Redefining Pediatric Sepsis and Septic Shock: The Role of the Phoenix Criteria

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Abstract

Background: Pediatric sepsis is a life-threatening syndrome caused by a dysregulated host response to infection and remains a major contributor to childhood mortality, organ dysfunction, and long-term disability worldwide. For many years, pediatric sepsis was defined using systemic inflammatory response syndrome–based criteria, although these criteria showed limited specificity, inconsistent bedside application, and inadequate discrimination of children at greatest risk of death. The Phoenix Sepsis Criteria were introduced to provide an evidence-based, globally applicable definition centered on infection-associated organ dysfunction. The Phoenix Sepsis Score evaluates respiratory, cardiovascular, neurological, and coagulation dysfunction, defining pediatric sepsis as suspected or confirmed infection accompanied by a score of at least 2 points. Septic shock is identified when a child with sepsis has at least 1 cardiovascular point based on severe age-adjusted hypotension, elevated blood lactate, or the requirement for vasoactive therapy.

Aim: This review aims to critically examine the Phoenix Sepsis Criteria in relation to pediatric septicemia, sepsis, and septic shock, with emphasis on their conceptual development, diagnostic components, prognostic performance, clinical applicability, and potential value in resource-limited settings. It also explores the relationship between the Phoenix Sepsis Score, inflammatory biomarkers, microbiological findings, organ dysfunction, and mortality. Particular attention is given to the distinction between bloodstream infection and the broader syndrome of sepsis, because septicemia or culture-confirmed bacteremia may be absent in many children who develop severe infection-associated organ dysfunction.

Conclusion: The Phoenix criteria represent an important transition from inflammation-based definitions toward an organ dysfunction–based framework that better identifies children with life-threatening infection and predicts adverse outcomes. Their simplified four-organ structure may support standardized diagnosis, epidemiological surveillance, clinical research, and comparison of pediatric sepsis outcomes across different health-care settings. Available clinical findings indicate that increasing total Phoenix scores and higher C-reactive protein concentrations may independently predict mortality, whereas individual cultured organisms or radiological respiratory findings may not consistently determine outcome. A total score threshold of approximately 5.5 may provide moderate discrimination for mortality, although its sensitivity and specificity remain insufficient for use as an isolated prognostic tool. Therefore, the Phoenix score should complement, rather than replace, early clinical assessment, sepsis screening systems, microbiological evaluation, biomarkers, and repeated evaluation of organ function. Further prospective multicenter validation is required, particularly among neonates, immunocompromised children, and populations in low-resource environments.

Keywords: Phoenix Sepsis Score; pediatric sepsis; septicemia; septic shock

1. Introduction

Pediatric sepsis is defined conceptually as life-threatening organ dysfunction resulting from a dysregulated host response to infection. It is not simply the presence of fever, inflammation, bacteremia, or a positive culture. The syndrome reflects the interaction between an infectious insult, host susceptibility, immune dysregulation, endothelial injury, altered perfusion, and progressive organ dysfunction. In 2024, the International Consensus Criteria for Pediatric Sepsis and Septic Shock operationalized this concept through the Phoenix Sepsis Score, replacing the previous systemic inflammatory response syndrome–based model with a framework emphasizing respiratory, cardiovascular, coagulation, and neurological dysfunction. This change represents one of the most important developments in pediatric sepsis classification since the 2005 consensus definitions. [1]

Sepsis remains a major global health burden despite vaccination, antimicrobial therapy, improved intensive care, and implementation of sepsis bundles. Global estimates indicate that almost half of all sepsis cases occur in children, particularly those younger than 5 years, with a disproportionate burden in low- and middle-income countries. The epidemiological burden is difficult to quantify because sepsis is frequently coded according to the underlying infection, diagnostic practices differ among institutions, and historical studies have used inconsistent definitions. Consequently, apparent changes in incidence may reflect altered recognition, coding, health-care access, and diagnostic criteria rather than true biological changes in disease frequency. [7]

