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Prehospital Management of Sepsis: Early Identification and Intervention

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ABSTRACT

Sepsis remains a leading cause of morbidity and mortality worldwide, with timely recognition and intervention being critical to survival. In the prehospital setting, paramedics are uniquely positioned to initiate early sepsis care, yet challenges in diagnosis, training, and standardized protocols persist. This review synthesizes current evidence on the role of paramedics in early sepsis identification and intervention. Screening tools such as qSOFA, NEWS2, and PRESS offer varying sensitivity and specificity, while clinical gestalt and real-time telemedicine support can complement structured scoring systems. Key prehospital interventions include fluid resuscitation, oxygen therapy, airway management, point-of-care lactate testing, and, in some systems, early antibiotic administration. Prehospital alerts and structured handover systems enhance continuity of care, reducing delays in hospital-based sepsis bundles. Despite promising evidence that early prehospital interventions improve time-to-treatment and outcomes, barriers such as diagnostic uncertainty, limited protocols, and regulatory restrictions remain. Future directions include integration of artificial intelligence, advanced point-of-care diagnostics, expanded paramedic scope of practice, and rigorous multicenter research to standardize and optimize care. Strengthening prehospital sepsis management has the potential to reduce mortality, improve patient outcomes, and alleviate healthcare system burdens.

Keywords: Sepsis; prehospital care; paramedics; emergency medical services; early recognition; screening tools; fluid resuscitation; prehospital antibiotics; telemedicine; patient outcomes

INTRODUCTION

Sepsis represents a critical global health challenge characterized by high incidence, morbidity, and mortality rates worldwide. In 2017, there were approximately 49 million sepsis cases globally, resulting in 11 million sepsis-related deaths, accounting for nearly 20% of all global deaths. The burden of sepsis is particularly pronounced in low- and middle-income countries, where incidence and mortality rates are highest, especially in sub-Saharan Africa, Oceania, and South Asia. Sepsis affects individuals across all age groups but disproportionately impacts the elderly and those with comorbidities. Beyond mortality,

survivors often endure significant long-term morbidity, including cognitive impairment and functional disabilities, further stressing healthcare systems (La Via et al., 2024).

The principle of "time is tissue" is central to sepsis care, emphasizing that early recognition and prompt intervention markedly improve patient outcomes. Each hour of delay in initiating treatment reduces survival rates by up to 8%. Early interventions such as timely antibiotics, fluid resuscitation, and hemodynamic support are critical components of sepsis management bundles shown to reduce morbidity and mortality. However, early identification is challenging due to the nonspecific and variable clinical presentations of sepsis, ranging from subtle symptoms to overt organ dysfunction, hampering timely diagnosis outside hospital settings. Prehospital diagnosis is further complicated by limited access to diagnostic tools and biomarkers traditionally used in hospitals. These diagnostic limitations contribute to delays in initiating life-saving interventions (Lazzarin et al., 2024a).

Paramedics play a unique and pivotal role as the first point of contact in the healthcare continuum for septic patients. Often serving as frontline providers in emergency medical services (EMS), paramedics have the opportunity to recognize sepsis during early clinical encounters and initiate prehospital interventions. Studies show that paramedics can identify sepsis with reasonable sensitivity and specificity using validated screening tools, although challenges remain in standardizing recognition and diagnosis protocols. Importantly, EMS care shortens time to initial assessment and can expedite hospital triage, which may improve outcomes compared to patients presenting without EMS involvement. Despite this, prehospital sepsis management including recognition, early fluid resuscitation, and antibiotic administration remains underutilized and under-researched (Green et al., 2016).

Focusing on prehospital management of sepsis bridges the critical gap between the community and hospital care. Early intervention in the prehospital setting complements and connects with emergency department (ED) and in-hospital sepsis bundles that follow evidence-based protocols to optimize outcomes. Coordinated care starting in the field can reduce treatment delays, improve hemodynamics prior to hospital arrival, and enhance seamless care transitions. This approach aligns with critical care system recommendations emphasizing regionalized and integrated sepsis care pathways (Seymour et al., 2012a).

The aim of this review is to synthesize current evidence regarding paramedics' role in the early identification and prehospital intervention of sepsis. It will analyze the effectiveness and challenges of screening tools, initial treatment strategies, and the integration of prehospital care within wider emergency and hospital sepsis protocols. By examining this evolving component of sepsis care, this review seeks to highlight gaps, opportunities, and future directions for enhancing prehospital sepsis management to ultimately improve patient survival and reduce the global burden of sepsis.

Pathophysiology and Clinical Significance of Sepsis

Sepsis is a life-threatening clinical syndrome defined by a dysregulated host response to infection, which results in organ dysfunction. The latest consensus definition, known as Sepsis-3, published in 2016, defines sepsis as "life-threatening organ dysfunction caused by a dysregulated host response to infection," where organ dysfunction is operationalized as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score. This represents a shift from older criteria such as the systemic inflammatory response syndrome (SIRS) criteria, which emphasized signs of systemic inflammation like fever, tachycardia, and leukocytosis but lacked specificity and sensitivity for predicting poor outcomes. Sepsis-3 emphasizes organ dysfunction and mortality risk rather than generalized inflammation alone, providing a more clinically relevant framework for early identification and treatment (Singer et al., 2016).

Pathophysiologically, sepsis begins with an infection that triggers an aberrant immune response. Recognition of pathogen-associated molecular patterns (PAMPs) by immune cells via toll-like receptors (TLRs) activates both pro-inflammatory and anti-inflammatory pathways, leading to a complex cascade

of immune activation. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukins (IL-1, IL-6, IL-8), and interferons initiate widespread inflammation, endothelial dysfunction, coagulation abnormalities, and complement activation. This inflammatory dysregulation causes vasodilatation, increased vascular permeability, microvascular thrombosis, and tissue hypoperfusion, leading to inadequate oxygen delivery and ultimately organ dysfunction. The systemic immune response also involves compensatory anti-inflammatory mechanisms and immune cell exhaustion, which can predispose patients to secondary infections and prolonged immunosuppression (Jarczak et al., 2021).

Clinically, sepsis progresses rapidly from infection to organ dysfunction and, if untreated, to septic shock, a subset characterized by profound circulatory and metabolic abnormalities including persistent hypotension despite fluid resuscitation and elevated serum lactate above 2 mmol/L. The time-sensitive nature of this progression necessitates prompt recognition and intervention. Early hemodynamic stabilization, primarily through fluid resuscitation and vasopressor support, aims to restore adequate tissue perfusion and oxygen delivery to prevent irreversible organ damage. Current guidelines recommend aggressive fluid administration, typically 30 mL/kg of crystalloid within the first hour, alongside vasopressors like norepinephrine to maintain a mean arterial pressure (MAP) of at least 65 mmHg. This early intervention period, sometimes called the “golden hour,” is critical to improving survival and minimizing organ injury (Lesur et al., 2018).

Epidemiology and Burden of Prehospital Sepsis

Sepsis is a common and life-threatening condition that arises when the body's response to infection causes organ dysfunction. Prehospital sepsis refers to patients with sepsis who are encountered by emergency medical services (EMS) before arrival at a hospital. The epidemiology and burden of sepsis in this prehospital context remain critical to understanding because early identification and intervention by paramedics can significantly affect patient outcomes.

