External validation of the Phoenix Sepsis Score in a multicentre cohort of emergency intensive care admissions

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ABSTRACT

Objectives

To describe the clinical characteristics and outcomes of children requiring emergency transport and paediatric intensive care unit (PICU) admission fulfilling the newly developed Phoenix Sepsis Score (PSS) sepsis definition and assess the association of PSS with mortality and ventilator-free days at day 30 (VFD-30).

Design

Multicentre prospective observational cohort study.

Setting

Emergency admission to PICU following transport in the South-East England, UK.

Patients

Children aged 0-16 years (n=663) of whom 444 had suspected/confirmed infection at the time of transport.

Interventions

None.

Measurements and main results

For each child with suspected/confirmed infection, the PSS was computed as a sum of four individual organ subscores (respiratory, cardiovascular, neurological and coagulation) using the worst values during transport. A cutoff of ≥2 points was used to identify children with sepsis; septic shock was defined as sepsis plus 1 or more cardiovascular subscore points. Receiver operating characteristic (ROC) curves and precision-recall (PR) curves were produced to test the accuracy of PSS in predicting the primary outcome (mortality). Sepsis criteria were met in 260/444 children with suspected/confirmed infection (58.6%) and septic shock criteria in 177/260 (39.9%). PSS sepsis criteria were met in diverse clinical infection syndromes including bronchiolitis (55.2%), meningoencephalitis (57.6%) and pneumonia (63.8%) as well in definite viral infections (49.2%). Overall, 14 (3.2%) children died, with 12 deaths in children with PSS ≥2 and 2 in children with PSS<2. PSS was predictive of mortality (area under the ROC curve 0.721, 95% CI 0.560–0.881; area under the PR curve 0.08) and correlated inversely with VFD-30 (adjusted R^2 0.11, $p<0.001$).

Conclusions

Over half of critically ill children with presumed infection satisfied sepsis criteria based on the newly developed PSS, including those with a clinical diagnosis of bronchiolitis, meningoencephalitis, and pneumonia. PSS was strongly associated with mortality and reduced VFD-30.

RESEARCH IN CONTEXT

- Sepsis is a syndrome that is commonly managed in paediatric critical care units, but its clinical definition has been challenging.
- A recent taskforce defined sepsis as life-threatening organ dysfunction, and developed and validated the Phoenix Sepsis Score (PSS) using data from several thousand hospital encounters, mainly from the emergency department; sepsis was defined as a PSS of 2 points or more.
- The validity of the PSS in a paediatric intensive care cohort, where organ dysfunction is expected to be more common, is unclear.

WHAT THIS STUDY MEANS

- Sepsis was identified in over half of transported emergency admissions to intensive care using the PSS criteria.
- Sepsis was present in over half of children with clinical infection syndromes such as bronchiolitis, meningoencephalitis, and pneumonia, as well as septic/toxic shock and severe sepsis.
- Changes to the definition of sepsis may have implications for epidemiology, clinical practice, and research.

INTRODUCTION

Sepsis is a life-threatening syndrome that is commonly treated on paediatric intensive care units (PICUs) worldwide(1-3). From 2005 until early 2024, the criteria to define paediatric sepsis were based on the presence of the systemic inflammatory response syndrome (SIRS) in children with presumed infection(4). However, SIRS criteria may simply reflect a functional response to infection and have a low ability to predict poor outcome, such as in-hospital mortality(5, 6). In 2016, the Sepsis-3 consensus criteria re-defined sepsis in adults as life-threatening organ dysfunction caused by a dysregulated host response to infection(7). This was operationalised by a two-point rise in the sequential (sepsis-related) organ failure assessment (SOFA) score in the context of suspected or confirmed infection, with enhanced ability to predict poor outcome in comparison to previous scores(8, 9).

