Pediatric Critical Care Medicine
XXX 2026 • Volume 28 • Number 00 • Pages XX–XX

FEATURED ORIGINAL RESEARCH ARTICLE

# Sepsis Point Prevalence Across Ibero-Latin America PICUs: The 2024 Sepsis Prevalence Assessment Database in Pediatrics (SPREAD PED IBERO-LATAM)

**OBJECTIVES:** To determine the prevalence and outcome of sepsis in PICUs across Ibero-Latin America; to identify patient- and institution-level factors associated with mortality; and to explore the prognostic performance of pediatric sepsis definitions.

**DESIGN:** Multinational, multicenter, prospective point prevalence study with follow-up to hospital discharge.

**SETTING:** One hundred sixty-eight PICUs in 21 countries across Latin America, Spain, and Portugal.

**PATIENTS:** Children of 28 days to 18 years with a clinical diagnosis of sepsis or septic shock admitted to participating PICUs between September 9 and September 13, 2024.

**INTERVENTIONS:** None

**MEASUREMENTS AND MAIN RESULTS:** Among 1318 screened PICU patients, 340 met criteria for clinical sepsis, yielding a point prevalence of 25.8% (95% CI, 23.5–28.2%). Complete outcome data were available for 324 patients. PICU mortality was 42 of 324 (13.0% [95% CI, 9.5–17.1%), and total in-hospital mortality was 49 of 324 (15.1% [95% CI, 11.4–19.4%]). Cardiovascular and respiratory dysfunction were most frequent, whereas multivariable logistic regression identified greater odds of PICU mortality associated with renal dysfunction (adjusted odds ratio [aOR], 3.2 [95% CI, 1.5–7.5]) and immunologic dysfunction (aOR, 12.7 [95% CI, 4.6–37.5]).In multivariable analysis, abnormal nutritional status, lack of vaccination, renal dysfunction, and admission to PICUs with intermediate or low resource availability were associated with greater odds of PICU mortality. In exploratory analyses, the Phoenix sepsis criteria identified 95.2% of PICU deaths, but the positive predictive value of the score for mortality was no different from the 2005 International Pediatric Sepsis Consensus Conference criteria.

**CONCLUSIONS:** In 2024, in Ibero-Latin American PICUs, sepsis affected approximately one in four admissions, and the diagnosis was associated with mortality. Both patient vulnerability and institutional resource availability were associated with greater odds of mortality, underscoring the potential influence of health system capacity on pediatric sepsis outcomes in the region.

**KEY WORDS:** critical care resources; health inequities; Ibero-Latin America; pediatric sepsis; prevalence study

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Sepsis is a life-threatening condition caused by infection that has global significance, as demonstrated in the 1990–2017 analysis for the Global Burden of Disease Study (1), and in May 2017 sepsis was recognized as a

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DOI: 10.1097/PCC.0000000000004077



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## RESEARCH IN CONTEXT

- Contemporary multinational data on pediatric sepsis across Ibero-Latin America are limited, with most reports derived from single-country cohorts.
- Furthermore, there may be variability in PICU resources for sepsis cases, and differences in outcomes.
- In September 2024, we coordinated a pediatric sepsis point prevalence study in 168 PICUs across 21 countries and determined patient- and institution-level factors associated with outcomes.

global health priority by the World Health Organization (2). In this context, between 2020 and early 2024, there were four key studies relevant to PICU practice worldwide. First, the Surviving Sepsis Campaign (SSC) produced the 2020 *International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction* in children (3). Second, in 2022, SLACIP (the Latin American Pediatric Intensive Care Society) provided consensus on the management of sepsis in children, with an emphasis on medical practice in low- and middle-income countries (LMICs) (4). Third, in 2023, the Society of Critical Care Medicine (SCCM) *Pediatric Sepsis Definition Taskforce* presented a position article on operationalizing appropriate sepsis definitions in children worldwide (5). Last, in February 2024, the SCCM Pediatric Sepsis Definition Taskforce reported the international consensus criteria for pediatric sepsis and septic shock, which are now called the Phoenix Criteria (6, 7).

Given the above, in 2023/2024, we coordinated a large, multinational, point prevalence study of the burden of pediatric sepsis in PICUs across Latin America, Spain, and Portugal. The three aims of the Sepsis PREvalence Assessment Database in PEDiatrics (SPREAD PED) study were: 1) to determine the prevalence and outcome of sepsis in PICUs across Ibero-Latin America; 2) to identify patient- and institution-level factors, across diverse health systems, associated with mortality; and 3) to explore the prognostic performance of pediatric sepsis definitions.