Population-based evidence demonstrates particularly high rates of sepsis among neonates and young children. A systematic review estimated millions of annual neonatal and pediatric cases, with mortality substantially higher among neonates and children with severe organ dysfunction. However, most available population-level studies were conducted in high- and middle-income countries, leaving major evidence gaps in regions where childhood infection, malnutrition, delayed presentation, limited critical-care capacity, and antimicrobial resistance are common. The Phoenix criteria may improve international comparability, but their implementation cannot compensate for absent surveillance systems or inequitable access to diagnostic and supportive care. [8]

The principal research gap is therefore not merely the absence of a standardized definition. It is the limited understanding of how the Phoenix criteria perform across different clinical environments, age groups, infectious etiologies, comorbidities, and resource levels. Additional uncertainty concerns whether the score can support bedside prognosis, whether it is sufficiently sensitive during early deterioration, and how it should be interpreted alongside biomarkers and microbiological findings. This review aims to examine these questions while clarifying the relationship between septicemia, bloodstream infection, pediatric sepsis, and septic shock. [4]

2. Septicemia, Bloodstream Infection, Sepsis, and Septic Shock

The terminology used in sepsis literature has evolved substantially. The 2005 International Pediatric Sepsis Consensus Conference defined pediatric sepsis as suspected or proven infection accompanied by systemic inflammatory response syndrome. Severe sepsis was defined by sepsis with cardiovascular dysfunction, acute respiratory distress syndrome, or dysfunction of at least two other organs, whereas septic shock referred to sepsis with cardiovascular dysfunction. These definitions supported research standardization but also classified many children with common febrile illnesses and physiological inflammation as having sepsis. [3]

“Septicemia” is an older and imprecise term that has been used to describe microorganisms or their products circulating in the blood, clinical deterioration associated with bloodstream infection, or sepsis in general. Contemporary terminology distinguishes bacteremia or bloodstream infection from sepsis. Bacteremia describes viable bacteria detected in blood, while bloodstream infection implies a clinically relevant pathogen in the circulation. Sepsis describes organ dysfunction caused by a dysregulated response to infection, regardless of whether microorganisms are recovered from blood. Therefore, a child may have bacteremia without sepsis, sepsis without bacteremia, or bacteremia accompanied by

septic shock. [13]

This distinction is clinically important because viral, fungal, parasitic, and localized bacterial infections can cause severe sepsis without positive blood cultures. Viral sepsis may result from respiratory syncytial virus, influenza, adenovirus, dengue, severe acute respiratory syndrome coronavirus 2, or other viral pathogens. Conversely, transient bacteremia or contamination with skin flora may occur without life-threatening organ dysfunction. The Phoenix criteria consequently require suspected or confirmed infection together with organ dysfunction rather than microbiological confirmation alone. [11]

The etiology of pediatric sepsis varies with age, geography, vaccination coverage, comorbidities, health-care exposure, and local antimicrobial resistance. Respiratory and bloodstream infections are common in intensive-care cohorts, whereas respiratory infections, diarrheal diseases, malaria, dengue, and neonatal infections contribute heavily to the burden in lower-resource regions. Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Candida species are important pathogens, but their relative frequency differs markedly across populations. Etiological heterogeneity supports the need for a syndrome definition that is not restricted to a particular organism or anatomical source. [10]

3. Pathophysiological Basis of Infection-Associated Organ Dysfunction

The pathogenesis of sepsis begins with recognition of pathogen-associated molecular patterns by innate immune receptors. This process activates intracellular signaling pathways and promotes the production of cytokines, chemokines, complement factors, acute-phase proteins, and procoagulant mediators. Cellular injury subsequently releases damage-associated molecular patterns that amplify inflammation even when the original microbial burden is declining. Sepsis therefore represents an evolving interaction among pathogen virulence, inflammatory activation, immune suppression, endothelial dysfunction, mitochondrial injury, and impaired cellular oxygen utilization rather than a simple excessive inflammatory response. [21]

Endothelial activation is central to progression from infection to organ dysfunction. Damage to the endothelial glycocalyx increases vascular permeability, promotes leukocyte adhesion, alters vasomotor regulation, and activates coagulation. Microvascular flow becomes heterogeneous, with areas of shunting adjacent to poorly perfused tissue. These changes may impair tissue oxygen extraction even when systemic blood pressure and cardiac output appear acceptable. Endothelial injury also links inflammation with capillary leakage, disseminated microthrombosis, acute respiratory distress syndrome, acute kidney injury, and neurological dysfunction. [20]

