

## Paediatric Sepsis 3

# Quality improvement programmes in paediatric sepsis from a global perspective

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Sepsis is a major contributor to poor child health outcomes around the world. The high morbidity, mortality, and societal cost associated with paediatric sepsis render it a global health priority, as summarised in Paper 1 of this Series. Sepsis is characterised by a dysregulated host response to infection that manifests as organ failure, and children are uniquely susceptible to sepsis, as discussed in Paper 2. The focus of this third Series paper is quality improvement in paediatric sepsis. The 2017 WHO resolution on sepsis outlined key aims to reduce the burden of sepsis. As of 2024, only a small number of countries have implemented systematic, paediatric-focused quality improvement programmes to raise sepsis awareness, enhance recognition of sepsis, promote timely treatment, and provide long-term support for paediatric sepsis survivors. We examine programme successes and systematic barriers to quality improvement targeting paediatric sepsis. We highlight the need for programme design to consider the entire patient journey, starting with prevention, caregiver awareness, recognition at home, education of the health-care workforce, development of health-care systems, and establishment of long-term family and survivor support extending beyond the intensive care unit. Building on lessons learnt from existing quality improvement programmes, we outline implementation strategies and measures to enable benchmarking. Ultimately, quality improvement on a global scale can only be accelerated through a global learning platform focusing on paediatric sepsis.

### Introduction

Children with sepsis present and require care at all levels of the health-care system.<sup>1-5</sup> Delivery of optimal management is highly reliant on adequate and rational allocation of health-care resources; however, substantial inequities are associated with access to nutrition, education, vaccination, and health care.<sup>6-9</sup> Extreme weather conditions, food insecurity, military conflicts, and pandemics are exacerbating global inequities.<sup>10-12</sup> Although patient outcomes of paediatric sepsis have marginally improved in high-income countries (HICs), the morbidity and mortality associated with paediatric sepsis remain high in low-income and middle-income countries (LMICs).<sup>2,13-15</sup> WHO's 2017 resolution on sepsis outlined key aims to reduce the burden of sepsis,<sup>16,17</sup> but as of 2024, few countries have launched systematic quality improvement programmes to raise sepsis awareness, improve recognition and diagnosis, promote timely and effective treatment, and provide long-term support for sepsis survivors. Most existing programmes are geared towards adults, with little emphasis on the unique needs and vulnerabilities of the paediatric population.

Some of the challenges of the COVID-19 pandemic exposed the dependency of health-care systems on a coordinated health-care response and highlighted the enormous benefits that can result from coordinated public health, academia, and industry efforts that combine strategies on prevention, education, research, and quality improvement.<sup>18</sup> The pandemic's effect on childhood vaccination programmes unveiled vastly unequal availability of medical supplies (including oxygen and personal protection equipment), specialist

health-care providers, and capacity to care for critically ill children.<sup>19</sup> Most of the children who died from COVID-19 lived in LMICs. Such data reinforce the vulnerability of children to life-threatening infection in regions with poor socioeconomic conditions and should inform action plans targeting sepsis in children.<sup>5</sup> Existing resources and initiatives for sepsis care are simply not optimised to serve the needs of paediatric populations in low-resource health-care settings.

### Paediatric sepsis is a failure of the health system

Multiple systemic barriers to the effective diagnosis, treatment, and follow-up of paediatric sepsis exist, including difficulty in early recognition, low socio-demographic status, cultural barriers, minimal sepsis education, and vulnerability of health-care systems (figure 1). Although paediatric sepsis occurs in all communities, it is predominantly a disease of poverty. Data from the Global Burden of Disease Study<sup>1</sup> showed that more than 80% of sepsis cases and sepsis-related deaths occur in settings with few resources that are often characterised by food and clean water insecurity, poor housing, environmental pollution, and low levels of parental education.<sup>20</sup>

Even within affluent countries, vulnerability to childhood sepsis will vary due to complex interactions of race, ethnicity, geographical residence, and sociodemographic issues (figure 2). In the USA, age-adjusted sepsis mortality rates in Hawaii were 5 times higher than in Los Angeles, California (14.4 deaths vs 2.7 deaths per 100 000 population).<sup>21</sup> In Australia, Aboriginal and Torres Strait Islander children with invasive infections who required intensive care unit (ICU) admission had

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For more on **health inequities and their causes** see <https://www.who.int/news-room/facts-in-pictures/detail/health-inequities-and-their-causes>

For the **WHO guidance on sepsis prevention and management** see <https://www.who.int/teams/integrated-health-services/infection-prevention-control/sepsis>

### Key messages

- The disproportionate effect of sepsis on child health across the world demands systematic and coordinated investment to improve awareness, enhance health-care worker training, and develop systems of care designed to prevent, recognise, treat, and follow up paediatric sepsis
- Sepsis has been termed a disease of systemic failures to learn, highlighting reoccurring patterns of missed recognition, delayed treatment, and delayed escalation to higher levels of care; these gaps might be exacerbated by poor sepsis awareness in the public, insufficient sepsis-specific training, difficulties in recognising the child with sepsis in a deteriorating condition, and delays in delivering treatment
- Previous quality improvement initiatives showed tremendous potential for improving outcomes for children with sepsis, such as reduced mortality and shorter intensive care stay; although most reports stem from highly specialised children's hospitals in high-income countries, sepsis quality improvement has been successful in low-income and middle-income countries too
- Several regional or national quality improvement initiatives targeting paediatric sepsis serve as models for coordinated approaches to improve knowledge, timely recognition, and deployment of effective treatment, and recommendations on how to establish a sepsis quality improvement programme with practical guidance on implementation of similar initiatives and evaluation using outcome, process, and balancing measures; where possible, sepsis quality improvement efforts should partner with antimicrobial stewardship efforts
- Despite ample observational evidence of long-term sequelae in childhood sepsis survivors, and contrary to best practice in very preterm infants or stroke survivors, services designed for paediatric post-sepsis care remain scarce

an age-standardised mortality rate 2·65 times higher than that of non-Indigenous children.<sup>22</sup>

Children in low sociodemographic index regions are disproportionately vulnerable to sepsis.<sup>20,23</sup> Approaches to improve the quality of paediatric sepsis management should therefore target these populations specifically. To this end, the WHO guidance on sepsis prevention and management recommends raising awareness of sepsis in low-income regions and among minority ethnic populations by developing and disseminating surveillance and early identification tools.