## MATERIALS AND METHODS

The SPREAD PED study across Ibero-Latin America PICUs was coordinated by the University of São Paulo, Brazil, supported by the Latin American Sepsis Institute (ILAS), with endorsement and participation from SLACIP, and funded by the Fundação de Apoio à Pesquisa do Estado de São Paulo (Grant no. 2017/21052-0). The study was approved by the Brazilian National Research Ethics Commission (CONEP No. 73764923.4.1001.0076; Approval Title: Pediatric Sepsis in Ibero-Latin American ICUs: Prevalence, Outcomes, and Resource Availability) in October 2023. Each participating center obtained local ethics approval in accordance with national regulations (see **Supplementary Digital Content [SDC]**, https://links.lww.com/PCC/C796; *Institutional Review Board [IRB] Approvals for Participating Centers in the SPREAD PED Ibero-Latin America Study*). Since observational, anonymized prevalence data were being collected, the need for parent/guardian consent for data collection was waived. All research procedures complied with local IRB requirements and adhered to the principles of the Declaration of Helsinki 1975.

### Participating PICUs and Patients

Potential sites were PICUs across 21 countries in Latin America, Spain, and Portugal, identified through national pediatric critical care societies, professional networks, and institutional registries. Hospitals were



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grouped into four predefined regional blocks to facilitate analysis and account for geographical heterogeneity: the Southern region (Brazil, Argentina, Chile, Uruguay, and Paraguay); the Andean region (Colombia, Peru, Bolivia, Ecuador, and Venezuela); the Northern region (Mexico, Guatemala, Cuba, Honduras, Panama, Costa Rica, El Salvador, Nicaragua, and the Dominican Republic); and the Iberian region (Spain and Portugal). PICUs were eligible to participate in the study if they provided 24/7 multidisciplinary intensive care for children of 28 days to 18 years. Neonatal-only ICUs were excluded.

The study population comprised children and adolescents aged 28 days to 18 years admitted to a participating PICU during the study window between September 9 and September 13, 2024. To estimate prevalence, a 1-day point prevalence assessment was conducted, in which eligible patients were identified on the designated study day within this period. Included patients were those clinically diagnosed with sepsis or septic shock by the treating medical team at any time during their PICU stay. Eligibility also encompassed patients who had sepsis-related organ dysfunction at any time during admission, even if the dysfunction was no longer present on the study day. No exclusion criteria were applied for the prevalence assessment.

Sepsis was defined pragmatically in patients with suspected or confirmed infection in whom a clinical decision was made by the treating physician to manage sepsis, including the administration of parenteral antibiotics and fluid boluses and/or inotropic support (**SDC Definitions**, https://links.lww.com/PCC/C796). This definition was aligned with regional consensus recommendations proposed by SLACIP and was selected because it reflected routine clinical practice across participating PICUs in Ibero-Latin America in 2024 (4). Hence, the standardized definition for this study was applied a priori across all sites. All patients meeting the clinical definition were subsequently evaluated for concordance with the 2024 Phoenix Sepsis Criteria (6, 7), using the Phoenix Sepsis Score, and with the 2005 International Pediatric Sepsis Consensus Conference (IPSCC) criteria based on systemic inflammatory response syndrome definitions (8). This two-step approach to definition enabled real-world case identification while also allowing subsequent exploratory comparison of the performance of these two pediatric sepsis definitions. Septic shock was defined as sepsis with cardiovascular dysfunction, operationalized as the requirement for vasoactive support or persistent signs of impaired perfusion despite appropriate fluid resuscitation (7).

## Data Collection

Participating PICUs were invited to complete a standardized, web-based questionnaire addressing institutional infrastructure, resource availability, and organizational characteristics relevant to pediatric sepsis care, including staffing, use of clinical protocols, and quality-of-care indicators. The survey was distributed electronically to the designated PICU coordinator at each site and completed by local investigators familiar with unit-level resources and practices. Information collected reflected routine clinical capacity during the study period and was used to characterize institutional readiness for sepsis management, using an institutional resource availability scoring system designed to reflect each site's capacity to adhere to the 1-hour SSC bundles, a technique previously used in a 2014 sepsis point prevalence study in adult patient ICUs in Brazil (9) (**SDC, Institutional resource availability scoring system**, https://links.lww.com/PCC/C796).

Each participating PICU designated a principal investigator responsible for patient identification, data entry, and local data quality oversight. Patient-level data were collected by trained clinicians using a standardized electronic case report form developed in Research Electronic Data Capture. Collected variables encompassed demographics, comorbidities, nutritional and vaccination status, infection characteristics, organ dysfunction, illness severity, and sepsis classification, using validated pediatric scoring systems, including the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score, the IPSCC score, the Phoenix-8 score, and the Phoenix Sepsis Score. Therapeutic interventions—such as fluid resuscitation, antimicrobial therapy, vasoactive support, mechanical ventilation, and corticosteroid use—were recorded within the first 24 hours following the onset of sepsis-related organ dysfunction.