Cardiovascular dysfunction in pediatric sepsis may involve hypovolemia, vasodilation, myocardial depression, altered afterload, or combinations of these mechanisms. Children can initially preserve blood pressure through tachycardia and peripheral vasoconstriction, making hypotension a relatively late and concerning sign. Lactate elevation may reflect inadequate oxygen delivery, impaired clearance, adrenergic stimulation, altered metabolism, or microcirculatory dysfunction. Consequently, lactate is a marker of severity and physiological stress but should not be interpreted as direct proof of tissue hypoxia or bacterial infection in isolation. [1]

Sepsis-associated acute kidney injury results from complex interactions among inflammation, endothelial dysfunction, altered renal microcirculation, tubular stress, nephrotoxic exposure, and hemodynamic instability. Renal injury can develop even without prolonged systemic hypotension and may worsen fluid accumulation, electrolyte abnormalities, acid-base disturbances, and drug toxicity. Although kidney dysfunction is clinically important and included in the expanded Phoenix-8 model, it was not retained in the four-organ Phoenix Sepsis Score because the final model prioritized mortality discrimination, feasibility, and parsimony. [19]

Coagulation dysfunction is another major pathway of organ injury. Inflammatory signaling promotes tissue factor expression, thrombin generation, platelet activation, endothelial disruption, and inhibition of natural anticoagulant pathways. Simultaneously, fibrinolysis may become suppressed. The resulting spectrum ranges from mild thrombocytopenia and laboratory coagulopathy to disseminated intravascular coagulation and thrombocytopenia-associated multiple-organ failure. The inclusion of

platelet count, international normalized ratio, D-dimer, and fibrinogen in the Phoenix score recognizes the prognostic relevance of disturbed coagulation in pediatric infection. [18]

4. Evolution From SIRS-Based Definitions to the Phoenix Criteria

The systemic inflammatory response syndrome framework was originally intended to identify an abnormal inflammatory response using temperature, heart rate, respiratory rate, and leukocyte abnormalities. In children, these parameters require age-specific thresholds and are influenced by fever, pain, anxiety, medication, dehydration, and many noninfectious conditions. Although SIRS can identify children requiring assessment, it has poor specificity for life-threatening infection and may be absent in children with significant organ dysfunction. It therefore functions more effectively as a physiological warning concept than as a definitive sepsis diagnosis. [3]

An international survey conducted by the Pediatric Sepsis Definition Taskforce demonstrated broad support for defining sepsis according to infection-associated life-threatening organ dysfunction rather than SIRS. Respondents also emphasized global applicability, feasibility in lower-resource settings, and the importance of distinguishing sepsis from uncomplicated infection. These findings aligned pediatric terminology with the conceptual direction of adult Sepsis-3 while acknowledging that adult thresholds and organ dysfunction scores could not simply be transferred to children without age-specific validation. [5]

The Pediatric Organ Dysfunction Information Update Mandate subsequently reviewed contemporary evidence for dysfunction across multiple organ systems. This work demonstrated that pediatric organ dysfunction is multidimensional and that no single physiological or laboratory measurement captures the full syndrome. It also provided evidence-based criteria that informed the evaluation of respiratory, cardiovascular, neurological, coagulation, renal, hepatic, endocrine, and immune dysfunction during development of the Phoenix models. [6]

A systematic review by the Pediatric Sepsis Definition Taskforce assessed demographic, clinical, physiological, laboratory, and organ dysfunction variables associated with sepsis, multiple-organ dysfunction, and mortality. Measures of altered consciousness, respiratory failure, cardiovascular compromise, coagulation disturbance, and overall organ dysfunction were more consistently associated with adverse outcomes than the presence of SIRS alone. Nevertheless, heterogeneity in study designs, definitions, populations, and outcome reporting limited the ability to select criteria exclusively through meta-analysis, necessitating the combination of empirical modeling and expert consensus. [4]