Global and Regional Incidence in EMS Populations

Globally, sepsis constitutes a major health challenge with an estimated 48.9 million incident cases in 2017 and 11 million deaths, accounting for approximately 20% of all global deaths. The incidence and mortality rates of sepsis vary substantially by geography, showing greater burden in low- and middle-income regions such as sub-Saharan Africa, South Asia, and Southeast Asia compared to high-income regions (Rudd et al., 2020).

In EMS populations specifically, sepsis is a frequent presentation, although its precise incidence depends on the EMS system and criteria used for identification. A large study from the U.S. estimated the incidence of severe sepsis at 3.3 per 100 EMS encounters, a rate higher than that for acute myocardial infarction (2.3/100) and stroke (2.2/100) in the same population. This finding underscores the substantial burden of sepsis within prehospital emergency care. Other EMS settings report a 1.8% to 3.3% incidence range for sepsis among ambulance transports (Piedmont et al., 2024).

Prevalence Compared with Other Emergencies

Sepsis, while less recognized by the public compared to emergencies like myocardial infarction (MI) or stroke, is at least as prevalent among EMS calls. Studies consistently show sepsis cases represent a significant proportion of EMS encounters and subsequent hospitalizations. For example, the Seattle study found sepsis incidence in EMS encounters surpassing that of MI and stroke, illustrating the critical frequency of prehospital sepsis (Seymour et al., 2012a).

However, public awareness of sepsis remains poor relative to MI and stroke, potentially contributing to delays in seeking care and challenges in prehospital recognition by EMS providers. Unlike MI and stroke, which have well-established public health campaigns and rapid prehospital protocols, sepsis identification protocols are evolving in EMS systems (Al-Orainan et al., 2020).

Mortality and Morbidity with Prehospital Delay

Delays in sepsis recognition and management are strongly linked to increased mortality and morbidity. Prehospital intervals, time from symptom onset or EMS contact to hospital admission, can influence outcomes significantly. Studies have found that longer prehospital delays correlate with higher severity of illness at hospital presentation and increased risk of death, even when subsequent in-hospital care is timely (Holmbom et al., 2021).

For bloodstream infections with sepsis, prehospital delay was identified as an independent risk factor for 30-day all-cause mortality. Non-survivors presented with higher severity scores on hospital arrival, indicating that delayed initial recognition and treatment in the prehospital phase worsens prognosis. Mortality for patients hospitalized with severe sepsis in EMS cohorts has ranged near 20%, indicating high fatality despite hospital treatment (Seymour et al., 2012).

Morbidity related to delayed sepsis care includes increased multi-organ failure, longer hospital stays, and greater likelihood of ICU admission. The rapid progression of sepsis to septic shock emphasizes the need for early intervention (Martel et al., 2020).

Cost Implications of Delayed Sepsis Recognition

Sepsis is associated with a high economic burden on healthcare systems due to prolonged hospital stays, ICU admissions, and complex treatments. Delayed sepsis diagnosis and management further exacerbate costs. In the United States alone, sepsis-related expenditures exceed billions annually, with estimates of $39,000 to $68,000 per case depending on severity and timing of diagnosis (Hollenbeak et al., 2023a).

Delayed recognition in the prehospital and early hospital phase leads to increased severity of illness, which drives up healthcare resource use and overall costs. Studies also indicate that earlier diagnosis using novel diagnostic tests or machine learning algorithms could reduce ICU stays and costly complications, underscoring the economic value of timely sepsis recognition (Hollenbeak et al., 2023).

Challenges of Sepsis Identification in the Prehospital Setting

Sepsis identification in the prehospital environment remains a major challenge for paramedics due to several factors, including clinical overlap with other common conditions, limitations inherent to the prehospital setting, and variability in paramedic training and protocols.

Clinical Overlap with Other Conditions

Sepsis presents with nonspecific clinical features that often mimic other illnesses such as seasonal influenza, community-acquired pneumonia, dehydration, and heart failure exacerbations. This overlap complicates accurate early identification because symptoms like fever, tachycardia, tachypnea, and altered mental status are common to many conditions encountered in the prehospital setting. Paramedics must often rely on clinical examination and history without access to advanced diagnostics, increasing the risk of misclassification or delayed recognition (Green et al., 2016).

Limitations of the Prehospital Environment

Paramedics face substantial environmental and system limitations impacting sepsis recognition:

- **Lack of Laboratory Tests:** Unlike hospital settings, prehospital care generally lacks access to laboratory diagnostics such as serum lactate, blood cultures, and biomarkers, which aid in confirming sepsis and assessing severity. The absence of these objective measures significantly restricts paramedics' ability to definitively diagnose sepsis, forcing reliance on clinical judgment and screening tools with variable sensitivities and specificities (Lazzarin et al., 2024).

- **Rapidly Changing Patient Status:** Patients with sepsis may deteriorate quickly, and clinical signs can evolve during transport. Paramedics must frequently reassess to detect clinical worsening, yet changing patient status combined with limited monitoring capabilities complicates timely intervention (Lazzarin et al., 2024).
- **Time Pressure and Resource Constraints:** EMS providers work under urgent conditions with limited time to conduct thorough assessments. Time-sensitive transport priorities and resource constraints, including staff shortages and equipment limitations, pressure paramedics to make rapid decisions, potentially impacting diagnostic accuracy (Green et al., 2016).

Variability in Paramedic Training and Protocols

The level of paramedic education, experience, and familiarity with sepsis varies widely across EMS systems, affecting the consistency of early recognition and intervention. Protocols and screening tools for sepsis used by paramedics are not universally standardized, and their sensitivity and specificity differ depending on the tool and local practices. Studies report a range of paramedic ability to identify sepsis, highlighting gaps in training and the need for validated, easy-to-use screening methods to support decision-making in the field (Smyth et al., 2016).

Prehospital Screening Tools and Early Recognition Strategies for Sepsis by Paramedics

Early recognition and timely intervention in sepsis are critical to improving patient outcomes, as sepsis is a time-sensitive condition with high morbidity and mortality. Paramedics play a vital role in prehospital care by identifying sepsis early and initiating appropriate management. Several screening tools and clinical strategies have been validated or studied in the paramedic setting to facilitate early recognition of sepsis, each with strengths and limitations.

qSOFA (Quick Sequential Organ Failure Assessment)

The qSOFA score is a simple bedside tool recommended to identify patients at increased risk of poor outcomes from sepsis outside intensive care settings. It includes three criteria: respiratory rate ≥ 22/min, altered mentation, and systolic blood pressure ≤ 100 mmHg. Studies in the prehospital environment have demonstrated that qSOFA has reasonable specificity but limited sensitivity, with sensitivity as low as 16.3% for severe sepsis identification by paramedics, though specificity may exceed 90%. Modifications adding clinical variables like pulse rate or age improve sensitivity but decrease specificity. Overall, qSOFA may be better used as a predictor of mortality risk rather than a sensitive screening tool for sepsis identification prehospital (Dorsett et al., 2017).