## Outcomes and Statistical Analyses

The primary outcome was the point prevalence of clinical sepsis and septic shock among PICU admissions. Secondary outcomes included patient- and



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institution-level characteristics associated with sepsis, including the distribution of organ dysfunctions, microbiological features of infection, duration of PICU and hospital length of stay (LOS), timing of death stratified by geographic region, and all-cause PICU and in-hospital mortality. In exploratory analyses, we assessed the ability of contemporary sepsis definitions, including the Phoenix sepsis criteria and the 2005 IPSCC criteria, to identify patients at risk of PICU mortality. For these analyses, the Phoenix Sepsis Score and IPSCC criteria were determined using the worst clinical and laboratory values recorded during the first 24 hours of PICU care. Sensitivity was calculated as the proportion of all PICU deaths identified by each definition, and specificity as the proportion of PICU survivors who did not meet each definition.

Analyses were both descriptive and inferential. Prevalence of sepsis was calculated considering all patients with clinical sepsis who were either already admitted or newly admitted to the PICU on the study day. Categorical variables were expressed as numbers, proportions, and percentages when the denominator of a proportion is more than 50. Differences in proportions are presented as mean difference in percentage with the 95% CI. Continuous variables were summarized as medians with the interquartile range (IQR). Between-group comparisons used the $\chi^2$ test for categorical variables; the Mann-Whitney *U* test was used for continuous variables. No correction to the *p* value has been made for multiple comparisons. Time-to-event outcomes (time to death) were analyzed using Kaplan-Meier estimates stratified by region.

To evaluate risk factors associated with PICU mortality, we used multivariable logistic regression. Variables were selected based on clinical plausibility and bivariate associations ($p < 0.05$). To reduce model complexity, we assessed multicollinearity using correlation matrices, retaining the clinically most relevant variable when overlap was present (e.g., Phoenix Sepsis Score vs. other organ dysfunction scores). Results are presented as adjusted odds ratios (aOR) with 95%CIs. Analyses were performed using R (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

Between September 9 and September 13, 2024, a total of 168 PICUs from 21 countries in Ibero-Latin America participated in the study (**Fig. S1**, https://links.lww.com/PCC/C796). These PICUs included 1,822 beds, within hospitals with an overall capacity of 62,244 beds. Overall, Brazil (30/168, 17.9%), Argentina (28/168, 16.7%), and Colombia (27/168, 16.1%) contributed the largest number of PICUs to the study, followed by Peru (15/168, 8.9%) and Spain (12/168, 7.1%) (**Fig. S2**, https://links.lww.com/PCC/C796). PICUs varied in size and capacity: 48.2% (81/168) had fewer than 10 beds, 39.8% (67/168) had 10–20 beds, and 11.9% (20/168) had more than 20 beds. Most units (128/168, 76.2%) were located in public hospitals, with marked regional variation (Iberia 14/14 vs. Andean region 109/168 [63.3%]), and 106 of 168 (61.4%) were affiliated with universities. Of the 168 participating PICUs, 155 of 168 (92.3%) were classified as high-resource, 10 of 168 (6.0%) as intermediate-resource, and 3 of 168 (1.8%) as low-resource units, according to the institutional resource availability scoring system (**Figs. S3** and **S4**, https://links.lww.com/PCC/C796).

A total of 1318 patients were screened during the study period, of whom 340 met inclusion criteria for clinical sepsis, yielding a point prevalence of 25.8% (95% CI, 23.5–28.2%) among PICU admissions. Complete outcome and severity data were available for 324 patients, who constituted the analytic cohort. Baseline clinical and demographic characteristics are presented in **Table 1**. There were 42 of 324 (12.9%) deaths. Mortality, as opposed to survival, was associated with a greater proportion of organ dysfunction assessed using the Phoenix-8 score, including coagulation, immunologic, and renal dysfunction (Table 1). Mortality, in comparison to survival, was also associated with higher median Phoenix Sepsis Score, Phoenix-8 score, and PELOD-2 score.

Microbiological data were available for all 324 patients, with 207 patients (64%) having at least one positive culture, most commonly from a respiratory source (**Table 2**). Gram-negative bacteria were the most frequent pathogens overall; however, *Staphylococcus aureus* was the single most commonly isolated organism, followed by *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Bloodstream infection was the most frequent site of microbiological isolation among children with sepsis.

After PICU admission, fluid resuscitation was administered in 137 of 324 (42.3%) patients. Vasoactive agents were used in 187 of 324 (57.7%) patients, with



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## TABLE 1.
### Demographic and Clinical Characteristics of Children With Sepsis or Septic Shock, Stratified by PICU Survival