5. Development of the Phoenix Sepsis Score

The Phoenix criteria were developed using data from more than 3.6 million pediatric health-care encounters across differently resourced settings. Children with suspected infection were identified using combinations of antimicrobial treatment and microbiological testing. Organ-specific subscores from eight existing organ dysfunction scores were calculated using data from the first 24 hours after presentation. Their ability to discriminate in-hospital mortality was assessed, and the best-performing components were entered into stacked regression models. The resulting models were then translated into an integer-based score suitable for clinical, epidemiological, and electronic applications. [2]

The initial expanded model included eight organ systems: respiratory, cardiovascular, coagulation, neurological, renal, hepatic, endocrine, and immunological dysfunction. A simplified four-organ model showed performance comparable with the expanded model and was selected because it was more feasible across diverse health systems. The final Phoenix Sepsis Score therefore included respiratory dysfunction scored from 0 to 3 points, cardiovascular dysfunction from 0 to 6 points, coagulation dysfunction from 0 to 2 points, and neurological dysfunction from 0 to 2 points, producing a maximum total score of 13. [2]

Sepsis is identified in a child with suspected or confirmed infection when the Phoenix Sepsis Score is at least 2. Septic shock is defined as sepsis accompanied by at least 1 cardiovascular point. The criteria generally apply to children younger than 18 years but are not intended for premature neonates whose postconceptional age is below 37 weeks. The term “severe sepsis” is no longer required because sepsis itself denotes potentially life-threatening organ dysfunction. [1]

The Phoenix criteria were named both for the location where they were introduced and for the symbolic concept of renewal. Their principal purpose is to standardize identification of children whose infection is accompanied by organ dysfunction associated with increased mortality. They were designed for clinical characterization, quality improvement, epidemiology, benchmarking, and research. They were not designed as an early screening instrument, a replacement for clinical judgment, or a mandate to delay treatment until the threshold of 2 points is reached. [34]

6. Components and Clinical Interpretation of the Phoenix Score

The respiratory component uses the arterial oxygen tension to inspired oxygen fraction ratio or the peripheral oxygen saturation to inspired oxygen fraction ratio, interpreted in relation to respiratory support. One point is assigned for impaired oxygenation while receiving respiratory support, whereas greater impairment during invasive mechanical ventilation generates 2 or 3 points. This structure attempts to distinguish mild oxygenation abnormalities from life-threatening respiratory dysfunction. However, respiratory support itself is influenced by local practice, resource availability, and thresholds for intubation, which may affect scoring across institutions. [1]

The cardiovascular component includes age-adjusted mean arterial pressure, serum lactate, and the number of vasoactive medications. One point may be assigned for moderately severe hypotension, lactate of 5 to 10.9 mmol/L, or use of one vasoactive medication. Two points are assigned for more profound hypotension, lactate of at least 11 mmol/L, or use of at least two vasoactive medications. Points from these variables may accumulate to a maximum cardiovascular subscore of 6. Because septic shock requires only 1 cardiovascular point in a child meeting sepsis criteria, shock can be identified without requiring simultaneous hypotension, hyperlactatemia, and vasoactive therapy. [2]

The coagulation component assigns 1 point for each abnormal variable, up to a maximum of 2 points. Relevant abnormalities include platelet count below $100 \times 10^3/\mu L$, international normalized ratio above 1.3, D-dimer above 2 mg/L fibrinogen-equivalent units, or fibrinogen below 100 mg/dL. The use of multiple interchangeable variables provides some resilience when individual tests are unavailable, but coagulation results may be influenced by liver disease, malignancy, transfusion, anticoagulant exposure, and pre-existing hematological abnormalities. Baseline status must therefore be considered when interpreting the score. [1]

The neurological component assigns 1 point for a Glasgow Coma Scale score of 10 or below and 2 points for bilaterally fixed pupils. Sedatives, neuromuscular blocking drugs, postictal states, traumatic brain injury, metabolic disturbances, and pre-existing neurological disability may confound assessment. The score should be based on the best clinically appropriate interpretation of neurological function rather than an uncritical extraction of a recorded value obtained during anesthesia or pharmacological paralysis. [6]

The Phoenix score is calculated using the most abnormal eligible values in the assessment window. Consequently, a score obtained retrospectively from the worst values during the first 24 hours is not equivalent to a score available at initial triage. A child may deteriorate from a score of 0 or 1 to a much higher score over several hours. Serial calculation may help describe the trajectory of organ dysfunction, but prospective evidence is still required to determine the optimal frequency, time window, and clinical actions associated with changing scores. [2]