### Failure of prevention

In LMICs, public health programmes that improve access to vaccines, nutrition, and sanitation are paramount to preventing paediatric sepsis. In the SPREAD-PED observational study<sup>24</sup> of childhood sepsis in a random sample of paediatric ICUs (PICUs) in Brazil, vaccination status was an independent predictor of

mortality (odds ratio 2·2 [95% CI 1·2–3·9] for incomplete vaccination; and 2·6 [1·3–5·2] for unknown vaccination status, compared with complete vaccination status).

In many regions of the world, insufficient vector control, sanitation, nutrition, and safe water supplies predispose children to sepsis. Nosocomial infections such as central line-associated bloodstream infection, surgical wound infection, and ventilator-associated pneumonia are preventable yet account for a considerable proportion of paediatric sepsis among children with comorbidities.<sup>25,26</sup> Finally, caregiver education on nutrition, sanitation, and infant health remains a highly effective intervention to reduce the incidence of childhood sepsis and is directly related to the Sustainable Development Goals.<sup>20</sup>

### Failure of recognition

Early recognition of a child with sepsis who presents among hundreds of febrile children is inherently challenging.<sup>15,27</sup> The non-specific symptoms in the early stages of sepsis make this complex disease difficult to define and diagnose, even for experienced physicians. Criteria used for sepsis recognition in adults, such as systemic inflammatory response syndrome (used until 2016) or the Quick Sequential Organ Failure Assessment Score (used currently), might not be reliable for recognising early and specific features of sepsis in children.<sup>28,29</sup> The 2024 Phoenix Sepsis Criteria operationalise paediatric sepsis on the basis of an extensive, international, data-driven development and validation process coupled with a modified Delphi study.<sup>30</sup> The criteria were developed and validated using data from the first 24 h of hospital admission for children with suspected sepsis, showing good sensitivity and precision for the prediction of hospital mortality.<sup>31</sup> Screening and early recognition tools that are trained on children and meet the Phoenix Sepsis Criteria are now needed. Previous studies have shown that screening tools in conjunction with clinician judgement might convey superior sensitivity and specificity than screening tools alone.<sup>32</sup> However, the challenge of early recognition of paediatric sepsis is aggravated by inadequate sepsis education and awareness among policy makers, health administrators, researchers, health professionals, and the general population. Delayed recognition by caregivers in turn contributes to delays in seeking care, resulting in late presentation to hospital and inferior outcomes. Root cause analyses have also emphasised the importance of ongoing staff training and education regarding paediatric sepsis.<sup>33</sup>

### Failure of treatment

The non-specific character of signs and symptoms during the early stages of sepsis, coupled with sensitive sepsis screening tools (eg, systemic inflammatory response syndrome criteria), presents an additional challenge for early treatment initiation. Physicians face the dilemma of promptly recognising clinical deterioration in children with sepsis and balancing