NEWS and NEWS2 (National Early Warning Score)

NEWS and its updated version NEWS2 incorporate multiple vital signs including respiratory rate, oxygen saturation, temperature, heart rate, blood pressure, and consciousness level to generate an aggregate score indicating severity. NEWS2 has been validated in prehospital contexts and has shown moderate sensitivity (approximately 0.52 at threshold >4) and positive predictive value (~0.22) for identifying sepsis that requires urgent hospital treatment. A NEWS2 score ≥ 7 in prehospital septic shock patients correlates with increased in-hospital and 30-90 day mortality risk, emphasizing its prognostic value. NEWS2 tends to outperform other early warning scores in accuracy and offers a balance between sensitivity and specificity, making it widely recommended in paramedic practice (Inada-Kim, 2022).

MEWS (Modified Early Warning Score)

MEWS uses vital signs including blood pressure, heart rate, respiratory rate, temperature, and level of consciousness to assess clinical deterioration risk. Studies show MEWS has moderate sensitivity (~53%) but somewhat lower specificity compared to NEWS or qSOFA when applied in the prehospital setting. It

remains in use due to its simplicity but is generally considered less accurate than NEWS2 (Jouffroy et al., 2018).

PRESEP and PRESS Scores

PRESEP is a score specifically designed for prehospital identification of septic patients and includes parameters such as heart rate, respiratory rate, blood pressure, temperature, and Glasgow Coma Scale. PRESS (Prehospital Severe Sepsis) score also incorporates EMS data on six risk factors. PRESEP and PRESS have demonstrated good sensitivity (about 49% for PRESEP and 86% for PRESS) but variable specificity (around 47–76%). PRESS showed high sensitivity but lower specificity in urban public hospital settings (Green et al., 2016).

Comparative Sensitivity and Specificity

No single screening tool achieves both high sensitivity and specificity universally in prehospital or hospital triage. For instance, qSOFA has lower sensitivity but high specificity, while NEWS2 offers a better trade-off. MEWS and PRESEP scores yield moderate performance. Positive predictive values are generally modest (<0.7), reflecting the challenge of sepsis diagnosis early in clinical presentation (Jouffroy et al., 2018).

Integration of Clinical Gestalt versus Algorithm-Based Screening

Several studies emphasize the critical role of paramedic clinical gestalt, the physician or paramedic's intuitive judgment in sepsis recognition. Physician gestalt in emergency settings has outperformed standardized screening tools in sensitivity and specificity, particularly within the first 15 minutes of encounter, suggesting that experience and clinical intuition complement algorithm-based tools. Combining algorithmic scores with clinical insight may enhance early identification (Knack et al., 2024).

Vital Signs Trend Monitoring

Monitoring trends in vital signs over time, rather than single measurements, is important for early sepsis detection. Continuous or repeated assessments of respiratory rate, heart rate, blood pressure, oxygen saturation, and temperature help identify deterioration or improvement trends, thus improving diagnostic accuracy and timing of interventions (Quinten et al., 2016).

Prehospital Interventions by Paramedics in Sepsis: Early Identification and Intervention

The prehospital management of sepsis by paramedics involves a structured approach encompassing initial assessment, airway and breathing support, circulatory support, consideration of early antibiotics, point-of-care diagnostics, and supportive monitoring. These interventions facilitate early recognition and timely treatment, which are vital to improving outcomes in sepsis patients.

Initial Assessment

Paramedics utilize the ABCDE approach Airway, Breathing, Circulation, Disability, Exposure as a universal, systematic framework to quickly assess and stabilize critically ill patients including those with sepsis. This approach prioritizes immediate life-threatening conditions: assessing and securing airway patency, evaluating breathing and oxygenation, managing circulatory status, performing rapid neurological assessment (including mental status), and finally inspecting for other clinical signs while initiating life-saving treatments simultaneously. Mental status, tissue perfusion, and respiratory effort should be rapidly evaluated to detect sepsis-related deterioration. Early recognition through structured tools improves paramedic diagnostic accuracy, achieving sensitivities and specificities over 70% using screening instruments tailored to sepsis identification (Thim et al., 2012).

Airway and Breathing Support

High-flow oxygen therapy is a cornerstone of prehospital care in sepsis to maintain adequate oxygen saturation, recommended to be ≥94%. Hypoxia is associated with increased mortality; thus, oxygen supplementation is critical to optimize outcomes. However, overly high oxygen levels may increase oxidative stress and mortality, suggesting targeted oxygen therapy should be employed to avoid hyperoxia (Huabbangyang et al., 2023a).

Ventilation support modalities available in ambulances range from non-invasive positive pressure ventilation (e.g., CPAP) to bag-valve-mask (BVM) ventilation and advanced airway management via supraglottic devices or endotracheal intubation. Supraglottic airways offer ease of placement and high success rates, especially in non-physician staffed services, while prehospital intubation success varies with provider expertise. Mechanical ventilation strategies supporting lung protection through low tidal volumes (<8 ml/kg ideal body weight) may improve prehospital septic shock outcomes (Pinto-Villalba et al., 2024).

Circulatory Support and Fluid Resuscitation

Vascular access for fluid administration can be established via intravenous (IV) or intraosseous (IO) routes. While IV access remains the preferred method due to its effectiveness, IO access presents a valuable rapid alternative, particularly in emergencies where IV access is challenging. IO sites differ in flow rates, with the sternal site providing the fastest flow, and humeral IO flow approaching IV rates under pressure infusion. Despite potential pain and complications, IO access allows early resuscitation for unstable patients (Lamhaut et al., 2010).

Fluid choice for sepsis resuscitation is generally isotonic crystalloids, with ongoing debate between balanced solutions (like lactated Ringer's) versus normal saline, the former potentially reducing renal complications. The Surviving Sepsis Campaign recommends an initial intravenous fluid bolus of 30 mL/kg, aiming to restore circulating volume and tissue perfusion; however, evidence for precise volume and timing in the prehospital setting remains limited and mixed. Risks such as fluid overload, especially in elderly or congestive heart failure patients, require careful clinical judgment. Guidelines emphasize individualized fluid titration based on responsiveness, blood pressure, capillary refill, and clinical context, with many EMS providers currently relying on clinical intuition for fluid decisions (Lazzarin et al., 2024).

Early Antibiotic Administration

The role of prehospital empiric antibiotic administration by paramedics is an evolving area. Some EMS systems in the US and Europe have piloted protocols allowing paramedics to initiate antibiotics based on sepsis recognition, with promising results including shortened time to antibiotic delivery and high protocol adherence rates. However, concerns remain regarding antibiotic stewardship, medication storage logistics, and integration with hospital care pathways. Meta-analyses indicate prehospital antibiotics can significantly reduce mortality, yet broader clinical trials are needed for conclusive evidence and widespread adoption (Varney et al., 2022).

Point-of-Care Diagnostics

Point-of-care lactate measurement devices have emerged as useful tools in EMS to assess sepsis severity, as elevated lactate correlates with worse outcomes and may guide fluid resuscitation strategies. Additionally, the increasing use of point-of-care ultrasound (POCUS) in prehospital settings shows promise for evaluating volume status and cardiac function, which could enhance individualized fluid management and early diagnostic accuracy without delaying transport (Green et al., 2016).