7. Relationship Between Phoenix Sepsis and Microbiologically Confirmed Septicemia

Blood culture remains essential when bacterial bloodstream infection is suspected because organism identification and antimicrobial susceptibility testing support definitive therapy. Nevertheless, culture has limited sensitivity. Low circulating bacterial density, inadequate blood volume, previous antimicrobial exposure, intermittent bacteremia, and technical factors can produce negative results. In pediatric and neonatal patients, obtaining sufficient blood volume may be difficult, and the diagnostic yield decreases when samples are collected after antimicrobials have been administered. [13]

Modern microbiological methods, including automated blood culture systems, multiplex polymerase chain reaction, pathogen-specific nucleic acid amplification, and mass spectrometry, can shorten the time to organism identification. However, molecular methods may detect microbial DNA without

proving viable bloodstream infection and may not provide complete susceptibility information. They also require financial, technical, and quality-assurance infrastructure that is unavailable in many settings. These methods complement rather than eliminate conventional cultures and clinical interpretation. [14]
Cultures should ideally be obtained before antimicrobial administration when this can be achieved without clinically important delay. Prospective evidence shows that blood culture positivity is lower after antimicrobial exposure for both Gram-positive and Gram-negative organisms. Nevertheless, in a child with shock or rapidly progressive organ dysfunction, treatment should not be delayed solely to obtain additional specimens. Diagnostic stewardship requires an appropriate number and volume of cultures, strict aseptic technique, and careful distinction between genuine bloodstream infection and contamination. [15]
The increasing prevalence of multidrug-resistant Gram-negative organisms complicates the relationship between pathogen identification and outcome. Klebsiella, Pseudomonas, Acinetobacter, and other resistant organisms may cause severe neonatal and pediatric sepsis, particularly in health-care-associated settings. However, mortality is not determined by organism identity alone. Host immunity, comorbidities, source control, antimicrobial susceptibility, treatment timing, organ dysfunction, and available supportive care may exert equal or greater influence. [12]
Consequently, neither a positive culture nor a specific organism automatically establishes Phoenix sepsis. A culture-positive child with no qualifying organ dysfunction does not meet the Phoenix definition, whereas a culture-negative child with suspected infection and a score of at least 2 does. This distinction explains why individual organisms may show no statistically significant association with mortality in a limited cohort even when the total organ dysfunction score is prognostically important. The Phoenix criteria classify the severity of the host response rather than the microbiological certainty of bloodstream invasion. [1]

8. Biomarkers and Hematological Indices

C-reactive protein, procalcitonin, interleukins, lactate, serum amyloid A, and other biomarkers have been investigated for diagnosis and prognosis in pediatric sepsis. C-reactive protein is inexpensive and widely available but rises after inflammatory stimulation and is not specific to bacterial infection. Procalcitonin may offer greater specificity for invasive bacterial disease in selected populations, although it can increase after surgery, trauma, severe shock, and other inflammatory states. Biomarker concentrations should be interpreted as dynamic probabilities rather than binary confirmation or exclusion of sepsis. [17]
Platelet count and platelet indices may provide additional information. Sepsis can cause platelet consumption, impaired production, endothelial adhesion, microthrombosis, and immune-mediated destruction. Mean platelet volume may increase as larger, younger platelets enter the circulation, and meta-analytic evidence suggests that it is often higher in neonatal sepsis than in controls. Nevertheless, variation among analyzers, sampling conditions, gestational age, and timing limits the use of mean platelet volume as a standalone diagnostic test. [16]
Thrombocytopenia and coagulation abnormalities are particularly relevant to the Phoenix score because they directly contribute to the coagulation subscore. Their presence may indicate systemic endothelial and coagulation activation, but alternative causes must be considered, especially in children with malignancy, chronic liver disease, bone marrow failure, massive transfusion, or pre-existing thrombocytopenia. In these populations, change from baseline may be more informative than a single absolute threshold, although the standard Phoenix calculation does not formally adjust for chronic dysfunction. [18]
In the study findings supplied for this review, increasing total score and C-reactive protein were independently associated with mortality, with reported odds ratios of 1.288 and 1.012, respectively. A total score cutoff of at least 5.5 produced an area under the receiver operating characteristic curve of 0.706, sensitivity of 68.6%, specificity of 64.7%, positive predictive value of 64.4%, negative predictive value of 83.3%, and overall accuracy of 65.8%. These results indicate moderate discrimination rather than definitive prediction. The comparatively higher negative predictive value suggests that lower scores