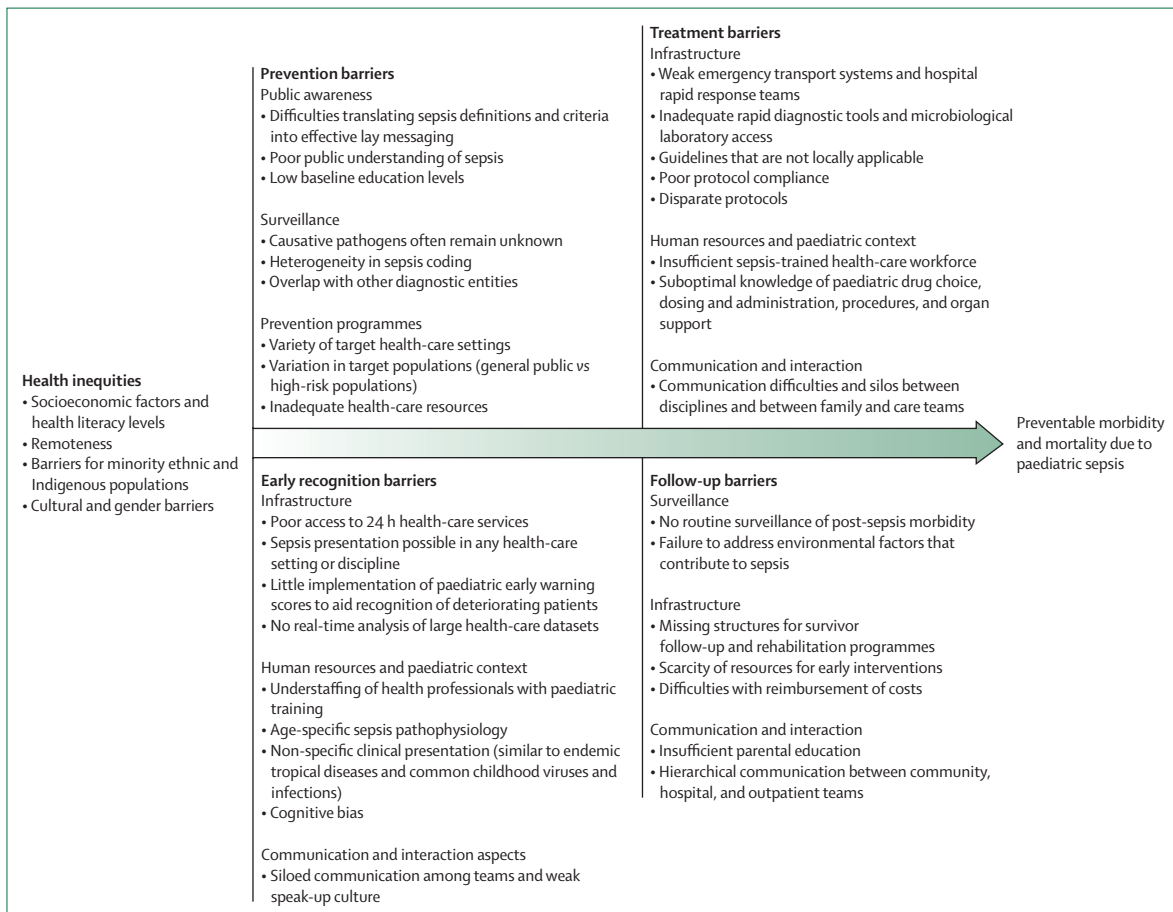


Figure 1: Causes of health system failures for quality improvement programmes in paediatric sepsis

concerns over resource allocation and antimicrobial misuse. Paediatric sepsis management requires effective systems of care that guarantee early recognition, timely emergency care, targeted antimicrobial therapy, source control, intensive monitoring, detection of clinical deterioration, and continued management of organ failure and complications.<sup>34,35</sup>

Multiple systems barriers contribute to failures in the management of paediatric sepsis, especially in LMICs. Overcrowding and understaffing in emergency departments, a shortage of paediatric specialists, inadequate resources for timely laboratory testing and imaging, and inappropriate use of antibiotics add up to a scenario of inadequate resources for paediatric sepsis management.<sup>36–38</sup>

Patient barriers to health-care access include travel difficulties, weaknesses in emergency health-care transport systems, and financial implications such as loss of income and out-of-pocket costs. Cultural aspects (such as protocol non-adherence), professional silos among medical staff, and the hierarchical relationship between staff and families might all negatively affect the quality of care for children with sepsis. The

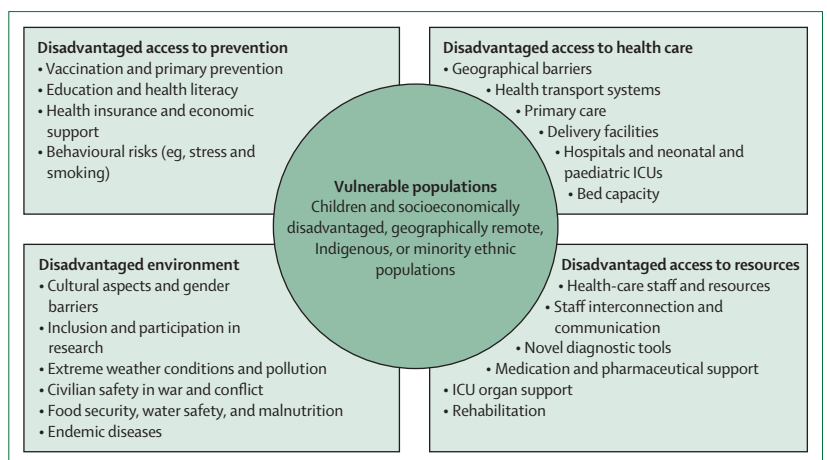


Figure 2: Relevance of targeting vulnerable populations in paediatric sepsis  
ICU=intensive care unit.

relationship between safety culture and prevention of health care-associated infections is well established and of key relevance to quality improvement programmes for paediatric sepsis.<sup>39</sup>

	Prevention and awareness	Early recognition	Treatment	Follow-up
Worldwide	Global Sepsis Alliance Surviving Sepsis Campaign			
Africa	African Sepsis Alliance			
Asia	Asia-Pacific Sepsis Alliance Eastern Mediterranean Sepsis Alliance			
Oceania	Australian Sepsis Network			
	Queensland Sepsis Program*			
Europe	European Sepsis Alliance UK Sepsis Trust* Swiss Sepsis National Program*			
	Sepsis Wissen*		German Sepsis Aid*	
North America	Sepsis Alliance	Children's Hospital of Philadelphia*		
		New York State Sepsis Care Improvement Initiative* Salt Lake City Hospital, Boston Children's Hospital, and Texas Children's Hospital,* Children's Hospital Association Rapid Cycle Collaborative, <sup>43</sup> American Academy of Pediatrics Septic Shock Collaborative, <sup>44</sup> Children's Hospital Improving Pediatric Sepsis Outcomes, <sup>45</sup>		
South America	Latin American Sepsis Institute Sepsis Mexico*			

**Figure 3: Geographical distribution and examples of current quality improvement programmes in paediatric sepsis**

\*Local example.

For the **Institute for Healthcare Improvement** see <https://www.ihl.org/>

### Failure of post-sepsis care

Despite accumulating evidence on often devastating, sometimes hidden, long-term sequelae after sepsis in children,<sup>15,40–42</sup> dedicated post-sepsis support for children and families remains largely unavailable in most settings around the world. Paediatric sepsis survivors generally do not have access to targeted rehabilitative support measures, and knowledge of health-care professionals on the needs of paediatric sepsis survivors remains scarce.

### Lessons from quality improvement programmes for paediatric sepsis

The past decade has seen the creation of large regional and national quality improvement programmes either specifically designed for children or with paediatric-specific components (figure 3). Many individual hospitals have also successfully undertaken quality improvement endeavours to improve sepsis outcomes in paediatric patients.<sup>46–50</sup> However, single institution programmes are often not generalisable or powered to detect sustainable differences in outcomes such as mortality.<sup>51</sup> In this

regard, quality improvement collaboratives such as those promoted by the Institute for Healthcare Improvement have been key in allowing more nuanced interpretation of improvements at scale.