Based on a similar conceptual framework(10, 11), new international consensus criteria for paediatric sepsis were presented at the Society of Critical Care Medicine Annual Congress in January 2024(12, 13). These recommend that children with sepsis are identified by a Phoenix Sepsis Score (PSS) of 2 or more points in the context of suspected infection. The PSS was developed using a data-driven derivation and validation approach based on electronic health record data from 3.1 million paediatric hospital encounters (172 984 of which related to suspected infection) following a global survey, and finalised after a Delphi consensus stage(13). The PSS was calculated as the sum of four individual organ system dysfunction scores (respiratory, cardiovascular, coagulation and neurological; Supplementary Digital Content, Table 1), based on the worst values in the first 24 hours of the hospital encounter. Septic shock was defined as sepsis with at least 1 point from the cardiovascular subscore.

The PSS was developed predominantly from emergency department encounters. There is a need for the PSS to be validated in the intensive care setting, where life-threatening organ dysfunction may be more common, and where the PSS may have a different predictive value for mortality in comparison with the diverse emergency department, inpatient and intensive care populations from high- and low-middle income settings used to derive the score(14). Therefore, we aimed to investigate the distribution of PSS in a cohort of children requiring emergency admission to PICU following transport. We describe the clinical characteristics, course, and outcomes of children with a sepsis and septic shock diagnosis based on the PSS criteria; and analyse the ability of PSS to predict mortality and ventilator-free days at day 30 (VFD-30) in children requiring paediatric intensive care.

MATERIALS AND METHODS

We analysed data collected as part of the Biomarkers of Acute Serious Illness in Children (BASIC) study(15). BASIC was a prospective cohort study that enrolled critically ill children admitted to four critical care units in the Southeast of England during emergency transport by the Children's Acute Transport Service (CATS). Children aged 0–16 years with an indwelling central venous or arterial catheter were eligible. Infants <36 weeks of corrected gestational age and those with agreed do-not-attempt-resuscitation plans were not recruited. The study was approved by the Health Research Authority (HRA, reference: 136866) and ethical approval was provided by the National Research Ethics Committee East Midlands—Nottingham 2 (reference: 13-EM-0399). Recruitment followed deferred consent processes, with written informed consent obtained by the study research team from parents/legal guardians within 24–48 hours(16).

Data

Detailed clinical phenotyping was undertaken in enrolled children in whom consent was available. For this study, patient demographic data (age; sex; ethnic category), clinical characteristics (suspected/confirmed infection, duration of acute illness prior to transport, pre-morbid Pediatric Overall Performance Category [POPC])(17), clinical severity markers such as the paediatric index of mortality (PIM-2) score and pediatric logistic organ dysfunction (PELOD-2) score on the day of transport(18, 19), interventions received during transport (invasive ventilation, vasoactive drugs) and PICU discharge outcome (vital status and duration of organ support) were extracted from the BASIC database. Detailed classification of infections (as ascertained at PICU discharge) as definite bacterial infection, definite viral infection, probable bacterial infection, probable viral infection, inconclusive for bacterial or viral infection using standardised published criteria(20, 21), and non-infectious conditions (respiratory, cardiovascular, neurological, trauma/head injury, metabolic/endocrine, other) was performed. In addition, children were grouped into specific clinical infection syndromes (bronchiolitis, meningoencephalitis, pneumonia/pleural effusion/empyema, severe sepsis, septic/toxic shock and other).

Statistical analysis

Categorical data are presented as frequency (%) and continuous data as medians (interquartile range [IQR]) or means with 95% confidence intervals (CI). Differences between proportions were calculated using the χ^2 test, and differences between continuous data with appropriate non-parametric tests (Wilcoxon rank sum and Kruskal-Wallis). Using the worst values during transport (assumed to represent the worst values within the first 24 hours of presentation to the community hospital), we computed four individual organ subscores (respiratory, cardiovascular, neurological and coagulation) for each child with

suspected/confirmed infection, and the PSS as a sum of individual organ-system subscores. We used the score cutoff of PSS ≥2 points to label children with a diagnosis of sepsis, and those with sepsis and at least 1 point from the cardiovascular subscore as septic shock. Children who had respiratory or neurological dysfunction and scored 1 or more points in a different organ system were labelled as having organ dysfunction remote to the site of infection.