Communication and System-level Integration in Prehospital Sepsis Management

Importance of Prehospital Alert Systems

Prehospital alert systems for sepsis, often termed “sepsis alerts,” function analogous to established protocols for stroke and STEMI (ST-segment elevation myocardial infarction) alerts. These specialized alert systems are designed to enable paramedics to identify suspected sepsis cases early and notify receiving hospitals in advance to trigger the activation of hospital sepsis response pathways. Implementation of such systems has demonstrated potential in streamlining care and improving outcomes by facilitating faster diagnostics and treatment initiation upon hospital arrival. Studies show that with prehospital sepsis alert systems, there is higher compliance with sepsis bundles and reduced time to essential interventions, including fluid resuscitation and antibiotic administration, all correlated with better patient survival rates and reduced hospital length of stay (Moutinho et al., 2025).

Digital platforms and structured scoring tools, such as the INEM Tool for Emergency Alert Medical System (iTeams™) and the Pre-hospital Sepsis Score (PSS), support paramedics by enabling systematic sepsis recognition and standardized alert triggers. These platforms integrate clinical data such as vital signs and lactate levels to inform alert generation on-site, which subsequently facilitates improved communication with hospital teams (Moutinho et al., 2025).

Structured Handover from Paramedics to Emergency Departments

Effective communication during the transition of care from prehospital providers to emergency department (ED) clinicians is critical to ensuring continuity and optimizing sepsis management. Structured handover protocols that emphasize clear transmission of key clinical information, including vital signs, suspected infection source, administered interventions (e.g., fluid resuscitation), and presence of red flag sepsis criteria, improve situational awareness and enable ED teams to prioritize care for septic patients promptly.

Research supports that standardized communication tools and team-based handover models reduce information loss and improve clinician preparedness, contributing to timelier initiation of sepsis bundles in the hospital. An effective handover integrates clinical findings, prehospital treatments performed, and the trajectory of the patient's condition, thereby maintaining the critical momentum of early sepsis care across the care continuum (Gross et al., 2025).

Role of Pre-notification to Hospitals

Pre-notification, meaning advance communication from paramedic teams to hospital emergency services about (Moutinho et al., 2025)an incoming septic patient, serves to mobilize hospital sepsis pathways before patient arrival. This mechanism primes ED and critical care teams, enabling activation of sepsis bundles, preparation of diagnostic resources, and prompt antibiotic and fluid administration.

Data from multiple observational studies highlight that prehospital notification can decrease door-to-treatment times, particularly for antibiotics and serum lactate measurements, core components of the Surviving Sepsis Campaign guidelines. Furthermore, it allows hospitals to allocate resources efficiently and tailor initial treatment strategies, such as designating a bed in the resuscitation area or assembling multidisciplinary teams (Kim et al., 2024).

Integration into Regional Sepsis Bundles and Time-to-Treatment Metrics

Integration of prehospital sepsis management into broader regional healthcare systems and sepsis bundles is vital for quality improvement and outcome standardization. Regional sepsis programs that coordinate education, protocols, and performance monitoring across prehospital and hospital settings demonstrate improved compliance with recommended care bundles, including early fluid resuscitation, blood cultures, and timely antibiotic therapy within defined time windows (Nardot et al., 2025).

Such system-level integration enables tracking of time-to-treatment metrics starting from the first EMS contact, thereby supporting accountability and continuous improvement. Metrics like "time-to-antibiotics"

and "time-to-lactate measurement" are used to assess adherence to clinical guidelines and identify bottlenecks. Coordinated sepsis pathways extending from the prehospital through hospital phases ensure that interventions are delivered within critical timeframes known to reduce mortality and morbidity (Nardot et al., 2025).

Regional programs also emphasize multidisciplinary collaborations among EMS, ED staff, ICU teams, and public health authorities to align protocols, share data, and optimize sepsis care continuum. The ultimate goal of this integration is to establish seamless, rapid, and standardized treatment pathways that reduce sepsis-related complications and improve patient outcomes (Nardot et al., 2025).

Training and Education of Paramedics

Current evidence highlights significant gaps in sepsis knowledge among EMS staff, particularly between different levels of training. Studies show that while most paramedics are aware of the term sepsis and understand its symptoms and initial management better than EMTs, knowledge is still insufficient for optimal early identification and intervention in the prehospital setting. For example, a survey in Saudi Arabia found only 48% of EMS personnel could correctly define sepsis, with paramedics performing better than EMTs but overall awareness and preparedness still lacking. Similarly, a US study reported that paramedics have better sepsis knowledge compared to firefighter-EMTs and EMTs, but many EMS providers believe sepsis is frequently missed out-of-hospital. These gaps underscore the need for targeted education (Ghazal et al., 2019).

Structured training modules and continuing education programs tailored for prehospital providers have demonstrated effectiveness in improving sepsis knowledge and clinical confidence. Leading EMS educators advocate for inclusion of sepsis-specific content covering pathophysiology, early recognition criteria, assessment skills, and treatment protocols as core components of EMS training curricula. Programs such as "Sepsis: First Response" provide accessible materials to prepare EMS personnel to rapidly identify sepsis and initiate early care.

Simulation-based learning plays a pivotal role in training paramedics to recognize subtle and variable sepsis presentations. Simulation scenarios, designed around key assessment techniques such as evaluating vital signs, recognizing infection sources, and differentiating sepsis from other conditions, enhance EMS providers' diagnostic accuracy and decision-making under realistic conditions. For instance, simulation training has been associated with improved sepsis recognition and faster treatment initiation among EMS providers. Simulation also helps overcome limitations of field assessment tools by facilitating practice in interpreting clinical signs despite lack of laboratory data.

The impact of comprehensive training on patient outcomes is notable. Field protocols and education enabling early identification and antibiotic administration have been correlated with improved survival rates and reduced morbidity. A pilot in the UK Isle of Wight trained paramedics to deliver the "Sepsis Six" bundle, including prehospital antibiotics, resulting in earlier treatment and a 93% accuracy rate in sepsis diagnosis, with favorable clinical outcomes. Similarly, US EMS systems adopting sepsis protocols with training components report lowered mortality rates due to earlier intervention. Quality improvement projects show increased clinician confidence and guideline adherence post-training, contributing to better sepsis care continuity from prehospital to hospital settings.

International Perspectives and Guideline Comparisons

Major international bodies and healthcare systems have developed sepsis position statements and prehospital protocols recognizing the EMS role in early sepsis management. The Surviving Sepsis Campaign (SSC), a key global initiative, emphasizes rapid identification and initiation of treatment bundles within "hour-1" of recognition, which has influenced many EMS systems to adopt structured sepsis care protocols. SSC guidelines encourage assessing infection suspicion combined with vital signs

to guide early intervention but leave implementation flexibility to local EMS capabilities (Huabbangyang et al., 2023).

In the United States, the American Heart Association (AHA) and National Association of EMS Educators (NAEMSE) support enhanced sepsis education and updated EMS scope of practice guidelines that include fluid resuscitation and airway management as core skills for paramedics treating sepsis. The AHA also promotes hospital "Code Sepsis" protocols to streamline emergency department transitions following prehospital recognition (CMTE, 2018).

Australian, Canadian, and various Asian EMS systems exhibit variability in sepsis management approaches, largely dependent on available paramedic training, scope of practice, and resources. Australian EMS often focus on education and rapid transport while some Canadian and Asian systems have piloted protocols for earlier interventions including fluid therapy, with antibiotic policies still varying according to regional antimicrobial resistance concerns and healthcare infrastructure (Huabbangyang et al., 2023).