In one of the first paediatric sepsis quality improvement collaboratives, 12 hospitals across the USA collected data from 1173 patients and showed that, although time to initial clinical assessment and first intravenous fluid bolus improved, 30-day mortality did not.<sup>43</sup> Study challenges included insufficient support for data collection at individual sites, dependence on ICD-9 codes (known to underestimate sepsis<sup>52</sup>), and heterogeneity in the operationalisation of a so-called time zero. Time zero has been variably defined as time of emergency department arrival, first abnormal vital signs, clinician determination and notation of meeting sepsis criteria, sepsis order set initiation, initiation of a best practice alert, and presence of an elevated paediatric early warning system score.

These lessons informed the American Academy of Pediatrics Pediatric Severe Sepsis Collaborative, which included 19 hospitals and focused on emergency department care.<sup>44</sup> The application of criteria for sepsis, standardised screening tools, and electronic health record (EHR)-embedded tools such as triage screens and sepsis order sets improved time to first clinical assessment, fluid bolus, and antibiotics, with an associated decrease in 30-day all-cause mortality from 2.3% to 1.4%. Even sites new to quality improvement work showed process metric improvement and mortality reductions, corroborating the benefits of the All Teach, All Learn method of quality improvement.<sup>53</sup>

In New York state (USA), where statewide sepsis care was mandated in 2013, improved adherence to timely delivery of a sepsis bundle to children with diagnosed sepsis or septic shock (ie, obtaining blood cultures, administering fluid bolus, and initiating antimicrobials) within 1 h of recognition was associated with a 41% mortality risk reduction relative to those who did not receive a sepsis bundle within 1 h.<sup>54</sup> Risk-adjusted compliance with this target was highly variable across the 54 participating institutions, ranging from 7% to 46% (median 33% [IQR 22–38%]), indicating the insufficient reliability in delivering care to the defined targets.

The Improving Paediatric Septic Shock Collaborative (IPSO), sponsored by the US Children's Hospital Association, is the most extensively reported paediatric septic shock collaborative to date.<sup>45,55,56</sup> As of 2024, the collaborative includes 64 hospitals and addresses care across the clinical continuum, including the emergency department, general wards, haematology and oncology units, and PICUs. IPSO was the first to publish a standardised definition of time zero, resulting in more valid conclusions regarding outcomes.<sup>56</sup> Collaborators standardised denominator definitions and interventions and prioritised abstracting data from the EHR, allowing for a sustainable submission rate of key variables of more

than 95%. Monthly data webinars, workshops every 2 years, and assignment of quality improvement consultants to each hospital have allowed for robust dissemination of key learning strategies and nuances of implementation science. In a large interim analysis of 24518 patients, IPSO identified an optimal bundle of intervention elements (including method of recognition, administration of fluid bolus in <60 min, and administration of intravenous antibiotics in <180 min) associated with a reduction in mortality from 4.8% to 2.4% ( $p<0.01$ ).<sup>45</sup> Sepsis-attributable mortality in the overall cohort dropped from 1.4% to 0.9%, representing a 35.7% relative reduction over the 3-year duration of the study ( $p<0.001$ ).

Using vetted quality improvement principles such as fishbone analysis, failure modes and effect analysis, and pareto charts, barriers to timely delivery of care were determined for each IPSO-affiliated institution. Solutions were thus idiosyncratic and included establishment of vascular access teams, prioritisation of intraosseous placement, standardised order sets with implemented clinical care guidelines, and order sets spanning a broad set of physiological conditions (eg, neonatal fever, febrile oncology, pneumonia, and urinary tract infection) to increase provider use. Clinicians were often hesitant to initiate all aspects of a shock treatment protocol, but implementation of two-tiered sepsis protocols for patients with and without shock increased acceptance of pathway initiation.<sup>57</sup> Septic shock clocks were implemented within the EHR and physically to alert clinicians to the first critical hours of resuscitation. Widespread communication of a so-called code sepsis event was communicated to key stakeholders, such as the pharmacy and ICU, to expedite antibiotic preparation and secure a critical care bed. Finally, skills days to deliver education on the use of pressure bags and push-pull devices for rapid delivery of intravenous fluids were instrumental in improving time to fluids for patients in shock.

A 2009 audit in the UK showed poor adherence to paediatric sepsis guidelines for severe sepsis management in 17 PICUs and two UK PICU transport services.<sup>58</sup> By 2014, the UK Sepsis Trust had developed the Paediatric Sepsis Six Initiative, which aimed to “empower medical and nursing staff to recognise sepsis early and initiate treatment rapidly” and thereby improve guideline adherence.<sup>59</sup> Although modelled on the adult Sepsis Six programme, the initiative’s broad diagnostic criteria had not been validated in clinical settings, and the risk of overtreatment limited uptake.<sup>60</sup> The introduction of the 2016 National Institute for Health and Care Excellence (NICE) sepsis guidance provided standardisation, but the concern around overidentification persisted. In a retrospective study at a single centre in Liverpool, UK, Romaine and colleagues<sup>61</sup> identified a set of seven paediatric early warning scores (PEWS) with excellent discrimination power for admission to critical care units (area under the

curve 0.91–0.95) and for predicting sepsis-related mortality (0.95–0.99). These findings support the use of PEWS for identifying suspected sepsis and improving outcomes in the paediatric emergency department, but more validation is necessary in other settings, particularly in resource-limited health-care settings. In addition to the patient’s clinical and demographic variables, PEWS incorporates concerns expressed by family members and nurses. The NICE sepsis guidance now integrates PEWS into its sepsis screening tool acute assessment (which also requires additional validation in diverse settings).

### Public awareness and the family perspective

Public messaging and training programmes about paediatric sepsis are challenging because early presentations of sepsis can be very difficult to differentiate from mild and self-limiting conditions. Increasing awareness of signs and symptoms of serious infection in children among the general public might improve the chances of recognising a shift from a simple uncomplicated infection to more severe illness. More than 20 years ago, a large public awareness campaign targeting meningococcal infection emphasised messages such as nuchal rigidity or skin pressure (also known as the Glass Test) to distinguish petechiae. Similar large-scale public awareness campaigns directed at HIV, myocardial infarction, and stroke might equally offer models that can be adopted and applied to public awareness and training campaigns targeting paediatric sepsis.