Using the PSS as a continuous variable, we produced receiver operating characteristic (ROC) curves and precision-recall curves and explored the ability of PSS to predict PICU mortality. In addition, we used ventilator-free-days at day 30 (VFD-30) and the composite outcome of death or needing ventilation at 30 days as markers of poor outcome.

RESULTS

Of the 1017 children who were eligible for the BASIC study, consent was available for 672 children (66.1%). Reasons for non-consent included decline of consent (n=114), missed by research team (n=34), child died prior to consent (n=30), discharged from hospital prior to consent (n=73), social/language barriers (n=49), later withdrawal of consent (n=2), and other (n=43). Nine children had missing data for suspected/confirmed infection at the time of transport to PICU, leaving data available for analysis from 663 children (Supplemental Digital Content, Figure 1). The clinical characteristics of the study cohort by suspected/confirmed infection status at the time of transport is shown in Table 1.

Of 663 children in the study cohort, 444 (70.0%) had suspected/confirmed infection at the time of transport to PICU and 219 (30.0%) did not. Compared to children without suspected/confirmed infection, there was a lower proportion of neonates (<1 month of age) with suspected/confirmed infection (58/219, 26.5% versus 54/444, 12.2%) and a higher proportion of children aged 1–11 months with suspected/confirmed infection (30/219, 13.7% versus 118/444, 26.6%).

Phoenix sepsis scores

PSS were calculated only in children with suspected/confirmed infection (n=444). Data availability for each of the clinical variables required to calculate the PSS is summarised in Supplemental Digital Content, Table 2. The median PSS was 2 (IQR 1-3), with the distribution of organ-specific subscores shown in Supplemental Digital Content, Table 3.

Children with suspected/confirmed infection and sepsis

Of 444 children with suspected/confirmed infection, 260 (58.6%) had a PSS ≥2 points (i.e., a diagnosis of sepsis) within 24 hours of transport to PICU (Table 2).

Of these 260 children, 177 (68.1%) had a PSS cardiovascular subscore ≥1 point (i.e., a diagnosis of *septic shock*). There was a non-significant difference in the proportion of children with a sepsis diagnosis by age group, with 38/260 (14.6%) neonates with a PSS ≥2 points and 16/184 (8.7%) neonates with a PSS <2 points (p=0.083 for neonates versus all other ages, p=0.29 for differences in all age groups, Table 2). Children with PSS ≥2 points (in comparison with children with PSS<2) were sicker with a higher admission Paediatric Index of Mortality-2 (PIM-2) score (median 6.4, IQR 3.6–11.7 versus median 4.3, IQR 1.6–6.9; p<0.001), and received more interventions (vasoactive infusions: 162/260, 62.3% versus 14/184, 7.3%, p<0.001; renal replacement therapy: 10/260, 3.8% versus 1/184, 0.5%, p 0.03).

Based on clinical syndromes allocated by clinicians at death/discharge from PICU, similar proportions of children with “bronchiolitis”, “meningoencephalitis”, “pneumonia/empyema” and “severe sepsis” (pre-2024 definition) had a PSS ≥2 points in comparison with PSS <2 points, whereas a higher proportion of children with PSS ≥2 points had “septic/toxic shock” in comparison with children with PSS <2 points (38/260, 14.7%, versus 8/184, 4.3%, p=0.001; median 3 [IQR 2–5] versus median 2, IQR [1–3]). However, as shown in Figure 2, more than half of children with each clinical syndrome fulfilled PSS sepsis criteria (bronchiolitis: 37/67, 55.2%; meningoencephalitis: 19/33, 57.6%; pneumonia/empyema: 30/47, 63.8%; septic/toxic shock: 38/46, 82.6%; and severe sepsis: 9/15, 60.0%). A high proportion of children with sterile site culture-proven bacterial infection had a sepsis diagnosis (46/58, 79.3% versus 12/58, 20.7%, p<0.001), although nearly half of children with a definite viral infection (clinically relevant pathogenic virus detected with CRP concentration <60 mg/L) also had a PSS sepsis diagnosis (58/118, 49.2% versus 60/118, 50.8%)