Prehospital antibiotic initiation policies demonstrate substantial variability internationally. Some systems have well-established prehospital sepsis pathways incorporating blood culture sampling and antibiotic delivery by trained paramedics, as seen in the Isle of Wight project in the UK, whereas others limit interventions to rapid transport with in-hospital treatment. Regions with mature pathways report benefits such as reduced time to antibiotics, lower mortality, and shorter hospital stays. These lessons highlight the importance of integrating prehospital and hospital sepsis care through education, protocol standardization, and interprofessional collaboration (Huabbangyang et al., 2023).

Outcomes of Prehospital Intervention

Impact of Early Fluid Resuscitation on Survival and ICU Stay

Early fluid resuscitation administered by paramedics is a critical intervention in prehospital sepsis care that may impact patient outcomes significantly. A large prospective observational study conducted in King County, Washington, among severe sepsis patients transported by EMS found that prehospital administration of intravenous fluids (median volume 500 mL) was associated with a statistically significant reduction in hospital mortality compared to no prehospital fluids (odds ratio 0.46, 95% CI 0.23-0.88, $p=0.02$). Even the placement of an intravenous catheter alone without fluid administration was linked to reduced hospital mortality (OR 0.3, 95% CI 0.17-0.57, $p<0.01$). These findings suggest that early fluid resuscitation during the prehospital phase supports organ perfusion and may reduce subsequent complications such as new organ failures, implying shortened ICU stays and improved survival chances (Seymour et al., 2014).

Other studies emphasize that prehospital fluid resuscitation is typically limited in volume, often less than what is recommended in hospital settings, potentially due to operational constraints in the field. Still, even limited fluid administration appears beneficial without significant adverse effects reported in large-scale data (Jouffroy, Saade, Muret, et al., 2018).

Hemodynamic strategies including balanced crystalloids and early use of vasopressors following initial fluid therapy may further optimize outcomes, though these are less commonly implemented prehospital.

Effectiveness of Paramedic-led Sepsis Screening in Reducing Time-to-Antibiotic in the ED

Paramedic identification and early suspicion of sepsis in the field have demonstrated the ability to reduce the time to antibiotic administration upon Emergency Department (ED) arrival, which is crucial for improving sepsis outcomes. Studies show that patients transported by Advanced Life Support (ALS) paramedics receive antibiotics significantly faster in the ED compared to Basic Life Support (BLS) or walk-in patients. One investigation highlighted that ALS care shortened door-to-antibiotic time by

approximately 43 minutes after adjustment for demographics and illness severity, though this did not always translate into statistically significant mortality reduction (Prekker & Puskarich, 2018).

Despite faster antibiotic initiation, clinical trials have shown mixed results on whether this timing difference alone impacts mortality in sepsis patients, indicating that early recognition must be paired with comprehensive sepsis bundle care for optimal outcomes (Peltan et al., 2018).

Studies on Prehospital Recognition Improving Mortality Outcomes

Recognition of sepsis by paramedics prehospital is associated with better outcomes. A retrospective study analyzing linked EMS and hospital records found that prehospital sepsis recognition decreased adjusted odds of hospital mortality by approximately 18% (OR 0.82, 95% CI 0.70-0.94). This recognition enables early alerting of hospital teams, activation of sepsis protocols, and expediting critical treatment (MacAllister et al., 2024).

Furthermore, patients identified with sepsis prehospital had higher acuity and mortality risk, underscoring the importance of this recognition for targeted care (Chatoor et al., 2024).

Studies Outcomes

Not all studies demonstrate clear mortality benefits from prehospital sepsis protocols or interventions, emphasizing the interplay of healthcare context, resources, and patient populations. For example, a pediatric sepsis protocol implemented in a limited-resource hospital in Bangladesh showed no mortality improvement post-implementation and was associated with higher fluid overload and cardiac complications, suggesting challenges adapting protocols developed for resource-rich settings to lower-resource environments (Kortz et al., 2017).

Operational challenges and the absence of universal standardized protocols, as well as variations in paramedic training and healthcare system integration, contribute to inconsistent outcomes in prehospital sepsis management. Hence, the success of interventions depends heavily on proper contextual adaptation, training, and system capacity (Draeger et al., 2025).

Barriers and Limitations in Prehospital Sepsis Management

Diagnostic Uncertainty in Undifferentiated Patients

Early sepsis diagnosis in the prehospital setting is complicated by nonspecific symptoms that overlap with other conditions, making paramedic diagnostic certainty challenging. The lack of rapid, reliable diagnostic tests to identify dysregulated immune responses within the critical early window creates uncertainty, risking missed or delayed diagnoses (Draeger et al., 2025).

Unawareness of baseline patient status, particularly in nonverbal or cognitively impaired individuals, adds to diagnostic difficulty, compounded by limited monitoring equipment availability on EMS units (e.g., thermometers).

Limited Protocols and Lack of Standardized Training Worldwide

There is a global lack of universally accepted, standardized training and protocols for prehospital sepsis recognition and management. This contributes to variable paramedic knowledge and inconsistent application of sepsis care guidelines. Studies report that many paramedics feel inadequately trained in fluid management and sepsis screening and express a desire for more education and protocol clarity.

Protocols also tend to be complex, resource-intensive, and not always user-friendly, reducing adherence, especially outside intensive care settings.

Operational Barriers: Time-sensitive Field Conditions and Overcrowded Systems

Paramedics operate in high-pressure, time-sensitive environments with multiple competing demands, which may limit the thoroughness of sepsis assessments and interventions. High patient volume, staffing shortages, interruptions, and limited time for assessments all negatively impact timely sepsis care delivery.

Overcrowded EMS systems and hospital EDs further exacerbate delays in care escalation and sepsis protocol activation.

Future Directions

The future of prehospital management of sepsis by paramedics is poised for transformative advancements through integration of cutting-edge technologies, expanded diagnostic capabilities, broadened paramedic roles, policy evolution, and rigorous research. These developments aim to significantly improve early identification, timely intervention, and long-term outcomes for septic patients.

Integration of artificial intelligence (AI) and machine learning (ML) in prehospital triage tools promises to revolutionize sepsis screening and decision-making. Current triage systems based on vital signs and scoring tools such as SIRS and SOFA criteria often lack specificity and sensitivity. AI/ML models can analyze complex prehospital data sets, including demographics, chief complaints, and physiological parameters, to predict sepsis risk with higher accuracy and earlier than conventional methods. Research shows ML frameworks can predict sepsis onset hours before clinical signs manifest, enabling paramedics to prioritize high-risk patients for immediate care and hospital notification. However, practical challenges remain in integrating these AI tools into EMS workflows with user-friendly interfaces and adequate provider training to interpret algorithm outputs effectively (Tyler et al., 2024).

Expansion of point-of-care (POC) diagnostics in EMS represents another pivotal future direction. Traditional laboratory-dependent sepsis diagnostics incur critical time delays incompatible with emergent prehospital care. Innovative POC technologies using microfluidics, lateral flow assays, and biosensors are increasingly capable of rapidly measuring sepsis biomarkers such as lactate, procalcitonin, and C-reactive protein from small blood samples even in resource-limited environments. These tools provide paramedics with real-time, actionable data to improve risk stratification, guide early interventions, and tailor transport decisions. Early adoption of POC testing in emergency settings has demonstrated reduced emergency room wait times and improved clinical outcomes. As device accuracy improves and costs decrease, their routine EMS implementation is anticipated to become feasible and advantageous (Oeschger et al., 2019).

