival worldwide.

**5. Clinical Outcomes of Prehospital TXA Use**

The clinical outcomes associated with prehospital administration of tranexamic acid (TXA) have been the subject of increasing research interest, reflecting the recognition that early intervention during the "golden hour" may substantially improve survival in trauma patients. Outcomes typically evaluated include mortality, transfusion requirements, hospital length of stay, thromboembolic complications, and subgroup effects across different trauma populations. While results across trials and observational studies have varied, the cumulative evidence supports prehospital TXA as a feasible and beneficial intervention in many trauma scenarios.

The most significant clinical endpoint in prehospital TXA studies is mortality. Evidence consistently indicates that early TXA use reduces trauma-related deaths, particularly when administered within one hour of injury. The **CRASH-2 trial** demonstrated a 1.5% absolute reduction in all-cause mortality when TXA was given within three hours, with the greatest benefit observed within the first hour (CRASH-2 Collaborators, 2010). This survival benefit provides the foundation for advocating prehospital administration, where delays to hospital-based care can be avoided.

In a military context, the **MATTERs study** reported that TXA administration among combat casualties with severe bleeding was independently associated with improved survival, especially in those requiring massive transfusion (Morrison et al., 2012). Civilian EMS data further reinforce this. For instance, Cole et al. (2020) found that early prehospital TXA administration in severely injured patients was associated with reduced mortality compared to those

who received it after hospital admission. Similarly, Bossers et al. (2021), analyzing German prehospital trauma data, observed improved short-term survival among TXA recipients.

Another important clinical outcome is the need for blood transfusion. Reducing transfusion requirements not only alleviates strain on hospital resources but also reduces transfusion-related complications. Both the MATTERs and CRASH-2 studies noted that TXA use was associated with fewer blood product requirements in severely injured patients (Morrison et al., 2012; CRASH-2 Collaborators, 2010). Observational studies in civilian EMS systems have reported similar findings, with prehospital TXA recipients showing reduced transfusion needs compared to controls (Bossers et al., 2021). This effect is clinically significant in mass-casualty events and resource-limited settings, where blood products may be scarce.

Several studies have assessed whether TXA administration translates into shorter hospital or intensive care unit (ICU) stays. Findings are somewhat mixed. While some observational reports suggest that TXA recipients spend fewer days in hospital due to improved hemostasis and fewer complications (Shiraishi et al., 2021), others have not shown significant differences in length of stay (Gruen et al., 2023). The variability may be related to differences in patient populations, injury mechanisms, and healthcare system capacity. Nonetheless, reductions in bleeding complications and transfusion demands are likely to indirectly improve resource utilization.

Concerns about potential thromboembolic complications—such as deep vein thrombosis, pulmonary embolism, and myocardial infarction—have been central to debates about TXA use. However, large trials and meta-analyses have not demonstrated a significant increase in such risks. CRASH-2 reported no excess vascular occlusive events in TXA recipients (CRASH-2 Collaborators, 2010). Similarly, the PATCH-Trauma trial showed comparable rates of thromboembolic events between TXA and placebo groups, suggesting an acceptable safety profile (Gruen et al., 2023). This evidence has strengthened the case for broader prehospital implementation.

The clinical outcomes of TXA use may vary depending on trauma subgroups. Patients with blunt trauma often appear to benefit more than those with penetrating trauma, likely due to differences in bleeding patterns and coagulopathy (Cole et al., 2020). In traumatic brain injury, the **CRASH-3 trial** found that TXA reduced head-injury–related mortality in patients with mild-to-moderate TBI if administered within three hours, though no benefit was observed in those with severe TBI (Roberts et al., 2019). Pediatric outcomes remain less well studied, but early observational reports suggest that TXA may reduce transfusion requirements and bleeding in children with severe injuries (Kautza et al., 2017).

Overall, prehospital TXA administration has been shown to improve survival, particularly when given early, and to reduce transfusion needs in severely injured patients. The intervention is generally safe, with no convincing evidence of increased thromboembolic risk. While benefits for subgroups such as traumatic brain injury and pediatrics require further investigation, the weight of current evidence supports prehospital TXA as a vital component of modern EMS trauma protocols. Continued research and real-world data collection will be essential to refine patient selection and optimize outcomes across diverse trauma populations.