Broad public awareness campaigns in Australia (the Queensland Sepsis Collaborative), the UK (the Sepsis Trust), the USA (the US Sepsis Alliance), and Brazil (the Latin American Sepsis Institute) have been implemented to increase public knowledge about sepsis. A shared feature of these campaigns is that they embedded child-specific messaging as part of wider sepsis campaigns. The UK Sepsis Trust used stickers on ambulances, advertising boards, and even plotlines in a popular daytime television show and other media outlets to disseminate simple messages about sepsis.

In observational studies, although not powered to investigate the role of parental concern in paediatric sepsis, data indicate that the presence of parental concern (expressed, for example, in response to being asked whether their child’s disease is different from previous diseases) is associated with severe bacterial infections.<sup>62,63</sup> Accordingly, sepsis pathways typically include parental concern as a potential trigger, as well as an additional safety net mechanism for children who are discharged from hospital.<sup>64</sup>

Importantly, messaging needs to be balanced by the risk of fever phobia, which might lead to inappropriate health-care use. General literacy, health literacy, and cultural appropriateness might pose additional challenges, particularly in LMICs and among socio-economically vulnerable groups and minority populations such as refugees and First Nations peoples

For more on the Queensland Sepsis Collaborative see <https://clinicalexcellence.qld.gov.au/priority-areas/safety-and-quality/sepsis/paediatric-sepsis>

For more on the UK Sepsis Trust see <https://sepsistrust.org>

	Prevention	Early recognition	Treatment	Follow-up
Policy and public health domain	<ul style="list-style-type: none"> <li>• Create mandatory infection prevention programmes (eg, food and water safety, prevention of influenza, and vaccination policy and campaigns)</li> <li>• Conduct surveillance by age and risk populations</li> <li>• Implement awareness campaigns</li> <li>• Cross-fertilise with antibiotic stewardship and other programmes</li> <li>• Promote health equity and access to care</li> </ul>	<ul style="list-style-type: none"> <li>• Include benchmarks for sepsis recognition in hospital performance reviews and accreditation</li> <li>• Mandate standards for sepsis recognition</li> <li>• Educate health-care workers (nursing, medical, and allied health)</li> <li>• Educate childcare workers and schoolteachers</li> <li>• Promote family-physician communication</li> <li>• Evaluate access to care</li> </ul>	<ul style="list-style-type: none"> <li>• Include benchmarks for sepsis treatment in hospital performance reviews and accreditation</li> <li>• Mandate standards and develop evidence-based and locally appropriate protocols for sepsis treatment</li> <li>• Include sepsis in health professional continuous education programmes</li> <li>• Assist governments in providing resources for sepsis management</li> </ul>	<ul style="list-style-type: none"> <li>• Mandate standards for routine follow-up</li> <li>• Assess burden of post-sepsis problems, define needs, and design intervention strategies</li> <li>• Negotiate health insurance coverage for post-sepsis follow up and rehabilitation</li> <li>• Establish link between paediatric health care and education providers (eg, schools, special needs support, etc)</li> </ul>
Clinical domain	<ul style="list-style-type: none"> <li>• Implement, monitor, and action hand hygiene programmes</li> <li>• Conduct programmes to reduce hospital-acquired infection, including perinatal and device-associated infections</li> <li>• Raise awareness in high-risk populations</li> <li>• Facilitate surveillance</li> <li>• Foster digitalisation of health-care tools</li> <li>• Mandate training provided by societies</li> </ul>	<ul style="list-style-type: none"> <li>• Clarify signs of sepsis to families (eg, giving clear written instructions)</li> <li>• Enhance communication across primary, secondary, and tertiary care</li> <li>• Promote multidisciplinary teamwork and speak-up culture</li> <li>• Install early recognition tools or action pathways</li> <li>• Help validate and apply AI algorithms</li> <li>• Embed sepsis recognition into systems of care, focusing on recognition of the patient in deteriorating condition</li> </ul>	<ul style="list-style-type: none"> <li>• Promote education on sepsis treatment as part of professional society requirements</li> <li>• Use core quality improvement principles to drive interventions (formal barriers assessment should drive highly reliable interventions focused on system change, not solely education)</li> <li>• Monitor adherence to sepsis bundles, best practices, and antibiotic stewardship</li> <li>• Build capacity in paediatrics</li> <li>• Implement laboratory, imaging, transfusion, organ support systems, and ICU standards</li> <li>• Integrate AI algorithms in care</li> </ul>	<ul style="list-style-type: none"> <li>• Schedule follow-up visits</li> <li>• Facilitate links for multidisciplinary cooperation</li> <li>• Ensure continuity of targeted rehabilitation measures from hospital to outpatient to family where feasible</li> </ul>
Society	<ul style="list-style-type: none"> <li>• Create, support, and link advocacy groups</li> <li>• Partner in research projects and awareness campaigns</li> <li>• Help with dissemination campaigns</li> </ul>	<ul style="list-style-type: none"> <li>• Lobby for paediatric specialised care</li> <li>• Educate parents and the public in regards to warning signs and addressing concerns to health-care teams</li> </ul>	<ul style="list-style-type: none"> <li>• Promote clinical trials in paediatric sepsis</li> <li>• Promote implementation science studies in paediatric sepsis</li> </ul>	<ul style="list-style-type: none"> <li>• Participate in patient support groups</li> <li>• Increase public awareness of post-sepsis sequelae</li> </ul>

**Figure 4: Strengthening quality improvement programmes in paediatric sepsis**  
AI=artificial intelligence. ICU=intensive care unit.

who might not speak the predominant language of the country in which they live. Use of appropriate and diverse media, including written, illustrated, verbal, and interactive material, and innovative social media platforms are key to achieving widespread dissemination and might benefit from codesign with consumer families. That these materials are written in language accessible to diverse audiences and nationalities is crucial.