The role of community paramedicine and telemedicine is expanding in sepsis follow-up and early detection. Community paramedics can perform longitudinal patient monitoring, chronic disease management, and post-discharge assessments, facilitating early recognition of evolving infections and sepsis recurrence outside hospital settings. Telemedicine enables remote consultation between paramedics, specialist clinicians, and rural hospitals, improving adherence to sepsis guidelines and timely decision-making in areas with limited access to expert care. Studies demonstrate tele-ED interventions enhance guideline compliance and clinical outcomes, particularly in rural or underserved populations. These capabilities reduce delays in treatment escalation and hospital transfers, supporting continuity of care across settings (Tu et al., 2025).

Policy changes to expand the paramedic scope of practice will be critical to enable enhanced prehospital sepsis care. Past regulatory updates have authorized paramedics to perform advanced interventions such as administration of narcotic antagonists and hemorrhage control measures. Similar expansions for sepsis management could authorize paramedic administration of broad-spectrum antibiotics, advanced hemodynamic monitoring, and sepsis-specific treatment bundles in the field. Such scope expansions depend on regulatory frameworks supported by evidence-based protocols, robust paramedic education, and ongoing clinical oversight to ensure safety and efficacy. National organizations are already

advocating for greater EMS involvement in sepsis care through updated standards and guidelines (Boehringer et al., 2021).

Finally, rigorous research remains essential to validate emerging technologies and practices in prehospital sepsis management. Multicenter randomized controlled trials (RCTs) evaluating the effectiveness of prehospital antibiotics, fluid resuscitation strategies, and sepsis screening tools will provide high-quality evidence to guide clinical practice and policy. For example, trials in Europe have assessed early administration of antibiotics by paramedics with mixed but promising results, showing feasibility and safety alongside potential reductions in time to treatment and hospital readmission rates. Research into AI triage tools and POC diagnostics is also needed to assess real-world impacts on patient outcomes and EMS operations. Strong evidence from multicenter studies will underpin acceptance and widespread adoption of advanced prehospital sepsis interventions (Alam et al., 2016).

CONCLUSION

Prehospital management of sepsis represents a pivotal opportunity to improve survival through earlier recognition and intervention. Paramedics, as the first point of contact, can accelerate care pathways by utilizing validated screening tools, structured assessment frameworks, and timely interventions such as oxygen supplementation, fluid resuscitation, and, where feasible, early antibiotic therapy. Communication systems, including sepsis alerts and structured handovers, further enhance integration with hospital sepsis bundles. Although evidence highlights the benefits of prehospital interventions in reducing treatment delays and improving outcomes, significant barriers remain, including diagnostic uncertainty, resource limitations, and regulatory restrictions. Addressing these challenges through standardized training, expanded scope of practice, and adoption of emerging technologies such as artificial intelligence and point-of-care diagnostics will be essential. Future research must evaluate the effectiveness and safety of these innovations to inform global guidelines. Ultimately, bridging the gap between community and hospital care through robust prehospital sepsis management can reduce mortality and contribute to global efforts in combating the burden of sepsis.

REFERENCES

1. Alam, N., de Ven, P. M. van, Oskam, E., Stassen, P., Kramer, M. H., Exter, P. van, & Nanayakkara, P. W. (2016). Study protocol for a Multi-centre, Investigator-initiated, Randomized Controlled Trial to Compare the Effects of Prehospital Antibiotic Treatment for Sepsis Patients with Usual Care after Training Emergency Medical Services (EMS) Personnel in Early Recognition (- The Prehospital ANTibiotics Against Sepsis (PHANTASi) trial. Acute Medicine, 15(4), 176–184.
2. Al-Orainan, N., EL-Shabasy, A. M., Al-Shanqiti, K. A., Al-Harbi, R. A., Alnashri, H. R., Rezqallah, R. A., & Mirghani, A. A. (2020). Public Awareness of Sepsis Compared to Acute Myocardial Infarction and Stroke in Jeddah, Saudi Arabia: Questionnaire Study. Interactive Journal of Medical Research, 9(2), e16195. https://doi.org/10.2196/16195
3. Boehringer, B., O'Meara, P., Wingrove, G., & Nudell, N. G. (2021). An Emergency Amendment to the National Scope of Practice for Paramedics in the Setting of a Global Pandemic. The Journal of Rural Health, 37(1), 191–193. https://doi.org/10.1111/jrh.12441
4. Chatoor, R., Sekhar, P., Mahony, E., Nehme, E., Cox, S., Cudini, D., Shao, J., Smith, K., Anderson, D., Nehme, Z., & Udy, A. (2024). The burden and prognostic significance of suspected sepsis in the prehospital setting: A state-wide population-based cohort study. Emergency Medicine Australasia, 36(3), 348–355. https://doi.org/10.1111/1742-6723.14357
5. CMTE, B. R., NREMTP, EdD, MPH, Rommie L. Duckworth, MPA, LP, EFO, FO, Chris Nollette, Ed D, NREMT-P, LP, Kevin Collopy, BA, FP-C, CCEMT-P, NRP. (2018, July 27). National Association of EMS Educators (NAEMSE) Position Paper on Sepsis. JEMS: EMS, Emergency Medical Services - Training, Paramedic, EMT News. https://www.jems.com/ems-training/national-association-of-ems-educators-naemse-position-paper-on-sepsis/