| Demographic and Clinical Characteristics | All | Died in the PICU | | *p* |
|---|---|---|---|---|
| | | No | Yes | |
| Total | 324 | 282 (87.1) | 42 (12.9) | |
| Male | 176 (54.3) | 150 (53.2) | 26/42 | 0.373 |
| Age (yr) | 2.00 (0.00–8.25) | 2.00 (0.00–8.00) | 1.00 (0.00–11.75) | 0.913 |
| Nutritional state | | | | **0.001** |
| Underweight | 103 (31.8) | 88 (31.2) | 15/42 | |
| Normal | 204 (63.0) | 184 (65.2) | 20/42 | |
| Obese | 17 (5.2) | 10 (3.5) | 7/42 | |
| Unvaccinated | 78 (24.1) | 61 (21.6) | 17/42 | **0.013** |
| Region | | | | 0.313 |
| Andean | 122 (37.7) | 107 (37.9) | 15/42 | |
| Northern | 52 (16.0) | 42 (14.9) | 10/42 | |
| Southern | 139 (42.9) | 122 (43.3) | 17/42 | |
| Iberian | 11 (3.4) | 11 (3.9) | 0 | |
| Phoenix criteria | 268 (82.7) | 228 (80.9) | 40/42 | **0.037** |
| International Pediatric Sepsis Consensus Conference criteria | 232 (71.6) | 200 (70.9) | 32/42 | 0.601 |
| Phoenix Sepsis Score | 3.00 (2.00–5.00) | 3.00 (2.00–5.00) | 5.00 (3.00–7.00) | **< 0.001** |
| Phoenix-8 score | 4.00 (2.00–6.00) | 4.00 (2.00–6.00) | 6.50 (4.25–8.00) | **< 0.001** |
| Pediatric Logistic Organ Dysfunction-2 score | 6.00 (3.00–9.00) | 6.00 (3.00–8.00) | 8.50 (6.00–12.00) | **< 0.001** |
| Organ dysfunction | | | | |
| Respiratory | 256 (79.0) | 221 (78.4) | 35/42 | 0.593 |
| Cardiovascular | 218 (67.3) | 187 (66.3) | 31/42 | 0.431 |
| Coagulation | 154 (47.5) | 122 (43.3) | 32/42 | **< 0.001** |
| Neurologic | 100 (30.9) | 82 (29.1) | 18/42 | 0.104 |
| Immunologic | 32 (9.9) | 19 (6.8) | 13/42 | **< 0.001** |
| Hepatic | 39 (12.1) | 34 (12.2) | 5/42 | 1 |
| Renal | 100 (30.9) | 77 (27.3) | 23/42 | **0.001** |

IQR = interquartile range.
Data are presented as *n* (%) or median (IQR), as appropriate. Comparisons were performed between survivors and nonsurvivors using $\chi^2$ or Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables.
*p* values <0.05 are shown in bold.

norepinephrine being the most common (**Table 3**). Corticosteroids were administered to 35 of 324 (10.8%) patients.

Overall PICU mortality was 42 of 324 (12.9% [95% CI, 9.5–17.1%]). The median time to death was 11.7 days (IQR, 9.5–24.3 d) in Northern PICUs, 20.8 days (IQR, 9.9–82.1 d) in Southern PICUs, and 30.7 days (IQR, 16.9–55.2 d) in Andean PICUs, with no deaths reported in Iberian units. Among survivors, the total median hospital LOS was 27.2 days (IQR, 14.0–54.3 d). The median PICU LOS was 16.1 days (IQR, 7.0–31.1 d) in survivors and 23.5 days (IQR, 10.9–59.4 d) in nonsurvivors ($p$ = 0.022). All-cause in-hospital mortality was 49 of 324 (15.1% [95% CI, 11.4–19.4%]).



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## TABLE 2.
### Microbiological Characteristics of Pediatric Sepsis Cases, Stratified by PICU Survival