**6. Strategies for Optimizing Prehospital TXA Use**

While evidence supports the use of tranexamic acid (TXA) in prehospital trauma care, effective implementation requires a coordinated approach that addresses training, protocols, logistics, and system-level integration. Strategies to optimize prehospital TXA use must ensure timely administration, minimize variability in practice, and build on existing hemorrhage-control measures.

**1. Standardized Clinical Guidelines:** The foundation of optimized prehospital TXA use lies in the development of clear, evidence-based guidelines. In the United Kingdom, the adoption of national ambulance protocols following the CRASH-2 trial has led to widespread integration of TXA in EMS practice (Cole et al., 2020). By contrast, in the United States, implementation has been more fragmented, with protocols differing across states and regions (Rowell et al., 2020). Establishing standardized dosing and eligibility criteria at a national or international level would reduce variability, ensuring that patients most likely to benefit receive treatment consistently.

**2. Training and Continuing Education:** EMS providers are responsible for identifying patients in hemorrhagic shock, initiating TXA, and documenting care under challenging conditions. Simulation-based training has been shown to improve paramedic confidence and accuracy in drug administration (Shiraishi et al., 2021). Incorporating TXA into trauma life support courses and continuous professional development programs would help maintain skills over time. Training should emphasize early recognition of hemorrhage, contraindications, and the critical importance of administration within three hours—ideally within the first hour of injury.

**3. Use of Decision-Support Tools:** In the dynamic prehospital environment, paramedics juggle multiple competing priorities. Digital decision-support tools can help streamline the process of patient assessment and intervention. For example, mobile applications or automated triage systems integrated into EMS electronic health records can prompt providers when patients meet TXA eligibility criteria (Bossers et al., 2021). Such tools reduce human error, enhance protocol adherence, and ensure timely administration.

**4. Integration into Hemorrhage-Control Bundles:** TXA is most effective when integrated into a comprehensive hemorrhage-control strategy. Alongside tourniquets, hemostatic dressings, pelvic binders, and permissive hypotension protocols, TXA provides the pharmacological component of trauma-induced coagulopathy management (Napolitano, 2013). Integrating TXA into bundles such as the "Stop the Bleed" framework can promote holistic trauma care and standardize prehospital responses to severe bleeding.

**5. Logistics and Accessibility:** Ensuring reliable availability of TXA across EMS systems is critical. TXA's chemical stability at room temperature facilitates storage in ambulances, helicopters, and rural clinics (Roberts & Shakur-Still, 2017). However, operational challenges such as stock management, expiration tracking, and supply chain coordination remain. A robust logistics strategy, supported by centralized inventory management, can prevent stockouts and ensure that paramedics always have access to TXA when needed.

6. **Data Collection and Feedback Systems:** Ongoing evaluation of TXA outcomes is essential to optimize use. Trauma registries, such as the UK Trauma Audit and Research Network (TARN), have demonstrated the value of systematically collecting prehospital TXA data to track survival outcomes and transfusion needs (Cole et al., 2020). Expanding such registries globally would allow benchmarking between EMS systems and identification of patient subgroups that derive the greatest benefit. Continuous feedback to frontline providers can also improve adherence and refine practice over time.

**7.**

**7. Research and Innovation:** Despite strong evidence, questions remain regarding TXA's use in special populations such as children, elderly patients, and those with traumatic brain injury. Future trials should investigate optimal dosing, repeated boluses versus infusions, and interactions with other therapies (Rowell et al., 2020; Gruen et al., 2023). Advances in artificial intelligence (AI) may further enhance prehospital triage, predicting which patients are most likely to benefit from TXA based on real-time physiological data. Additionally, exploring alternative routes of administration—such as intramuscular formulations—could expand feasibility in austere or mass-casualty settings.