6. Dorsett, M., Kroll, M., Smith, C. S., Asaro, P., Liang, S. Y., & Moy, H. P. (2017). qSOFA Has Poor Sensitivity for Prehospital Identification of Severe Sepsis and Septic Shock. Prehospital Emergency Care, 21(4), 489–497. https://doi.org/10.1080/10903127.2016.1274348
7. Draeger, L., Fleischmann-Struzek, C., Gehrke-Beck, S., Heintze, C., Thomas-Rueddel, D. O., & Schmidt, K. (2025). Barriers and facilitators to optimal sepsis care – a systematized review of healthcare professionals' perspectives. BMC Health Services Research, 25, 591. https://doi.org/10.1186/s12913-025-12777-8
8. Ghazal, H. S., Alkhunein, A. A., Alkhazi, A. A., Aldeheshi, S. A., Alhusain, F. A. M., & Al Jerian, N. (2019). Understanding the Knowledge and Attitude of Prehospital Sepsis Care among Emergency Medical Service Personnel. Journal of Emergencies, Trauma, and Shock, 12(2), 123–127. https://doi.org/10.4103/JETS.JETS_130_18
9. Green, R. S., Travers, A. H., Cain, E., Campbell, S. G., Jensen, J. L., Petrie, D. A., Erdogan, M., Patrick, G., & Patrick, W. (2016). Paramedic Recognition of Sepsis in the Prehospital Setting: A Prospective Observational Study. Emergency Medicine International, 2016, 6717261. https://doi.org/10.1155/2016/6717261
10. Gross, C. L., Cowgill, C. D., Selph, B. A., Cowgill, J. M., Saqr, Z., Allen, B. R., Southwick, F. S., & Hwang, C. W. (2025). Prehospital to emergency department handoff: Can team-based reporting improve markers of clinical efficiency in an adult emergency department? BMJ Open Quality, 14(2). https://doi.org/10.1136/bmjoq-2024-002948
11. Hollenbeak, C. S., Henning, D. J., Geeting, G. K., Ledeboer, N. A., Faruqi, I. A., Pierce, C. G., Thomas, C. B., & O'Neal, H. R. (2023a). Costs and Consequences of a Novel Emergency Department Sepsis Diagnostic Test: The IntelliSep Index. Critical Care Explorations, 5(7), e0942. https://doi.org/10.1097/CCE.0000000000000942
12. Hollenbeak, C. S., Henning, D. J., Geeting, G. K., Ledeboer, N. A., Faruqi, I. A., Pierce, C. G., Thomas, C. B., & O'Neal, H. R. (2023b). Costs and Consequences of a Novel Emergency Department Sepsis Diagnostic Test: The IntelliSep Index. Critical Care Explorations, 5(7), e0942. https://doi.org/10.1097/CCE.0000000000000942
13. Holmbom, M., Andersson, M., Berg, S., Eklund, D., Sobczynski, P., Wilhelms, D., Moberg, A., Fredrikson, M., Balkhed, Å. Ö., & Hanberger, H. (2021). Prehospital delay is an important risk factor for mortality in community-acquired bloodstream infection (CA-BSI): A matched case–control study. BMJ Open, 11(11), e052582. https://doi.org/10.1136/bmjopen-2021-052582
14. Huabbangyang, T., Klaiangthong, R., Jaibergban, F., Wanphen, C., Faikhao, T., Banjongkit, P., & Kuchapan, R. (2023a). Pre-hospital Prognostic Factors of 30-Day Survival in Sepsis Patients; a Retrospective Cohort Study. Archives of Academic Emergency Medicine, 11(1), e48. https://doi.org/10.22037/aaem.v11i1.2029
15. Huabbangyang, T., Klaiangthong, R., Jaibergban, F., Wanphen, C., Faikhao, T., Banjongkit, P., & Kuchapan, R. (2023b). Pre-hospital Prognostic Factors of 30-Day Survival in Sepsis Patients; a Retrospective Cohort Study. Archives of Academic Emergency Medicine, 11(1), e48. https://doi.org/10.22037/aaem.v11i1.2029
16. Huabbangyang, T., Klaiangthong, R., Jaibergban, F., Wanphen, C., Faikhao, T., Banjongkit, P., & Kuchapan, R. (2023c). Pre-hospital Prognostic Factors of 30-Day Survival in Sepsis Patients; a Retrospective Cohort Study. Archives of Academic Emergency Medicine, 11(1), e48. https://doi.org/10.22037/aaem.v11i1.2029
17. Inada-Kim, M. (2022). NEWS2 and improving outcomes from sepsis. Clinical Medicine, 22(6), 514–517. https://doi.org/10.7861/clinmed.2022-0450
18. Jarczak, D., Kluge, S., & Nierhaus, A. (2021). Sepsis—Pathophysiology and Therapeutic Concepts. Frontiers in Medicine, 8, 628302. https://doi.org/10.3389/fmed.2021.628302
19. Jouffroy, R., Saade, A., Ellouze, S., Carpentier, A., Michaloux, M., Carli, P., & Vivien, B. (2018a). Prehospital triage of septic patients at the SAMU regulation: Comparison of qSOFA, MRST, MEWS and PRESEP scores. The American Journal of Emergency Medicine, 36(5), 820–824. https://doi.org/10.1016/j.ajem.2017.10.030

20. Jouffroy, R., Saade, A., Ellouze, S., Carpentier, A., Michaloux, M., Carli, P., & Vivien, B. (2018b). Prehospital triage of septic patients at the SAMU regulation: Comparison of qSOFA, MRST, MEWS and PRESEP scores. The American Journal of Emergency Medicine, 36(5), 820–824. https://doi.org/10.1016/j.ajem.2017.10.030
21. Jouffroy, R., Saade, A., Muret, A., Philippe, P., Michaloux, M., Carli, P., & Vivien, B. (2018). Fluid resuscitation in pre-hospital management of septic shock. The American Journal of Emergency Medicine, 36(10), 1754–1758. https://doi.org/10.1016/j.ajem.2018.01.078
22. Kim, H.-J., Ko, R.-E., Lim, S. Y., Park, S., Suh, G. Y., & Lee, Y. J. (2024). Sepsis Alert Systems, Mortality, and Adherence in Emergency Departments: A Systematic Review and Meta-Analysis. JAMA Network Open, 7(7), e2422823. https://doi.org/10.1001/jamanetworkopen.2024.22823
23. Knack, S. K. S., Scott, N., Driver, B. E., Prekker, M. E., Black, L. P., Hopson, C., Maruggi, E., Kaus, O., Tordsen, W., & Puskarich, M. A. (2024). Early Physician Gestalt Versus Usual Screening Tools for the Prediction of Sepsis in Critically Ill Emergency Patients. Annals of Emergency Medicine, 84(3), 246–258. https://doi.org/10.1016/j.annemergmed.2024.02.009
24. Kortz, T. B., Axelrod, D. M., Chisti, M. J., & Kache, S. (2017). Clinical outcomes and mortality before and after implementation of a pediatric sepsis protocol in a limited resource setting: A retrospective cohort study in Bangladesh. PLOS ONE, 12(7), e0181160. https://doi.org/10.1371/journal.pone.0181160
25. La Via, L., Sangiorgio, G., Stefani, S., Marino, A., Nunnari, G., Cocuzza, S., La Mantia, I., Cacopardo, B., Stracquadanio, S., Spampinato, S., Lavalle, S., & Maniaci, A. (2024). The Global Burden of Sepsis and Septic Shock. Epidemiologia, 5(3), 456–478. https://doi.org/10.3390/epidemiologia5030032
26. Lamhaut, L., Dagron, C., Apriotesei, R., Gouvernaire, J., Elie, C., Marx, J.-S., Télion, C., Vivien, B., & Carli, P. (2010). Comparison of intravenous and intraosseous access by pre-hospital medical emergency personnel with and without CBRN protective equipment. Resuscitation, 81(1), 65–68. https://doi.org/10.1016/j.resuscitation.2009.09.011
27. Lazzarin, T., Ballarin, R. S., Zornoff, L., Tanni, S. E., Paiva, S. A. R. de, Azevedo, P. S., & Minicucci, M. F. (2024a). Sepsis management in pre-hospital care – the earlier, the better? BMC Emergency Medicine, 24, 220. https://doi.org/10.1186/s12873-024-01137-0
28. Lazzarin, T., Ballarin, R. S., Zornoff, L., Tanni, S. E., Paiva, S. A. R. D., Azevedo, P. S., & Minicucci, M. F. (2024b). Sepsis management in pre-hospital care – the earlier, the better? BMC Emergency Medicine, 24(1), 220. https://doi.org/10.1186/s12873-024-01137-0
29. Lesur, O., Delile, E., Asfar, P., & Radermacher, P. (2018). Hemodynamic support in the early phase of septic shock: A review of challenges and unanswered questions. Annals of Intensive Care, 8, 102. https://doi.org/10.1186/s13613-018-0449-8
30. MacAllister, S. A., Fernandez, A. R., Smith, M. J., Myers, J. Brent., & Crowe, R. P. (2024). Prehospital Sepsis Recognition and Outcomes for Patients with Sepsis by Race and Ethnicity. Prehospital Emergency Care, 28(7), 898–904. https://doi.org/10.1080/10903127.2023.2294269
31. Martel, T., Melmer, M. N., Leaman, S. M., Kassen, N., Kozlowski, S., Pangia, J., Gutovitz, S., & Jehle, D. (2020). Prehospital Antibiotics Improve Morbidity and Mortality of Emergency Medical Service Patients with Sepsis. HCA Healthcare Journal of Medicine, 1(3). https://doi.org/10.36518/2689-0216.1063
32. Moutinho, A., Fontes, J., Ferreira, L., Lopes, J., Martins, F., Mega, S., Gil, M., Barros, F., & Correia, A. M. (2025). Sepsis Alerts in the Pre-hospital Setting: An Observational Retrospective Study of Emergency Medical Services' Response in Portugal (2020–2023). Cureus. https://doi.org/10.7759/cureus.82528
33. Nardot, A., Lacorre, C., Lanneluc, A., Paulet, D., Gauriat, M., Moesch, C., Feydeau, P., Valantin, E., Dupuy, P., Blondel, M., Karam, H. H., Baïsse, A., Herafa, I., Blanchet, A., Dumolard, M., Daix, T., & Lafon, T. (2025). A program to improve sepsis management in the Emergency Department: A multicenter prospective study in France. Internal and Emergency Medicine. https://doi.org/10.1007/s11739-025-03877-8