Remote organ dysfunction in children with a sepsis diagnosis

Of all patients with sepsis, 171/260 (65.8%) had a respiratory subscore >0, 177/260 (68.1%) had a cardiovascular subscore >0, 10/260 (3.9%) had a coagulation subscore >0 and 172/260 (66.2%) had neurological subscore >0. Remote organ dysfunction was present in 215/260 children (82.7%) with PSS sepsis. However, most children were ventilated and sedated (which automatically assigned them a neurological subscore of >0 When children who only had respiratory and neurological organ system dysfunction were excluded, only 161/260 (61.9%) had remote organ dysfunction.

PSS for prediction of poor outcome in children with suspected/confirmed infection

In children with suspected/confirmed infection, 14 (3.2%) children died, and 27 (6.1%) children either died within 30 days or were still receiving mechanical ventilation at day 30. Children who died had a greater PSS than survivors (median 4, IQR 3–5 versus median 2, IQR 1–3, p=0.004); and children who died or were still receiving mechanical ventilation at day 30 had a greater PSS compared to those discharged prior to day 30 (median 4, IQR 3–5, p<0.001; Figure 1B). There was a negative association between PSS and ventilator-free-days, indicating a longer duration of invasive mechanical ventilation with increased PSS (adjusted R^2=0.11, p<0.001, Figure 1C).

PSS was predictive of mortality (area under the ROC [AUROC] curve 0.721, 95% CI 0.560–0.881, Figure 3A; area under the PR curve 0.07, Figure 3B), and predictive of either mortality or still receiving mechanical ventilation at 30 days (AUROC 0.719, 95% CI 0.610–0.829, Figure 3C, area under the PR curve 0.14, Figure 3D). The Youden's method optimum cut-off for prediction of mortality was a PSS of 3 (sensitivity 0.857, IQR 0.572–0.982, specificity 0.598, IQR 0.550–0.644).

As expected, PPV for mortality changed with increased PSS (SDC, Figure 2A), as did PPV for mortality or still receiving mechanical ventilation at day 30 (SDC, Figure S2B). We visually examined the trade-off between sensitivity and PPV for the prediction of mortality, or for mortality or still receiving mechanical ventilation at day 30 (SDC, Figure 3). With PSS ≥2 points, there was a sensitivity of 0.857 (95% CI 0.643–1) and PPV 4.7% (95% CI 3.6%–5.6%) for mortality; and a sensitivity of 0.815 (95% CI 0.667–0.926) and PPV 8.5% (95% CI 6.9%–10.0%) for mortality or still receiving mechanical ventilation at 30 days.

DISCUSSION

We have described the clinical characteristics, course, and outcome of a multicentre cohort of critically ill children from England with a diagnosis of sepsis based on the newly published Phoenix Sepsis Score (PSS) criteria. Data completeness for the variables that contributed to the PSS ranged from 0% for international normalised ratio, D-dimer and fibrinogen to 100% for vasoactive support. Over half of the cohort fulfilled a sepsis diagnosis, including in clinical infection syndromes such as bronchiolitis, meningoencephalitis, pneumonia/empyema, severe sepsis, and septic shock. Similarly, 40% of the cohort fulfilled the septic shock definition. The PSS was predictive of mortality and correlated inversely with ventilator-free days in this cohort.

A new paediatric sepsis definition was published by the Society of Critical Care Medicine (SCCM) task force in 2024, based on the newly developed Phoenix Sepsis Score (PSS)(12). Previously, the International Pediatric Sepsis Consensus Conference (IPSCC) defined paediatric sepsis as suspected or confirmed infection in the presence of a systemic inflammatory response syndrome (SIRS)(4). The PSS has been shown to outperform the IPSCC criteria in identifying life-threatening organ dysfunction with infection (sepsis). The PSS was developed from predominantly emergency department encounters, but it has not yet been applied to an external cohort to identify cases of sepsis and septic shock, especially a critical care cohort where life-threatening organ dysfunction may be more common.