may be more useful for identifying a lower-risk group than higher scores are for establishing inevitable mortality. The cutoff requires external validation and should not be generalized without assessing calibration, prevalence, case mix, and treatment effects.

The absence of statistically significant associations between mortality and individual organisms or radiological diagnoses should also be interpreted cautiously. A negative association does not establish biological irrelevance and may reflect small subgroup sizes, overlapping infections, antimicrobial exposure, or limited statistical power. Pneumonia, acute respiratory distress syndrome, and extensive radiological opacification may contribute to the respiratory Phoenix subscore, but the prognostic effect is mediated through the severity of gas-exchange impairment and organ dysfunction rather than the radiological label alone.

9. Prognostic Performance and External Validation

In the original development and validation study, mortality increased progressively with higher Phoenix scores. A threshold of at least 2 provided a higher positive predictive value and similar or higher sensitivity for mortality than previous pediatric consensus criteria across several higher- and lower-resource datasets. The score's discrimination varied among sites because outcome prevalence, data completeness, respiratory support documentation, and available laboratory testing differed. These findings demonstrate that performance is context dependent even when the same thresholds are applied. [2]

A subsequent nine-center United States validation included 25,680 critically ill children with suspected or confirmed infection. Approximately 43% met Phoenix sepsis or septic shock criteria, and mortality among those meeting the criteria was approximately 9%. The Phoenix criteria generally discriminated mortality more effectively than the 2005 consensus criteria across age, malignancy, and technology-dependence subgroups. Importantly, children meeting Phoenix but not older consensus criteria had higher mortality than those meeting older criteria without Phoenix-defined sepsis, supporting the emphasis on organ dysfunction rather than SIRS. [28]

External validation among children hospitalized with suspected community-acquired sepsis in Australia and New Zealand showed performance broadly comparable with the original study. However, important limitations were identified. More than 95% of hospitalized children with suspected sepsis did not meet the Phoenix criteria, the score depended on the worst values during the first 24 hours, and a substantial proportion of children who died were not identified by the binary sepsis threshold. These observations reinforce that the criteria are optimized for defining life-threatening organ dysfunction, not for capturing the entire clinical workload of suspected sepsis or providing an early rule-out test. [29]

A Korean pediatric intensive-care validation evaluated both worst values during 24 hours and values obtained close to admission. The Phoenix score remained associated with mortality under both approaches and generally performed better than older consensus definitions. Nevertheless, discrimination was influenced by low mortality prevalence and the selected assessment window. Such findings support use of the score for prognostic characterization while highlighting the need for prospective studies evaluating real-time calculation and treatment decisions at presentation. [30]

A large population-based study from Hong Kong evaluated the Phoenix-4 and Phoenix-8 scores across more than 140,000 hospitalizations with presumed infection. Children meeting Phoenix-8 criteria had substantially higher mortality than those classified as having uncomplicated infection, and mortality discrimination was strong. Phoenix-8 performed better than pediatric SOFA and similarly to Phoenix-4 and PELOD-2 in several analyses. The study also revealed that electronic availability of required variables differed considerably among scores, demonstrating that feasibility depends on how clinical data are recorded and indexed. [31]

Not all external studies have shown uniformly strong performance. A 2026 multicenter Chinese intensive-care cohort reported only moderate mortality discrimination for the original score, with an area under the curve of approximately 0.60. A modified model incorporating comorbidities, demographic characteristics, and vital signs performed better. These results do not invalidate the Phoenix definition but demonstrate that a parsimonious diagnostic classification may not be the optimal

standalone mortality prediction model in every population. Definitions, severity scores, screening tools, and prognostic models serve related but different purposes. [32]