#### Training the health-care workforce

Although many sepsis quality improvement programmes such as the New York State Sepsis Care Improvement Initiative include requirements for health-care worker education on sepsis, reports on the effectiveness of such education are scarce. Developing an effective paediatric sepsis education programme requires a multifaceted approach across the continuum of care ranging from primary care, paramedics, and rural and remote medical services to private hospitals, tertiary training facilities, and rehabilitation to home. Reports have confirmed the importance of multi-professional and multidisciplinary quality improvement interventions in sepsis, including the empowerment of nurses.<sup>65</sup> The majority of paediatric quality improvement works in HICs have been focused on large paediatric hospitals that are able to provide care for complex and comorbid patients, where paediatric-specific education is provided regularly and staff might be more familiar

with quality improvement work. By contrast, regional and mixed facilities often account for a disproportionate burden of paediatric sepsis, and integration of paediatric-specific sepsis material into adult-based efforts is pivotal.

#### Leveraging interdependencies of quality improvement and systematic approaches to improve the recognition of children in deteriorating condition

The effective implementation of sepsis quality improvement is directly dependent on the overall quality of health care. Sepsis quality improvement might also benefit other aspects of safe paediatric care. Systematic screening, alerting, and escalation procedures for paediatric sepsis should be embedded in hospital-wide systems to recognise children in deteriorating condition. Although the introduction of PEWS has not improved paediatric arrest outcomes,<sup>66</sup> the application of these scores in either paper-based or digital form is increasingly considered a pillar of safety net implementation within hospitals in HICs.<sup>27</sup> However, studies are needed to confirm the feasibility and effectiveness of such scores in diverse settings within LMICs. In Uganda, the introduction of a digital screening platform<sup>67</sup> was associated with an 11-min reduction in time from screening to antibiotic administration and a 34-min reduction among children prioritised as an emergency, which suggests that the potential benefits of such interventions can extend to low-resource health-care settings.

### Post-discharge support

Data to inform systems of paediatric sepsis care beyond hospitalisation are sparse. In Australia, the Queensland Paediatric Sepsis Program codesigned a multimodal education package for families affected by sepsis and implemented a novel family support structure to improve care after childhood sepsis.<sup>68</sup> The first sepsis survivorship programme in the USA is a multi-disciplinary paediatric follow-up clinic managed by the Children's Hospital of Philadelphia (Philadelphia, PA).<sup>69</sup> However, important questions around who is most likely to benefit from rehabilitation, what makes an optimal rehabilitative strategy, how to overcome logistic challenges in organising follow-up across geographically diverse regions, and how rehabilitative interventions might be adapted to low-resource health-care settings remain unanswered.

### A global framework to enhance quality improvement in paediatric sepsis

National action plans for sepsis that identify relevant barriers and targets can seed the development of strategies to overcome current gaps.<sup>36,70,71</sup> In Australia, for example, the Stopping Sepsis National Action Plan<sup>71</sup> recommended the establishment of the National Sepsis Program, which in turn paved the way for a national Sepsis Clinical Care Standard.<sup>72</sup>

Where feasible, such programmes should incorporate key stakeholders and leverage experience from the COVID-19 pandemic.<sup>18</sup> As many children are cared for in mixed-age facilities, often by staff without much paediatric-specific training, initiatives might benefit from an all-age approach that emphasises paediatric-specific considerations. Importantly, given the dominance of adult health care in terms of facilities, providers, and funding, identifying unique paediatric needs and ensuring adequate prioritisation of funding and resources are imperative to ensure quality improvement measures succeed in targeting paediatric sepsis.

Large de novo quality improvement programmes can be highly resource-intensive, and sometimes prohibitively so. Strategies therefore need careful optimisation. For example, cost-benefit analyses should consider the entire health-care system and society,<sup>73</sup> and cross-fertilisation with existing health-care programmes (eg, vaccination programmes) can build on available structures, experience, and personnel. Low-cost innovations include grassroot initiatives, social media, and frugal technologies, and leveraging externally tested materials and strategies with appropriate local and regional adaptation can increase efficiency.

### Core components of systematic quality improvement in paediatric sepsis

Paediatric sepsis quality improvement interventions can be optimised along the patient journey to address public

	Feasibility from an LMIC perspective
<b>Public health</b>	
Proportion of children vaccinated against specific pathogens	High—can be nested within vaccination programmes
Number of deaths with infection-associated ICD code	Medium—depends on availability and accuracy of death registries and coding inconsistencies
Number of deaths with sepsis-specific ICD code	Medium to low—depends on availability and accuracy of death registries and coding inconsistencies
Number of sepsis cases per 1000 hospital admissions	Medium—requires hospital-based statistics
<b>Public awareness</b>	
Proportion of parents who receive information on sepsis (during pregnancy and after birth or during childhood)	Medium—requires alignment with existing obstetric and paediatric structures (such as in antenatal visits, immunisation appointments, a paediatric health booklet, or during specialised consultations for high-risk populations)
Awareness of the condition of paediatric sepsis in the public	Medium—costly, dependent on existing local structures (eg, information could be disseminated via schools and monitoring could potentially come through the education department)
<b>Health-care worker education</b>	
Number of programmes or hours of paediatric sepsis coverage in medical and nursing school curricula	Medium—overview of national training programmes might vary and curriculum might be updated slowly
Number of programmes or hours of paediatric sepsis coverage in post-graduate specialist and general practitioner or health-care worker training	Medium—overview of national specialist programmes might vary and specialist training programme requirements might be unlikely to change
Proportion of hospitals and health-care facilities with mandatory sepsis-specific onboarding for staff	Low—overview of institutional programmes is usually insufficient unless made part of accreditation requirements; however, institutional level interventions such as targeting personnel (eg, training cleaners, clerks, low-level nurses, community health-care workers, security personnel, etc) who play an integral role in operational system flow might have high yield
<b>Process measures in health-care settings</b>	
Proportion of children screened for sepsis	High if screening is digital; low if paper-based or manual (sampling might increase feasibility)
Proportion of health-care units with access to monitoring devices, laboratories, drugs, blood products, oxygen therapy, and organ support systems	High—dependent on reliability of inventory documentation
Time from presentation to sepsis screening	High if digital, low if paper-based or manual (sampling might increase feasibility)
Time to receipt of laboratory results	High if digital, low if paper-based or manual (sampling might increase feasibility)
Sepsis bedside huddle (rapid response team) activations	Low—clinical huddles generally have poor documentation
Time from trigger or screening to initiation of sepsis order set and to first care bundle	High if digital, low if paper-based or manual (sampling might increase feasibility)
Time to intravenous antibiotics	Medium—must consider nuances of patients already on antibiotics, correct broad-spectrum antibiotic, and documentation
Time to first intravenous fluid bolus	Medium—must consider fluid-sensitive conditions and correct amount of fluid, which might result in the need for manual review