Our finding that over half of the BASIC cohort had ‘sepsis’ is surprising, in the context of a previous large international point prevalence study in intensive care units (The Sepsis Prevalence, Outcomes, and Therapies Study, SPROUT) reporting a sepsis prevalence of 8.2% based on physician diagnosis or IPSCC criteria(22). Both physician diagnosis and IPSCC criteria were met in less than half of the patients(23). Potential reasons for this discrepancy may relate to the high acuity of our cohort (only emergency admissions from community hospitals, vast majority invasively ventilated, all with indwelling arterial or central venous lines), a fundamental shift in the conceptual definition of ‘sepsis’, and a high number of children sedated in our cohort which assigned them all at least one point on the neurological subscore making it easier to have a PSS≥2. Organ dysfunction remote to the site of infection was common in children with sepsis, similar to the PSS derivation/validation study; however, respiratory and neurological organ dysfunctions were correlated due to the high proportion of children ventilated and sedated.

Our study has several implications for epidemiology, practice, and research. First, the large proportion of children fulfilling the sepsis definition may make it challenging to compare the epidemiology of sepsis from before and after introduction of the PSS definition. Benchmarking of sepsis rates across sites may be confounded by the change in the definition of sepsis. Second, several sepsis identification quality improvement programmes are ongoing in hospitals, which focus on early diagnosis of sepsis and timely administration of treatments such as systemic antibiotics, fluid boluses and vasoactive medications(24). It is likely that at least in the critical care setting, the high proportion of children with a PSS-based sepsis diagnosis might increase antibiotic use and other invasive therapies. Finally, identification of children for clinical trials of interventions in sepsis may be altered in the future by changes to the definition.

The strengths of our study are the size, diversity of the cohort in terms of age, ethnicity and diagnosis, and multicentre setting which make the findings generalisable to other similar healthcare systems; the detailed phenotyping of patients at the end of PICU stay by their infection aetiology and clinical syndrome; and the early enrolment of children into the study during transport, prior to PICU admission. In addition, this is the first study to validate the PSS in an external critical care cohort unrelated to the derivation/validation study.

This study has several limitations. First, since consent was not available in nearly 40% of eligible children, the sample may have been biased. This is particularly evident in the number of deaths – while there were 27 deaths in the consented cohort, there were an additional 30 deaths prior to consent. This may be one reason why there was a mortality rate difference between this cohort (4%) and the PSS cohort (7%). Previous studies have shown that most children with sepsis who die will do so within the first 24 hours of hospital admission(25). Second, data required to calculate the PSS was missing in many patients, especially related to coagulation markers such as D-dimers and fibrinogen level; however, this may be a common problem in emergency/early critical care, where results from diagnostic tests are likely to be pending or unavailable. Unavailability of missing values means that the real PSS could have been higher than what is reported. Third, the predictive performance of PSS for mortality in this study was lower than in the PSS derivation/validation study (AUROC 0.72 versus 0.88-0.92), likely reflecting the differences between the cohorts.

CONCLUSION

In children with suspected/confirmed infection requiring emergency admission to PICU following transport, over half satisfied sepsis criteria based on the newly developed PSS. This included children with a clinical diagnosis of bronchiolitis, meningoencephalitis, and pneumonia. PSS was strongly associated with mortality and reduced ventilator-free days indicating that it serves as a good organ dysfunction severity score.

TABLES AND FIGURES

Table 1. Characteristics of the study cohort.