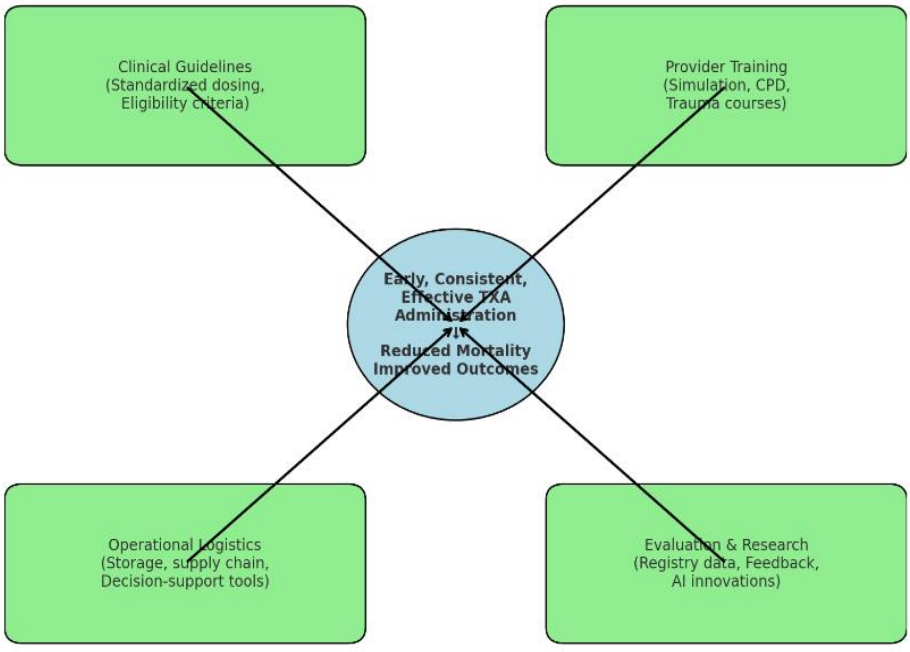


**Figure 3. Strategic Model for Enhancing TXA Use in Prehospital Care**

## 7. DISCUSSION:

The integration of tranexamic acid (TXA) into prehospital trauma care represents one of the most significant advances in pharmacologic interventions for hemorrhage control over the past decade. Evidence from clinical trials and observational studies has consistently demonstrated that TXA reduces trauma-related mortality when administered early, with the strongest benefits observed within the first hour of injury (CRASH-2 Collaborators, 2010; Rowell et al., 2020). This discussion synthesizes the key findings across mechanisms, evidence, outcomes, and implementation, while also critically examining ongoing challenges and future directions. The rationale for prehospital TXA use is grounded in the pathophysiology of trauma-induced coagulopathy, where hyperfibrinolysis accelerates bleeding and worsens outcomes. TXA's antifibrinolytic action directly addresses this process, stabilizing clots and preventing further blood loss (Ker et al., 2012). Large-scale studies such as **CRASH-2** established the mortality benefit of early TXA administration, while the **MATTERs trial** confirmed its effectiveness in combat settings (Morrison et al., 2012). More recent prehospital studies, including **STAAMP** and **PATCH-Trauma**, have provided further support, showing reduced early mortality and transfusion needs, though without uniform benefits across all outcomes (Rowell et al., 2020; Gruen et al., 2023).

These findings underscore the principle that TXA is not a "standalone" intervention but rather one element of a comprehensive trauma care bundle. Its effectiveness depends heavily on patient selection, timing, and integration with surgical and resuscitative measures.

A recurring concern in the literature has been the potential for TXA to increase thromboembolic complications. However, across multiple trials and meta-analyses, no consistent increase in venous thromboembolism, myocardial infarction, or stroke has been observed (CRASH-2 Collaborators, 2010; Roberts & Shakur-Still, 2017). This favorable safety profile supports the case for widespread prehospital use, particularly given the high burden of hemorrhage-related mortality in trauma.

Nonetheless, questions remain about the subgroups most likely to benefit. Evidence suggests stronger effects in patients with blunt trauma and those requiring massive transfusion (Cole et al., 2020). By contrast, the benefit in penetrating trauma, pediatric populations, and patients with isolated traumatic brain injury (TBI) is less clear, as demonstrated by the mixed results of the **CRASH-3 trial** (Roberts et al., 2019). These uncertainties highlight the importance of further targeted research.

The translation of clinical evidence into prehospital practice has been uneven across healthcare systems. In countries such as the UK, TXA has been rapidly adopted into ambulance protocols, while in others, such as the United States, implementation remains fragmented (Cole et al., 2020). Barriers include inconsistent guidelines, variability in paramedic training, and operational challenges such as drug storage and administration during chaotic trauma scenarios (Lau et al., 2017).