(Table continues on next page)

awareness, health-care worker education, prevention, recognition, timeliness of treatment (including antimicrobial stewardship considerations and escalation of advanced PICU treatment), and post-discharge support for patients and families (figure 4). Efforts can start with

For more on the **sepsis survivorship programme** see <https://www.chop.edu/services/sepsis-survivorship-program>

## Feasibility from an LMIC perspective

(Continued from previous page)

## Outcome measures in health-care settings

Sepsis mortality in hospital (consider 3-day and 30-day mortality)	High—quality is dependent on coding
Sepsis incidence with onset in hospital	High—quality is dependent on coding
Hospital, ICU, and high-dependency unit admissions due to sepsis	High—quality is dependent on coding
Hospital and ICU free days for patients with sepsis	Medium
Organ support-free days (days free of ventilation and inotropes or vasoactive agents)	Low—difficult to ascertain in an automated fashion, especially for those with pre-existing conditions
Cost of sepsis care for the health system and the patient	Medium—dependent on cost and charges documentation

## Balancing measures in health-care settings

Number of intravenous antibiotic days	Medium—extraction through electronic health records is very feasible
ICU admissions	High—quality is dependent on coding

## Structural measures (follow-up) in health-care settings

Proportion of children with sepsis who receive targeted follow-up	Low due to an absence of follow-up structures in most settings and little integration of post-discharge data with hospital data
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## Research

Proportion of research expenditures and programmes on sepsis, at local and national levels	High at national level; low for non-federally funded grants
Proportion of research expenditures and sepsis programmes that are controlled by a country's government (eg, ministries of health)	High at national level; low for non-federally funded grants

Sampling options might include random sample selection, selection of sites and hours of shifts, patients with particular procedures (such as blood cultures), or patients with particular conditions (such as positive blood cultures). Each option has benefits and drawbacks in relation to feasibility, generalisability, and representativeness. LMIC=low-income and middle-income country. ICU=intensive care unit.

Table: Quality indicators for paediatric sepsis, by domain

For Australia's National Sepsis Program see <https://www.safetyandquality.gov.au/our-work/national-sepsis-program>

family education, community campaigns, basic infection prevention strategies such as handwashing, and facilitating access to health-care expertise through telehealth platforms and remote health-care worker empowerment. Health-care responders situated across the patient journey, including prehospital care providers, paramedics, physicians, advanced practice providers, nurses, respiratory therapists, specialised transport teams, and pharmacists should all be reached by quality improvement and educational programmes (eg, through dedicated paediatric sepsis champions).<sup>74</sup>

Non-governmental organisations play an important role in advocating for sepsis awareness and protocol development. For example, the Rory Staunton Foundation in the USA runs education campaigns, fundraises, and hosts annual forums that have proven effective.

The design of such quality improvement programmes must reflect careful consideration of appropriate and feasible measures to assess the effectiveness of the programme (in terms of process, outcome, and

balancing measures), provide feedback to the health-care workforce in an iterative process (such as the Plan-Do-Study-Act problem-solving model), and facilitate reporting to administrators and the public (table). The medical literature offers a large range of quality improvement matrices, usually centred on in-hospital process measures related to the speed of sepsis bundle delivery and outcome measures such as length of stay or mortality.<sup>38,56,57,75</sup> However, in LMICs, many paediatric deaths happen outside the health system, and linking multiple sources of information might be necessary where available to track deaths related to infection.<sup>76</sup> The increasing availability of EHR-based data capture is a step towards designing standardised measures that can be extracted in a robust and harmonised way for paediatric sepsis surveillance and benchmarking.<sup>27,77,78</sup> Where high-quality, EHR-derived data are not available, random sampling might reduce the manual workload of data capture.<sup>79</sup> Sepsis is often undercoded, so the definition of the metric calculation denominator must include broad criteria beyond those of the ICD-9 or ICD-10.

Process measures include the therapeutic timepoints from time of sepsis recognition. Time zero is often difficult to glean from a singular electronic timestamp, so surrogates such as time of a sepsis screen, order set use, first therapeutic intervention, or time of presentation (for community-acquired sepsis) are useful alternatives that can be presented in statistical process control charts for quality improvement dashboards.

The risks of tying incentives to process metrics and related concerns about overtreatment of children in whom sepsis is ultimately not confirmed have fuelled controversy over the suitability of process measures for sustainable quality improvement programmes.<sup>80</sup> Commonly used outcome metrics include in-hospital mortality and measures of morbidity, such as hospital and ICU length of stay, and might be accessible through mandatory hospital and public health datasets and ICU registries.

Sepsis management is dependent on resource allocation and requires community, government, and health service involvement. Major challenges include sustainability and scalability. In Brazil, Machado and colleagues<sup>81</sup> showcased successful sepsis quality improvement programmes in both public and private hospitals, although the mortality reduction was sustained in private hospitals only. Reasons for this difference between public and private health-care settings include case mix differences, delayed emergency room arrival, resource shortages, and staff turnover. Solutions involve prevention, education, and governmental prioritisation of sepsis.