	All (n=663)	Suspected or confirmed infection (n=444)	Infection not suspected or confirmed (n=219)
Age group			
0 to <1 month	112 (16.9)	54 (12.2)	58 (26.5)
1-11 months	148 (22.3)	118 (26.6)	30 (13.7)
12-23 months	89 (13.4)	63 (14.2)	26 (11.9)
2-4 years	123 (18.6)	86 (19.4)	37 (16.9)
5-11 years	132 (19.9)	83 (18.7)	49 (22.4)
≥12 years	54 (8.1)	37 (8.3)	17 (7.8)
Missing	5 (0.8)	3 (0.7)	2 (0.9)
Sex			
Male	365 (55.1)	244 (54.9)	121 (55.3)
Female	292 (44.0)	195 (43.9)	97 (44.3)
Missing	6 (0.9)	5 (1.1)	1 (0.5)
Ethnic category			
White	311 (46.9)	210 (47.3)	101 (46.1)
Asian	75 (11.3)	51 (11.5)	24 (10.9)
Black	53 (8.0)	38 (8.6)	15 (6.9)
Mixed	23 (3.5)	18 (4.1)	5 (2.3)
Other	19 (2.9)	13 (2.9)	6 (2.7)
Missing	182 (27.5)	114 (25.7)	68 (31.1)
Comorbidities*			
None	292 (44.0)	203 (45.7)	89 (40.6)
Respiratory	109 (16.4)	83 (18.7)	26 (11.9)
Cardiac	71 (10.7)	41 (9.2)	30 (13.7)
Neurological	131 (19.8)	87 (19.6)	44 (20.1)
Genetic/Syndrome	61 (9.2)	49 (11.0)	12 (5.5)
Metabolic/Endocrine	33 (4.9)	21 (4.7)	12 (5.5)
Haematology/Oncology	13 (1.9)	6 (1.4)	7 (3.2)
Multisystem	8 (1.2)	7 (1.6)	1 (0.5)
Other	102 (15.4)	66 (14.9)	36 (16.4)
POPC status prior to admission			
Normal	431 (65.0)	278 (62.6)	153 (69.9)
Mild disability	38 (5.7)	28 (6.3)	10 (4.6)
Moderate disability	56 (8.5)	43 (9.7)	13 (5.9)
Severe disability	62 (9.3)	46 (10.4)	16 (7.3)
Missing	76 (11.4)	49 (11.0)	27 (12.3)
Time from onset of symptoms to first contact with transport team			
< 6 hours	108 (16.3)	52 (11.7)	56 (25.6)

6-24 hours	148 (22.3)	97 (21.9)	51 (23.3)
24-72 hours	160 (24.1)	120 (27.0)	40 (18.3)
3-7 days	118 (17.8)	94 (21.2)	24 (10.9)
>7 days	70 (10.6)	54 (12.2)	16 (7.3)
Missing	59 (8.9)	27 (6.1)	32 (14.6)
Interventions prior to/during transport to PICU			
Invasive ventilation	639 (96.3)	428 (96.4)	211 (96.3)
Received >40 ml/kg fluid bolus	107 (16.1)	92 (20.7)	15 (6.9)
Vasoactive agents	271 (40.9)	176 (39.6)	95 (43.4)
Median Paediatric Index of Mortality-2 score predicted mortality risk, % (IQR)	5.6 (3.1,10.7)	5.5 (2.8,9.7)	5.9 (3.7,13.2)
Median ventilator-free days at day 30 (IQR)	25 (22,27)	25 (22,27)	26 (22,28)
PICU mortality (%)	27 (4.1)	14 (3.2)	13 (5.9)
Median hours of invasive ventilation (IQR)	95 (46,186)	98.5 (51,190.5)	76 (30,168)

*Each patient may have more than co-morbidity. Abbreviations: POPC: Pediatric Overall Performance Category; PICU: paediatric intensive care unit; IQR: inter-quartile range

Table 2. Characteristics and outcomes of children with suspected/confirmed infection with a sepsis diagnosis based on PSS criteria.