34. Oeschger, T., McCloskey, D., Kopparthy, V., Singh, A., & Erickson, D. (2019). Point of Care Technologies for Sepsis Diagnosis and Treatment. Lab on a Chip, 19(5), 728–737. https://doi.org/10.1039/c8lc01102h
35. Peltan, I. D., Mitchell, K. H., Rudd, K. E., Mann, B. A., Carlbom, D. J., Rea, T. D., Butler, A. M., Hough, C. L., & Brown, S. M. (2018). Prehospital Care and Emergency Department Door-to-Antibiotic Time in Sepsis. Annals of the American Thoracic Society, 15(12), 1443–1450. https://doi.org/10.1513/AnnalsATS.201803-199OC
36. Piedmont, S., Goldhahn, L., Swart, E., Robra, B.-P., Fleischmann-Struzek, C., Somasundaram, R., & Bauer, W. (2024). Sepsis incidence, suspicion, prediction and mortality in emergency medical services: A cohort study related to the current international sepsis guideline. Infection, 52(4), 1325–1335. https://doi.org/10.1007/s15010-024-02181-5
37. Pinto-Villalba, R. S., Balseca-Arellano, D., & Leon-Rojas, J. E. (2024). Septic shock in the prehospital setting: A scoping review. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 32, 113. https://doi.org/10.1186/s13049-024-01282-2
38. Prekker, M. E., & Puskarich, M. A. (2018). Emergency Department Sepsis Care: Could It Matter Who Is in the Ambulance? Annals of the American Thoracic Society, 15(12), 1398–1400. https://doi.org/10.1513/AnnalsATS.201808-554ED
39. Quinten, V. M., Meurs, M. van, Maaten, J. C. ter, & Ligtenberg, J. J. M. (2016). Trends in vital signs and routine biomarkers in patients with sepsis during resuscitation in the emergency department: A prospective observational pilot study. https://doi.org/10.1136/bmjopen-2015-009718
40. Rudd, K. E., Johnson, S. C., Agesa, K. M., Shackelford, K. A., Tsoi, D., Kievlan, D. R., Colombara, D. V., Ikuta, K. S., Kissoon, N., Finfer, S., Fleischmann-Struzek, C., Machado, F. R., Reinhart, K. K., Rowan, K., Seymour, C. W., Watson, R. S., West, T. E., Marinho, F., Hay, S. I., … Naghavi, M. (2020). Global, regional, and national sepsis incidence and mortality, 1990–2017: Analysis for the Global Burden of Disease Study. The Lancet, 395(10219), 200–211. https://doi.org/10.1016/S0140-6736(19)32989-7
41. Seymour, C. W., Cooke, C. R., Heckbert, S. R., Spertus, J. A., Callaway, C. W., Martin-Gill, C., Yealy, D. M., Rea, T. D., & Angus, D. C. (2014). Prehospital intravenous access and fluid resuscitation in severe sepsis: An observational cohort study. Critical Care, 18(5), 533. https://doi.org/10.1186/s13054-014-0533-x
42. Seymour, C. W., Rea, T. D., Kahn, J. M., Walkey, A. J., Yealy, D. M., & Angus, D. C. (2012a). Severe Sepsis in Pre-Hospital Emergency Care. American Journal of Respiratory and Critical Care Medicine, 186(12), 1264–1271. https://doi.org/10.1164/rccm.201204-0713OC
43. Seymour, C. W., Rea, T. D., Kahn, J. M., Walkey, A. J., Yealy, D. M., & Angus, D. C. (2012b). Severe Sepsis in Pre-Hospital Emergency Care: Analysis of Incidence, Care, and Outcome. American Journal of Respiratory and Critical Care Medicine, 186(12), 1264–1271. https://doi.org/10.1164/rccm.201204-0713OC
44. Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G. R., Chiche, J.-D., Coopersmith, C. M., Hotchkiss, R. S., Levy, M. M., Marshall, J. C., Martin, G. S., Opal, S. M., Rubenfeld, G. D., van der Poll, T., Vincent, J.-L., & Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA, 315(8), 801–810. https://doi.org/10.1001/jama.2016.0287
45. Smyth, M. A., Brace-McDonnell, S. J., & Perkins, G. D. (2016). Identification of adults with sepsis in the prehospital environment: A systematic review. BMJ Open, 6(8), e011218. https://doi.org/10.1136/bmjopen-2016-011218
46. Thim, T., Krarup, N. H. V., Grove, E. L., Rohde, C. V., & Løfgren, B. (2012). Initial assessment and treatment with the Airway, Breathing, Circulation, Disability, Exposure (ABCDE) approach. International Journal of General Medicine, 5, 117–121. https://doi.org/10.2147/IJGM.S28478
47. Tu, K. J., Wymore, C., Tchangalova, N., Fuller, B. M., & Mohr, N. M. (2025). The impact of telehealth in sepsis care: A systematic review. Journal of Telemedicine and Telecare, 31(1), 3–13. https://doi.org/10.1177/1357633X231170038

48. Tyler, S., Olis, M., Aust, N., Patel, L., Simon, L., Triantafyllidis, C., Patel, V., Lee, D. W., Ginsberg, B., Ahmad, H., & Jacobs, R. J. (2024). Use of Artificial Intelligence in Triage in Hospital Emergency Departments: A Scoping Review. Cureus. https://doi.org/10.7759/cureus.59906
49. Varney, J., Motawea, K. R., Kandil, O. A., Hashim, H. T., Murry, K., Shah, J., Shaheen, A., Akwari, J., Awad, A. K., Rivera, A., Mostafa, M. R., Swed, S., & Awad, D. M. (2022). Prehospital administration of broad-spectrum antibiotics for sepsis patients: A systematic review and meta-analysis. Health Science Reports, 5(3), e582. https://doi.org/10.1002/hsr2.582