## Antimicrobial stewardship

Early use of antimicrobials remains one of the pillars of successful sepsis management, but antimicrobials must be used appropriately.<sup>82,83</sup> Antimicrobial stewardship refers to a set of coordinated strategies and actions



aimed at optimising the use of antimicrobial agents in order to preserve their effectiveness, and many countries have started to implement targeted strategies against antimicrobial resistance. Antimicrobial resistance is considered one of the ten top threats to global health by WHO and was accountable for 5 million deaths in 2019. 1.3 million antimicrobial resistance-related deaths, many of which were in the paediatric population, were attributable to bacterial antimicrobial resistance.<sup>84</sup>

Accordingly, antimicrobial stewardship is an essential element of tackling sepsis, and paediatric sepsis quality improvement programmes must strengthen antimicrobial stewardship. Specifically, antimicrobial stewardship programmes should ensure that age-appropriate antibiotics are initiated promptly and in line with local epidemiology and resistance patterns relevant to life-threatening childhood infections. Sepsis quality improvement programmes can partner with antimicrobial stewardship pharmacists and paediatric infectious disease physicians to educate staff on optimal antimicrobial choice, dosing, administration, and duration to promote best prescribing practice.

Future programmes should place more focus on the importance of ruling out sepsis and antibiotic de-escalation and include antibiotic prescribing compliance measures in their quality improvement metrics. Combining sepsis and antimicrobial resistance initiatives creates invaluable benefits in terms of education, tailored protocols, data monitoring, and interdisciplinary teamwork, as evidenced by the UK's Infection Management Coalition.

### Education platforms

In 2019, resolute that education is key to reducing the sepsis burden in Latin America, the Latin American Sepsis Institute launched a free online education programme for health professionals, covering topics related to the management of sepsis in newborn babies, children, and adults. Given shortfalls in paediatric sepsis knowledge across hospitals, such educating strategies should be embedded in structured and mandatory undergraduate and postgraduate training programmes.<sup>85,86</sup>

In 2024, the US Centers for Disease Control and Prevention published the Hospital Sepsis Program Core Elements of successful sepsis quality improvement programmes in hospitals.<sup>87</sup> Although these core elements were designed for the US health-care system, they are adaptable to different health-care settings and patient populations. The components target a range of actors, stakeholders, and processes such as hospital leadership, local incentive programmes, and accountability and transparency mechanisms. Multiprofessional expertise and structural support are delivered to departments, patients and families, and case management teams, and dedicated sepsis coordinators navigate data collation, implementation, and real-time case review. Interventions must be based on quality improvement processes and implementation science. Finally,

### Search strategy and selection criteria

We searched the PubMed database using the MeSH terms ("sepsis" OR "septic shock" OR "trial") AND ("child" OR "Paediatric") for studies published between Jan 1, 2000, and June 30, 2023, with no language restrictions; we did specific sub-searches adding the terms "quality improvement" OR "quality of healthcare" OR "quality assurance", "prevention", "sepsis campaign", and "sepsis collaborative". In addition, reference lists from key papers of interest were searched for additional related important publications. Publications where abstracts were not available in English, Portuguese, Spanish, or German were not considered.

robust operationalisation of the target population, performance benchmarking, and education for both clinical staff and patients are emphasised as essential actions to optimise patient care and help clinicians, hospitals, and health systems to improve the hospital management and outcomes of sepsis.

A global platform for the exchange of education, materials, and databases on paediatric sepsis quality improvement is urgently needed to reduce the costs of establishing new programmes, increase the efficiency of existing programmes, and foster a global learning health-care system for children with sepsis. Duplication of effort among settings and other inefficiencies can be avoided, precious resources for paediatric-specific needs can be prioritised, and global learning can be accelerated. Such work should ideally be coupled with implementation research through data platforms such as the Pediatric Sepsis Data CoLaboratory (Sepsis CoLab), a global collaborative network dedicated to reducing paediatric sepsis mortality and morbidity. Rapid feedback protocols will enhance the effectiveness of future work. Members of CoLab enjoy networking, mentorship, and access to the Sepsis CoLab Dataverse repository, which facilitates the use of guidelines, tools, and resources, along with secure data storage and sharing under established agreements. Effective collaboration and data transfer to such platforms require a data transfer agreement between parties, outlining terms for data processing and protection. Additionally, smaller-scale educational platforms include those by Open Pediatrics and the Latin American Society of Pediatric Emergency Physicians, with similar initiatives by the Latin American Sepsis Institute.

### Conclusion

To reduce the burden of paediatric sepsis on patients, families, and societies across the world, multifaceted local and global efforts and coordination by policy makers, health-care administrators, researchers, and clinicians in all health-care environments will be required. Reducing this burden involves implementing educational programmes for health-care professionals, developing

For the **Infection Management Coalition** see <https://theimc.org/>

For the **Sepsis CoLab** see <https://wfpiccs.org/pediatric-sepsis-colab/>

For the **Hospital Sepsis Program Core Elements** see <https://www.cdc.gov/sepsis/hcp/core-elements/index.html>

standardised protocols for recognising and managing paediatric sepsis, improving communication and handover processes, enhancing health-care system resources, and promoting public awareness and education, all of which improve the resilience of health-care systems. The number of dedicated paediatric sepsis quality improvement initiatives has increased in the past decade but primarily in HICs. Informed by these collaboratives, the paediatric community must establish a global learning platform to enhance the implementation, adaptation, and effectiveness of paediatric sepsis quality improvement.

#### Contributors

LJS, NK, and DCdS conceptualised the Series paper and wrote the first draft. LJS, NK, AA, and DCdS had full access to all the data in the manuscript and take responsibility for the integrity of the data. RM created the figures. LJS, NK, AA, DCdS, RP, RM, JS, RJ, EL, AH, SAA, MA, and SQ contributed to the literature search, interpretation, and the writing of the manuscript. All authors revised the manuscript and approved the final version.

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