10. Clinical Application and Management Implications

The Phoenix score should be used only after infection is suspected or confirmed. Clinical pathways are still required to recognize children at risk before advanced organ dysfunction becomes evident. Abnormal appearance, altered interaction, prolonged capillary refill, weak pulses, respiratory distress, oliguria, altered consciousness, temperature instability, and rapidly changing vital signs should activate urgent assessment even when the current Phoenix score is below 2. The score must never be used to justify withholding evaluation or treatment from a deteriorating child. [1]

Current pediatric Surviving Sepsis Campaign guidance emphasizes early recognition, repeated reassessment, appropriate cultures, timely antimicrobial therapy, source control, individualized fluid resuscitation, vasoactive support when indicated, and organ support. Treatment should be initiated according to the probability and severity of infection rather than delayed until retrospective score completion. The Phoenix criteria and management guidelines are therefore complementary: one standardizes the definition of organ dysfunction, while the other guides actions during suspected or established sepsis and septic shock. [22]

Quality-improvement initiatives demonstrate that standardized pathways can reduce delays in recognition and treatment. Implementation of mandated pediatric sepsis care in New York was associated with improved protocol completion and lower mortality when key elements were completed promptly. However, process targets must be balanced with individualized assessment, particularly because aggressive fluid or antimicrobial strategies may cause harm when applied indiscriminately to children without bacterial infection or circulatory compromise. [23]

Antimicrobial stewardship remains essential in the Phoenix era. Children meeting the criteria may have bacterial, viral, fungal, or parasitic infection, and some may ultimately have a noninfectious sepsis mimic. Empirical therapy should reflect age, infection source, immune status, previous antimicrobial exposure, local resistance, and health-care association. Once microbiological and clinical information becomes available, therapy should be narrowed, modified, or discontinued when appropriate. The seriousness of organ dysfunction does not remove the obligation to reassess the diagnosis and minimize avoidable antimicrobial harm. [24]

Electronic health records may support automatic Phoenix calculation, case identification, benchmarking, and research enrollment. Nevertheless, automated systems are vulnerable to missing data, incorrect inspired oxygen documentation, sedation-related Glasgow Coma Scale values, and misclassification of chronic organ dysfunction. An electronic alert should present the contributing variables and their timing rather than generate an unexplained binary label. Clinical governance, local validation, and monitoring for alert fatigue are necessary before the score is linked to mandatory treatment pathways. [35]

11. Application in Lower-Resource Settings

The Phoenix criteria were deliberately developed using data from differently resourced settings, and their four-organ structure is simpler than many existing organ dysfunction scores. Oxygen saturation can substitute for arterial oxygen measurements, age-adjusted blood pressure can identify cardiovascular dysfunction when lactate is unavailable, and the coagulation component allows different qualifying abnormalities. These features support broader implementation, but they do not eliminate the effects of limited monitoring, laboratory testing, oxygen delivery, vasoactive medications, or mechanical ventilation. [1]

In lower-resource environments, interventions included in the score may be unavailable or initiated late. A child who would receive mechanical ventilation or vasoactive therapy in a tertiary center may not receive these treatments elsewhere, producing a lower intervention-based score despite greater clinical risk. Conversely, delayed presentation may result in profound hypotension or neurological dysfunction and a very high score at first assessment. Local validation must therefore examine missingness, referral patterns, treatment availability, and deaths occurring before hospital or intensive-care admission. [33]

Clinical decision-support tools for resource-limited settings must be feasible, interpretable, and

connected to actions that can actually be delivered. Tools requiring unavailable tests may worsen inequity or produce misleading comparisons between institutions. The Phoenix score can standardize part of the diagnostic framework, but world-oriented implementation also requires investment in pulse oximetry, reliable blood-pressure measurement, essential laboratory testing, antimicrobial access, oxygen systems, referral pathways, and trained pediatric personnel. [34]

12. Limitations of the Phoenix Criteria

The first limitation is that the Phoenix criteria define established organ dysfunction rather than early risk. A child can be in the initial phase of rapidly progressive sepsis while having a score below 2. Screening instruments, pediatric early-warning systems, clinician concern, and repeated observation remain necessary. Studies comparing emergency screening tools show that no single tool identifies every child who later meets Phoenix sepsis or septic shock criteria, reinforcing the need for layered recognition strategies. [35]

Second, the score includes interventions and measurements that depend on practice patterns. Respiratory support, mechanical ventilation, vasoactive therapy, lactate testing, coagulation testing, and neurological documentation are not applied uniformly. A score may therefore reflect both illness severity and the local health-care response. This is particularly relevant when comparing hospitals, countries, or historical periods with different treatment thresholds and resource availability.