| Microbiological Characteristics | All | Died in the PICU | | *p* |
|---|---|---|---|---|
| | | No | Yes | |
| Total | 324 | 282 (87.0) | 42 (12.9) | |
| Culture source | | | | 0.144 |
| Any | 207 (63.9) | 180 (63.8) | 27/42 | |
| Blood | 94 (29.0) | 75 (26.6) | 19/42 | |
| Urine | 13 (4.0) | 12 (4.3) | 1/42 | |
| Cerebrospinal fluid | 4 (1.2) | 4 (1.4) | 0 | |
| Tracheal | 45 (13.9) | 41 (14.5) | 4/42 | |
| Other | 51 (15.7) | 48 (17.0) | 3/42 | |
| Type of infection | | | | **0.025** |
| Community acquired | 194 (59.9) | 176 (62.4) | 18/42 | |
| Hospital acquired | 130 (40.1) | 106 (37.6) | 24/42 | |
| Pathogen | | | | 0.361 |
| Gram-negative bacteria | 76 (23.5) | 60 (21.3) | 16/42 | |
| *Pseudomonas* | 17 (5.2) | 13 (4.6) | 4/42 | |
| *Klebsiella* | 28 (8.6) | 21 (7.4) | 7/42 | |
| *Escherichia coli* | 16 (4.9) | 13 (4.6) | 3/42 | |
| *Enterobacter* | 10 (3.1) | 8 (2.8) | 2/42 | |
| Acinetobacter | 5 (1.5) | 5 (1.8) | 0 | |
| Gram-positive bacteria | 55 (17) | 50 (17.7) | 5/42 | |
| *Streptococcus pneumoniae* | 14 (4.3) | 12 (4.3) | 2/42 | |
| *Staphylococcus aureus* | 31 (9.5) | 29 (10.3) | 2/42 | |
| Methicillin-sensitive *Staphylococcus aureus* | 14 (4.3) | 13 (4.6) | 1/42 | |
| Methicillin-resistant *Staphylococcus aureus* | 17 (5.2) | 16 (5.7) | 1/42 | |
| *Staphylococcus epidermidis* | 4 (1.2) | 3 (1.1) | 1/42 | |
| *Enterococcus* | 6 (1.9) | 6 (2.1) | 0 | |
| Fungal | 15 (4.6) | 12 (4.3) | 3/42 | |
| *Candida* | 14 (4.3) | 11 (3.9) | 3/42 | |
| *Aspergillus* | 1 (0.3) | 1 (0.4) | 0 | |
| Viral | 28 (8.6) | 26 (9.2) | 2/42 | |
| Rhinovirus | 7 (2.2) | 7 (2.5) | 0 | |
| Respiratory syncytial virus | 5 (1.5) | 5 (1.8) | 0 | |
| Adenovirus | 2 (0.6) | 2 (0.7) | 0 | |
| Cytomegalovirus | 1 (0.3) | 0 (0.0) | 1/42 | |
| SARS-Cov-2 | 1 (0.3) | 1 (0.4) | 0 | |
| Influenza | 3 (0.9) | 3 (1.1) | 0 | |
| Metapneumovirus | 6 (1.9) | 6 (2.1) | 0 | |
| Dengue | 3 (0.9) | 3 (1.1) | 0 | |
| Other | 33 (10.2) | 31 (11.0) | 2/42 | |

Data are expressed as *n* (%). Comparisons were performed between survivors and nonsurvivors using $\chi^2$ or Fisher exact test, as appropriate. Culture sources include any positive bacterial, viral, or fungal pathogen isolated from blood, urine, cerebrospinal fluid, tracheal aspirate, or other sterile sites. Hospital-acquired infection was defined as onset ≥ 48 hr after hospital admission. *p* values <0.05 are shown in bold.



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## TABLE 3.
### Therapeutic Interventions and Management Strategies Among Children With Sepsis, Stratified by PICU Survival

| Therapies and Management | All | Died in the ICU | | *p* |
|---|---|---|---|---|
| | | No | Yes | |
| Total | 324 | 282 (87.1) | 42 (12.9) | |
| Vasoactives | | | | |
| Norepinephrine | 130 (40.1) | 115 (40.8) | 15/42 | 0.648 |
| Epinephrine | 96 (29.6) | 81 (28.7) | 15/42 | 0.457 |
| Dobutamine | 19 (5.9) | 14 (5.0) | 5/42 | 0.152 |
| Dopamine | 3 (0.9) | 3 (1.1) | 0 | 1 |
| Milrinone | 38 (11.7) | 33 (11.7) | 5/42 | 1 |
| Vasopressin | 22 (6.8) | 17 (6.0) | 5/42 | 0.279 |
| None | 137 (42.3) | 122 (43.3) | 15/42 | 0.449 |
| Fluid | | | | |
| Any | 137 (42.3) | 120 (42.6) | 17/42 | 0.931 |
| Saline | 67 (20.7) | 59 (20.9) | 8/42 | 0.941 |
| Balanced | 70 (21.6) | 61 (21.6) | 9/42 | 1 |
| Simple ringers | 11 (3.4) | 11 (3.9) | 0 | 0.398 |
| Lactated ringers | 57 (17.6) | 49 (17.4) | 8/42 | 0.962 |
| Plasmalyte | 4 (1.2) | 3 (1.1) | 1/42 | 1 |
| Broad-spectrum antibiotics | 311 (96.0) | 269 (95.4) | 42/42 | 0.318 |
| Hydrocortisone | 35 (10.8) | 32 (11.3) | 3/42 | 0.581 |
| Mechanical ventilation | 186 (57.4) | 163 (58.0) | 23/42 | 0.818 |
| Monitoring devices | | | | |
| Central venous catheter | 218 (67.3) | 94 (33.3) | 12/42 | 0.662 |
| Arterial line | 101 (31.2) | 90 (31.9) | 11/42 | 0.571 |

Data are presented as *n* (%). Comparisons were performed between survivors and nonsurvivors using $\chi^2$ or Fisher exact test, as appropriate. Broad-spectrum antibiotics include third- and fourth-generation cephalosporins, carbapenems, or glycopeptides administered within the first 24 hr after recognition of sepsis.

Among children with clinical sepsis, abnormal nutritional status (both underweight and obesity), lack of vaccination, and selected comorbidities, including cardiovascular, hemato-oncological, and congenital conditions, were associated with greater odds of PICU mortality (**Table 4**). Admission to a PICU with intermediate- or low-resource availability was also associated with greater odds of mortality. In multivariable logistic regression, independent factors associated with greater adjusted odds of PICU mortality included the Phoenix Sepsis Score, immunologic dysfunction, renal dysfunction, abnormal nutritional status, unvaccinated status, and admission to a PICU with intermediate or low resource availability (Table 4).