	Sepsis (PSS >/=2) (n=260)	**Not sepsis (PSS <2) (n=184)**	**P value**
Age group			0.29
0 to <1 month	38 (14.6)	16 (8.7)	
1-11 months	73 (28.1)	45 (24.5)	
12-23 months	34 (13.1)	29 (15.8)	
2-4 years	48 (18.5)	38 (20.7)	
5-12 years	43 (16.5)	40 (21.7)	
>12 years	23 (8.8)	14 (7.6)	
Missing	1 (0.4)	2 (1.1)	
Male sex	142 (54.6)	102 (55.4)	0.87
One or more comorbidities	139 (53.5)	102 (55.4)	
Diagnosis at PICU discharge			<0.001
Infection	162 (62.3)	104 (56.5)	
Bronchiolitis	37 (14.2)	30 (16.3)	
Meningoencephalitis	19 (7.3)	14 (7.6)	
Pneumonia/empyema	30 (11.5)	17 (9.2)	
Septic/toxic shock	38 (14.7)	8 (4.3)	
Severe sepsis*	9 (3.5)	6 (3.3)	
Other	25 (9.7)	25 (13.0)	
Missing			
Respiratory/Airway	57 (21.9)	31 (16.8)	
Aspiration pneumonia	5 (1.9)	1 (0.5)	
Asthma/Wheeze	2 (0.8)	8 (43.)	
Croup	2 (0.8)	2 (1.1)	
Primary pulmonary hypertension	8 (3.1)	0 (0.0)	
Other	40 (15.4)	20 (10.9)	
Neurological	15 (5.8)	37 (20.1)	
Coma	0 (0.0)	5 (2.7)	
Status epilepticus	13 (5.0)	29 (15.8)	
Other	2 (0.8)	3 (1.6)	
Cardiac	10 (3.8)	6 (3.3)	
Cardiac arrest	1 (0.4)	1 (0.5)	
Congenital heart disease	1 (0.4)	0 (0.0)	
Myocarditis	2 (0.8)	1 (0.5)	
Other	6 (2.3)	4 (2.2)	
Trauma/Head injury	2 (0.8)	0 (0.0)	
Endocrine/Metabolic	3 (1.2)	2 (1.2)	
Other	9 (3.5)	4 (2.2)	
Aetiology of Infection			0.003
Definite bacterial	46 (17.1)	12 (6.2)	

Definite viral	58 (22.3)	60 (32.6)	
Probable bacterial	30 (11.5)	18 (9.3)	
Probable viral	13 (5.0)	12 (6.2)	
Inconclusive	79 (30.4)	50 (25.9)	
Non-infectious	32 (12.3)	32 (17.4)	
Missing	2 (0.8)	0 (0.0)	
Interventions during admission			
Invasive ventilation	255 (98.1)	173 (94.0)	0.02
Vasoactive agent use	162 (62.3)	14 (7.6)	<0.001
Renal replacement therapy	10 (3.8)	1 (0.5)	0.03
Extracorporeal life support	12 (4.6)	0 (0.0)	0.002
Median Paediatric Index of Mortality-2 score predicted mortality risk (IQR)	6.4 (3.6, 11.7)	4.3 (1.6, 6.9)	<0.001
Median hours of vasoactive therapy (IQR)	24 (0,75)	0 (0,0)	<0.001
Median ventilator-free days at day 30 (IQR)	24 (20, 26)	26 (24, 28)	<0.001
Median hours of invasive ventilation (IQR)	121 (72,208.5)	69.5 (33,127.5)	<0.001
PICU mortality (%)	12 (4.6)	2 (1.1)	0.05

***** severe sepsis was defined as per the international Paediatric Sepsis Consensus Conference (IPSCC) criteria

FIGURES

Figure 1. Phoenix Sepsis Score within the first 24 hours of transport to PICU. A. Number of children with suspected/confirmed infection status at time of transport to PICU. B. Number of children with suspected/confirmed infection who were discharged alive and received mechanical ventilation <30 days, survived to 30 days but still receiving mechanical ventilation at 30 days, and died within 30 days of transport. C. Proportion of children (%) with suspected/confirmed infection who were discharged alive and received mechanical ventilation <30 days, survived to 30 days but still receiving mechanical ventilation at 30 days, and died within 30 days of transport.