Third, the simplified score excludes renal, hepatic, endocrine, and immune dysfunction. A child with severe infection-associated acute kidney injury or hepatic failure could have clinically important sepsis while accumulating fewer than 2 points if the four included systems remain relatively preserved. The Phoenix-8 score may provide a more complete description for research, but it requires additional data and may be less feasible for routine use. The four-organ score should not narrow the clinician's assessment of multiple-organ dysfunction.

Fourth, chronic disease can confound score components. Baseline thrombocytopenia in malignancy, chronic hypoxemia in cyanotic heart disease, neurological impairment, or dependence on respiratory support may generate points unrelated to an acute infectious deterioration. Original studies generally used available encounter data without consistently distinguishing new from chronic abnormalities. Prospective implementation should document baseline function and interpret acute changes within the clinical context.

Finally, the Phoenix score was derived using mortality as the principal outcome. Mortality is important but does not capture new disability, cognitive impairment, reduced quality of life, technology dependence, readmission, or family psychological effects. A score optimized to discriminate death may not identify all children at risk of substantial long-term morbidity. Pediatric sepsis research should therefore combine mortality with patient- and family-centered outcomes. [27]

13. Outcomes Beyond Hospital Survival and Future Directions

Survivors of pediatric sepsis may experience physical weakness, respiratory limitations, neurological impairment, feeding problems, emotional disturbance, cognitive difficulties, and reduced participation in school and social activities. These effects may occur as part of pediatric post-intensive-care syndrome and can also affect parents and siblings. Organ dysfunction scores, vasoactive requirements, cardiopulmonary resuscitation, neurological events, immunocompromised status, and extracorporeal support have been associated with poorer functional outcomes. [25]

Long-term outcome trajectories are heterogeneous. Some children recover rapidly, whereas others have persistent or newly recognized disability months after discharge. Follow-up studies of community-acquired pediatric septic shock demonstrate that mortality and health-related quality-of-life morbidity continue beyond the acute hospitalization. Future Phoenix validation should therefore determine whether the score or its trajectory predicts late mortality, functional status, neurodevelopment, health-related quality of life, and family burden. [36]

A core outcome set for pediatric critical care has been developed to reduce heterogeneity in outcome reporting. Incorporating standardized survival, functional, cognitive, emotional, and quality-of-life outcomes into sepsis studies would allow more meaningful comparison of interventions. Future research

should also evaluate whether combining Phoenix components with age, comorbidity, infection source, biomarkers, host-response phenotypes, and treatment-response variables improves individualized prognosis without producing an impractical or opaque model. [27]

The most promising future approach may separate three linked functions: early screening, diagnostic classification, and outcome prediction. Early-warning tools should prioritize sensitivity and timely escalation; the Phoenix criteria should provide a reproducible definition of infection-associated organ dysfunction; and prognostic models should estimate individual risks using additional clinical and biological variables. Treating one score as though it performs all three functions risks missed early disease, overtreatment, and inaccurate counseling.

Conclusion

The Phoenix Sepsis Criteria provide a major conceptual and practical advance by defining pediatric sepsis through infection-associated organ dysfunction rather than systemic inflammation alone. They clarify that septicemia or bloodstream infection is neither necessary nor sufficient for sepsis and that septic shock represents sepsis with cardiovascular dysfunction. The score offers valuable standardization for research, surveillance, quality improvement, and clinical characterization, but its prognostic performance varies across populations and it is not an early screening tool. Optimal use requires integration with repeated bedside assessment, microbiological evaluation, biomarkers, baseline organ function, and timely guideline-directed management. Prospective multicenter studies are required to refine real-time application, validate higher prognostic thresholds, and determine how Phoenix score trajectories relate to survival, disability, and long-term quality of life.

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