The prognostic performance of sepsis definitions was evaluated among patients with a clinical diagnosis of sepsis (**Fig. 1**). At admission day, Phoenix criteria identified 268 of 324 patients (82.7%), of whom 40 of 268 (14.9%) died during the PICU stay, corresponding to a sensitivity of 95.2% and specificity of 19.1% for PICU mortality. In contrast, the IPSCC criteria on admission day identified 232 of 324 patients (72%), including 32 of 232 deaths (13.8%), yielding a sensitivity of 76.2% and specificity of 29.1% (**Table S1**, https://links.lww.com/PCC/C796). Of note, given the pretest probability of death of 0.129, the positive predictive values (PPV) of both scoring systems were no different, ~0.140. Although patients meeting Phoenix criteria accounted for a larger



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## TABLE 4.
### Risk Factors Associated With PICU Mortality Among Children With Sepsis: Bivariate and Multivariable Logistic Regression Analyses

| Risk Factor for ICU Mortality | Bivariate Analysis OR (95% CI) | Multivariable Analysis,* Adjusted OR (95% CI) |
|---|---|---|
| Phoenix Sepsis Score | 1.34 (1.2–1.5) | 1.4 (1.2–1.6) |
| Nutritional status | | |
| Normal | Reference category | Reference category |
| Underweight | 1.6 (0.8–3.2) | 2.3 (1.0–5.7) |
| Obese | 6.4 (2.1–18.7) | 7.6 (2.0–29.4) |
| Unvaccinated | 2.5 (1.2–4.8) | 3.2 (1.4–7.5) |
| Cardiovascular comorbidity | 2.2 (1.1–4.6) | |
| Congenital comorbidity | 2.9 (1.4–5.7) | |
| Immunologic dysfunction | 6.2 (2.7–13.8) | 12.7 (4.6–37.5) |
| Renal dysfunction | 3.2 (1.7–6.3) | 3.2 (1.5–7.5) |
| Coagulation dysfunction | 4.2 (2.1–9.3) | |
| Hospital-acquired infection | 2.2 (1.2–4.3) | |
| PICU with medium or low resources | 4.3 (1.7–10.1) | 3.7 (1.3–10.6) |

OR = odds ratio.

Only risk factors independently associated with ICU mortality in multivariable analysis are included. Data are presented as ORs with 95% CIs. The multivariable model included variables with $p < 0.05$ in bivariate analysis or considered clinically relevant. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test ($p = 0.83$).

*The multivariable logistic regression model included variables with $p < 0.05$ in bivariate analysis or considered clinically relevant.

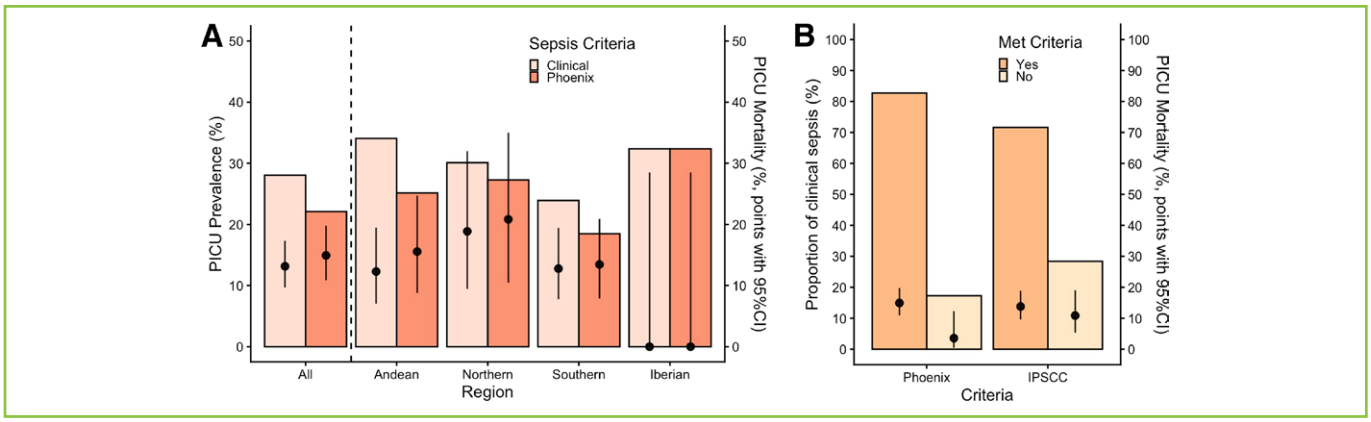



**Figure 1.** Prevalence and mortality of pediatric sepsis according to diagnostic criteria and region. **A**, Proportion of patients with clinical sepsis who met the Phoenix Sepsis Score or the International Pediatric Sepsis Consensus Conference (IPSCC) criteria on the day of admission. *Circles* represent PICU mortality (%) with 95% CIs. **B**, PICU prevalence and mortality of clinical and Phoenix-defined sepsis across Ibero-Latin American regions. *Bars* show prevalence of sepsis among total PICU admissions; *circles* indicate PICU mortality (%) with 95% CIs.

proportion of PICU deaths, absolute PICU mortality rates were comparable when stratified by IPSCC criteria. These findings reflect differences in case identification rather than differences in outcome. Importantly, in-hospital mortality was similar across definitions, at 16.8% among patients meeting Phoenix criteria and 16.4% among those meeting IPSCC criteria.