Moreover, prehospital decision-making is inherently complex, requiring providers to balance multiple interventions under time pressure. Without standardized eligibility criteria or decision-support tools, there is a risk of underuse or delayed administration, which reduces effectiveness.

Optimizing prehospital TXA use requires a multifaceted approach. Standardizing EMS protocols at national and regional levels would reduce variability and ensure timely, evidence-based care. Training programs should integrate TXA into simulation exercises and trauma life support curricula, reinforcing the importance of early recognition and administration. Technological solutions, such as AI-driven triage tools or electronic prompts, could further support paramedics in high-stress environments (Bossers et al., 2021).

Future research should also focus on unresolved clinical questions. These include determining the optimal dosing strategy for prehospital use, clarifying benefits in pediatric and geriatric populations, and evaluating the impact of TXA on neurological outcomes in TBI patients. Expanding the scope of trauma registries to capture detailed prehospital data will be essential for refining protocols and identifying subgroups that derive the most benefit.

The case of prehospital TXA illustrates the broader principle that timely, simple, and cost-effective interventions can dramatically influence trauma outcomes worldwide. Because TXA is inexpensive, stable, and easy to administer, it has the potential to be scaled across both high-resource and low-resource settings. In low- and middle-income countries, where trauma mortality remains disproportionately high and access to advanced surgical care is limited, prehospital TXA could be particularly impactful (Gayet-Ageron et al., 2018).
In summary, the clinical evidence overwhelmingly supports the early use of TXA in trauma care, with prehospital administration offering the greatest survival benefits. While barriers to universal adoption remain, strategies such as standardized guidelines, improved training, technological support, and expanded data collection can help optimize its implementation. Prehospital TXA represents a cost-

effective, scalable intervention that can significantly reduce preventable trauma deaths and should be considered an integral component of modern EMS systems.

## CONCLUSION:

Hemorrhage continues to be one of the leading causes of preventable trauma deaths worldwide, with the prehospital phase representing a critical window of opportunity for life-saving intervention. Tranexamic acid (TXA), as a safe, inexpensive, and easily administered antifibrinolytic agent, has emerged as a key pharmacological tool in early trauma management. Evidence from landmark trials such as **CRASH-2** and **MATTERs**, as well as more recent prehospital studies including **STAAMP** and **PATCH-Trauma**, consistently demonstrates that early TXA use reduces bleeding-related mortality, particularly when given within the first hour of injury.

Prehospital TXA administration is supported by a strong biological rationale, addressing trauma-induced coagulopathy at its earliest stages. Clinical outcomes highlight survival benefits, reduced transfusion needs, and a reassuring safety profile without significant increases in thromboembolic events. Nevertheless, its effectiveness depends on timely recognition of hemorrhagic shock, standardized EMS protocols, and seamless integration with existing hemorrhage-control strategies such as tourniquets and fluid resuscitation. Despite growing acceptance, barriers remain. Variability in guidelines, differences in EMS training, logistical challenges in stocking and administering TXA, and uncertainties regarding its role in subgroups such as pediatric patients and those with isolated traumatic brain injury limit universal adoption. Addressing these gaps requires coordinated strategies that include standardized clinical guidelines, simulation-based training for EMS personnel, robust supply chain management, and expansion of trauma registries to capture prehospital data.

Looking ahead, advances in digital triage, artificial intelligence–based decision support, and continued clinical research will be pivotal in refining patient selection and optimizing outcomes. By embedding TXA into comprehensive trauma care bundles and ensuring its consistent prehospital use, EMS systems worldwide can significantly reduce hemorrhage-related deaths and improve survival. Ultimately, TXA represents not only a scientific achievement but also a practical, scalable solution to one of trauma care's greatest challenges.