## DISCUSSION

In this September 2024, multinational, multicenter point prevalence study including 168 PICUs across 21 countries in Ibero-Latin America, approximately one-in-four PICU admissions met criteria for clinical sepsis. Among children with sepsis, all-cause PICU



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## WHAT THIS STUDY MEANS

- In September 2024, across 168 Ibero-Latin PICUs, we found that pediatric sepsis accounted for one-in-four admissions and was associated with 13% PICU mortality.
- Mortality was associated with renal and immunologic dysfunction, abnormal nutritional status, lack of vaccination, and admission to PICUs with intermediate or low resource availability, underscoring the interaction between patient vulnerability and system capacity.
- Early recognition of organ dysfunction and timely access to essential sepsis care resources may be opportunities for practice improvements.

mortality was ~13.0%, with an in-hospital mortality of 15.1%, and no significant differences in mortality across geographic regions. In exploratory analyses, the 2024 Phoenix criteria had greater sensitivity but lower specificity for PICU mortality than the 2005 IPSCC criteria; however, their PPVs were similar.

The prevalence observed in September 2024 is consistent with other estimates of the global burden of pediatric sepsis; however, mortality appeared lower than that reported in earlier regional and global studies. For example, the international point prevalence Sepsis Prevalence, Outcomes, and Therapies (SPROUT) study conducted between June 2013 and March 2014 reported an overall in-hospital mortality of 25%, with lower mortality in the South America subgroup, comparable to that found in our cohort (10). More recently, the national, multicenter PICU study from Bolivia (11, 12), with data from 2023, had a mortality of 33%. Our findings in September suggest lower mortality across the region. This pattern aligns with the idea that sepsis remains frequent but is associated with improved survival, in keeping with the 1990–2017 analysis for the Global Burden of Disease Study (1). In March 2019, the Brazilian SPREAD PED point prevalence study found a comparable prevalence of pediatric sepsis to the current study in September 2024, around 25%. Also, there was comparable in-hospital mortality to the current study (19.8% vs. 15.1%; mean difference, 4.7% [95% CI, –1.3% to 10.8%]; $p = 0.13$), which reinforces a substantial regional burden of disease alongside a consistent signal of outcome (13).

The factors associated with mortality in the multivariable model underscored the intersection between patient vulnerability and structural inequities across the region. Malnutrition and obesity are opposite extremes of nutritional risk, and both were associated with greater odds of death. This observation highlights how metabolic fragility amplifies the physiologic burden of sepsis in children, as described in the nutrition in PICU point prevalence study of malnutrition in Latin America in 2021 (14). Likewise, lack of vaccination and underlying immunological disease were also associated with greater odds of mortality, likely reflecting impaired host defense mechanisms (15). Renal dysfunction, a marker of systemic hypoperfusion and inflammatory injury, was associated with three-fold greater odds of mortality, which is consistent with what is now being learnt about a renal phenotype in pediatric sepsis (16–20).

Beyond individual characteristics, the most striking finding was the association between resources odds of mortality. That is, sepsis patients managed in PICUs with intermediate or low resource availability (defined by restricted access to timely laboratory diagnostics, vasoactive agents, and monitoring technology) had close to four-fold greater odds of mortality, even after adjustment for illness severity. This gradient suggests that in Ibero-Latin America, outcome disparities in pediatric sepsis are not only associated with biological vulnerability but also with organizational limitations that hinder the timely implementation of evidence-based interventions (21). However, this finding should be interpreted with caution. The limited representation of intermediate- and low-resource PICUs, together with the relatively wide 95% CI, restricts the precision of the estimated effect size and suggests that our results may reflect a best-case scenario within the region. As such, the true magnitude of the association between resource availability and mortality may be underestimated. Nevertheless, the consistency of the observed direction supports the hypothesis that structural/organizational constraints contribute meaningfully to outcome disparities. Further studies targeting resource-limited settings are warranted to better understand this relationship.

Our findings suggest that greater timeliness and more consistent application of core resuscitation



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measures—including early antimicrobial therapy, initiation of vasoactive support, and basic physiologic monitoring—may be associated with improved clinical outcomes, as described in the March 2019 Brazilian SPREAD PED point prevalence (13). Although overall mortality did not differ across regions, heterogeneity in time to death may reflect differences in the capacity to sustain advanced care, including infrastructure, referral pathways, continuity of support, and infection control (21, 22).

In the exploratory analyses, comparing the 2024 Phoenix sepsis criteria and the 2005 IPSCC criteria for identifying children at risk of death, we are unable to favor one scoring system over the other. Both result in PPV for mortality that is ~0.140. That is, although the Phoenix criteria identified a greater proportion of patients who ultimately died, absolute hospital mortality did not differ meaningfully between patients classified by Phoenix vs. IPSCC criteria. These findings suggest that the observed differences are driven by case capture and sensitivity rather than true differences in outcome, reinforcing that sepsis definitions may influence risk stratification without necessarily altering underlying mortality risk. The Phoenix criteria authors have discussed the sepsis score and the potential limitations, such as using interventions in the criteria, which may be a problem when interventions are unavailable (23); using stages of sepsis when definitions are too inclusive (24); or the need for world-oriented criteria relevant in LMICs (25, 26); and the problem of parsimony in the scoring elements, that is, four vs. eight components (27). Regarding the latter, we used the Phoenix-8 rather than the Phoenix-4, but it may be that the Phoenix-4 would have resulted in a different relationship with the outcome. Further understanding of these relationships is needed for future epidemiological investigations of sepsis and septic shock across world regions, such that we, as a worldwide PICU community, are better able to address the epidemiological challenges of the Global Sepsis Alliance "2030 Global Agenda for Sepsis" (28). In particular, of the five strategic pillars: Pillar 2, Health System Readiness for Sepsis and Its Sequelae; and Pillar 4, Sepsis Research and Innovations.

This study has some limitations that warrant discussion. First, the point prevalence design precludes causal inference and limits the assessment of clinical trajectories, the identification of incident sepsis occurring outside the sampling window, and the evaluation of long-term outcomes, which hinders comparison with studies such as SPROUT that used a different study design (10). In addition, although the study included PICUs from multiple countries, time zones, and climatic regions, it did not capture seasonal variability in sepsis epidemiology. Therefore, the estimated prevalence should be interpreted as a cross-sectional snapshot rather than an annual burden. Nonetheless, our study in September 2024 is the largest pediatric, multicenter cohort from our region. Second, participating PICUs were not randomly selected, and more than 90% were classified as high-resource units, introducing the potential for selection bias and suggesting that observed outcomes may approximate a best-case performance scenario rather than regional averages. However, these units constitute a large and geographically diverse sample of regional referral centers and allow the description of contemporary trends in resource availability for early sepsis care. Third, our multivariable analysis of factors associated with greater odds of PICU mortality among children with sepsis may be subject to overfitting given the events-per-variable ratio of less than 10:1. External validation of these findings is warranted. Last, although geographic coverage was broad, some countries contributed a limited number of PICUs, restricting the precision of national-level inferences.

In conclusion, our September 2024 multinational, point prevalence study found that clinical sepsis accounted for approximately one quarter of PICU admissions across the Ibero-Latin America region. Across participating units, intermediate or low availability of critical care resources was associated with greater odds of mortality, highlighting the influence of structural/organizational capacity on outcomes. The SPREAD PED Ibero-Latin America study provides a contemporary, large-scale, multinational description of pediatric sepsis in the region and demonstrates the feasibility of collaborative networks to generate comparable data across diverse health systems.

## ACKNOWLEDGMENTS

This work was organized by the Latin American Sepsis Institute in collaboration with the Latin American Society of Pediatric Intensive Care and the University of São Paulo. We express our deep gratitude to the



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national coordinators, site investigators, and PICU teams from 21 participating countries for their dedication and commitment to data collection. We also extend our sincere gratitude to the Red Colaborativa Pediatrica de Latinoamerica Network for its collaboration and support in the dissemination of this research. We also thank the families and institutions that enabled this research and recognize the contribution of the Sepsis PREvalence Assessment Database in PEDiatrics Latin America Iberia network to advancing collaborative pediatric critical care research in the region.

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*This work was supported by a research grant from Fundação de Apoio à Pesquisa do Estado de São Paulo (Grant no. 2017/21052-0). Dr. Fernández-Sarmiento received grant support from Universidad de La Sabana through the MED 65-2026. Name of the research project: Pediatric Sepsis in Ibero-Latin American ICUs: Prevalence, Outcomes, and Resource Availability.*

*Dr. De Souza's institution received funding from Fundação de Apoio à Pesquisa do Estado de São Paulo. Dr. Fernandez-Sarmiento's institution received funding from Universidad de La Sabana through the MED 65-2026. Dr. Sanchez-Pinto's institution received funding from the National Institutes of Health (NIH) (R01HD105939); He received support for article research from the NIH. Drs. Marques and Marquez disclosed government work.*



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*Dr. Machado received funding from Baxter; she received support for article research from Conselho Nacional de Pesquisa. The remaining authors have disclosed that they do not have any potential conflicts of interest.*

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