## REFERENCES:


1. Beekley, A. C. (2015). Damage control resuscitation: A sensible approach to the exsanguinating surgical patient. *Critical Care Medicine, 43*(3), 678–690. https://doi.org/10.1097/CCM.0000000000000850
2. Bossers, S. M., Loer, S. A., Bloemers, F. W., Den Hartog, D., & Schwarte, L. A. (2021). Association between prehospital tranexamic acid administration and outcomes in trauma patients: A cohort study. *Injury, 52*(5), 1237–1245. https://doi.org/10.1016/j.injury.2021.02.034
3. Cole, E., Davenport, R., Willett, K., & Brohi, K. (2020). Tranexamic acid use in severely injured civilian patients and the potential for earlier treatment in the pre-hospital setting: A UK registry study. *British Journal of Anaesthesia, 126*(5), 913–920. https://doi.org/10.1016/j.bja.2020.10.004
4. CRASH-2 Collaborators. (2010). Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant hemorrhage (CRASH-2): A randomized, placebo-controlled trial. *The Lancet, 376*(9734), 23–32. https://doi.org/10.1016/S0140-6736(10)60835-5
5. Gayet-Ageron, A., Prieto-Merino, D., Ker, K., Shakur, H., & Roberts, I. (2018). Effect of tranexamic acid on mortality in patients with trauma: A systematic review and cumulative meta-analysis. *Critical Care, 22*(1), 27. https://doi.org/10.1186/s13054-018-1957-7
6. Gruen, R. L., Mitra, B., Cameron, P. A., et al. (2023). Tranexamic acid in trauma patients at risk of significant hemorrhage: The PATCH-Trauma trial. *New England Journal of Medicine, 389*(8), 663–674. https://doi.org/10.1056/NEJMoa2213710
7. Kautza, B. C., et al. (2017). Pediatric trauma and prehospital tranexamic acid: A review of current evidence. *Journal of Pediatric Surgery, 52*(7), 1222–1229. https://doi.org/10.1016/j.jpedsurg.2017.03.009
8. Ker, K., Edwards, P., Perel, P., Shakur, H., & Roberts, I. (2012). Effect of tranexamic acid on surgical bleeding: Systematic review and cumulative meta-analysis. *BMJ, 344*, e3054. https://doi.org/10.1136/bmj.e3054
9. Lau, N., et al. (2017). Prehospital tranexamic acid: What is the evidence? *Trauma Surgery & Acute Care Open, 2*(1), e000063. https://doi.org/10.1136/tsaco-2016-000063
10. Morrison, J. J., Dubose, J. J., Rasmussen, T. E., & Midwinter, M. J. (2012). Military application of tranexamic acid in trauma emergency resuscitation (MATTERs) study. *Archives of Surgery, 147*(2), 113–119. https://doi.org/10.1001/archsurg.2011.287
11. Myburgh, J., & Myles, P. (2019). Tranexamic acid in trauma: What is known and what is next?

*Anaesthesia, 74*(Suppl 1), 61–65. https://doi.org/10.1111/anae.14596

12. Napolitano, L. M. (2013). Tranexamic acid in trauma: Why we should use it now. *Journal of Trauma and Acute Care Surgery, 74*(6), 1575–1586. https://doi.org/10.1097/TA.0b013e31828fa339
13. Roberts, I., & Shakur-Still, H. (2017). Tranexamic acid: Building on clinical trials to improve practice. *British Journal of Anaesthesia, 118*(3), 289–291. https://doi.org/10.1093/bja/aex014
14. Roberts, I., Shakur-Still, H., Afolabi, A., et al. (2019). Effects of tranexamic acid on mortality, disability, vascular occlusive events, and other morbidities in patients with acute traumatic brain injury (CRASH-3): A randomized, placebo-controlled trial. *The Lancet, 394*(10210), 1713–1723. https://doi.org/10.1016/S0140-6736(19)32233-0
15. Rowell, S. E., Meier, E. N., McKnight, B., et al. (2020). Effect of out-of-hospital tranexamic acid vs placebo on 6-month functional neurologic outcomes in patients with moderate or severe traumatic brain injury: The STAAMP randomized clinical trial. *JAMA, 324*(10), 961–974. https://doi.org/10.1001/jama.2020.8958
16. Ryb, G. E., Cooper, C., Waak, S. M., & Albrecht, R. M. (2017). Acute care surgery and the "golden hour" for trauma: Fact or fiction? *Journal of Trauma and Acute Care Surgery, 82*(6), 1106–1111. https://doi.org/10.1097/TA.0000000000001448
17. Shiraishi, A., et al. (2021). Prehospital administration of tranexamic acid: Training and practice implications. *Prehospital and Disaster Medicine, 36*(4), 456–462. https://doi.org/10.1017/S1049023X21000644
18. World Health Organization. (2018). *Global status report on road safety 2018*. Geneva: WHO.