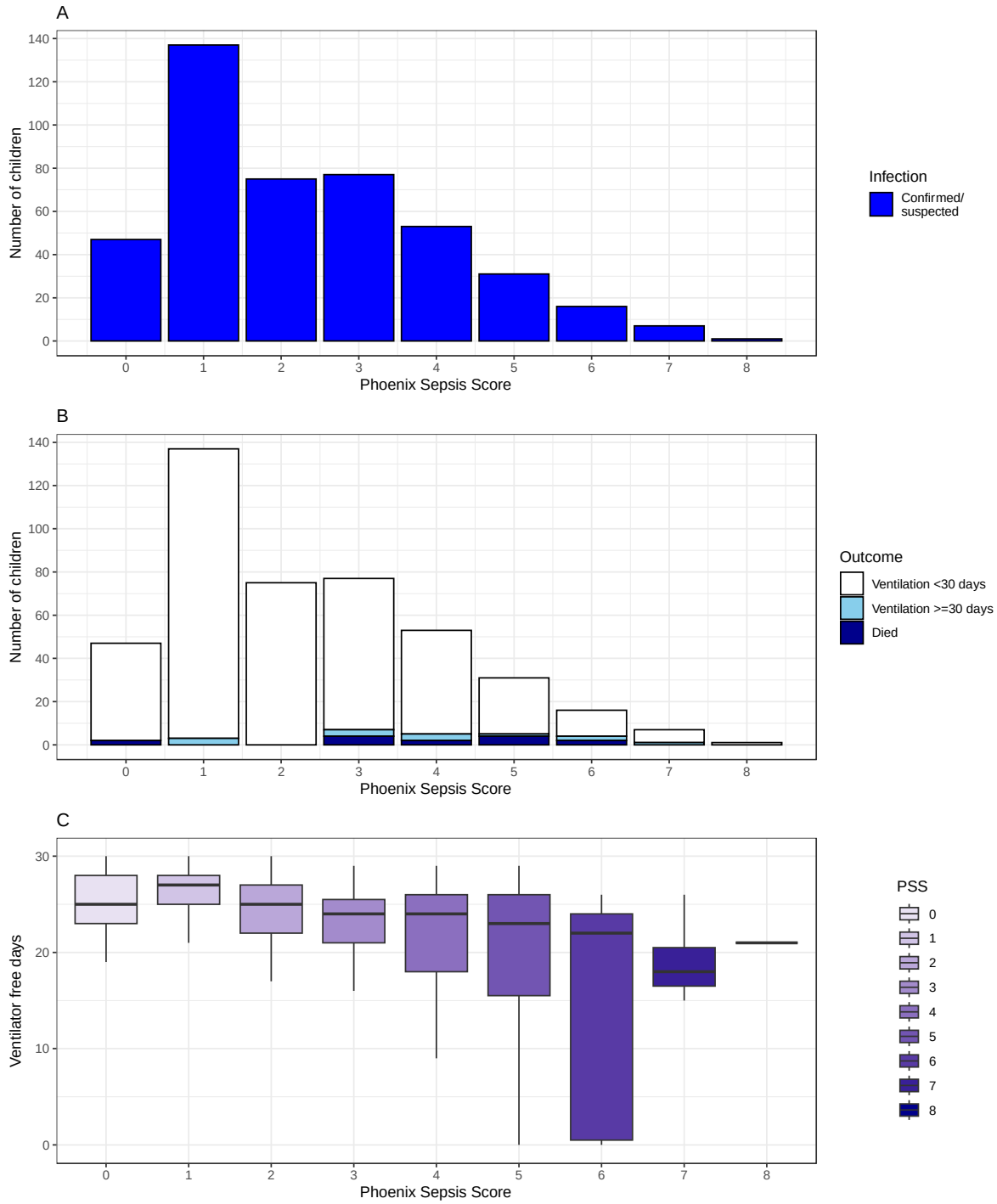
A
Number of children
Phoenix Sepsis Score
Infection
Confirmed/ suspected
B
Number of children
Phoenix Sepsis Score
Outcome
Ventilation <30 days
Ventilation >=30 days
Died
C
Ventilator free days
Phoenix Sepsis Score
PSS
0
1
2
3
4
5
6
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Figure 2. Proportion of children with suspected/confirmed infection in the BASIC cohort meeting PSS criteria for sepsis (PSS ≥2 points) by clinical infection syndrome

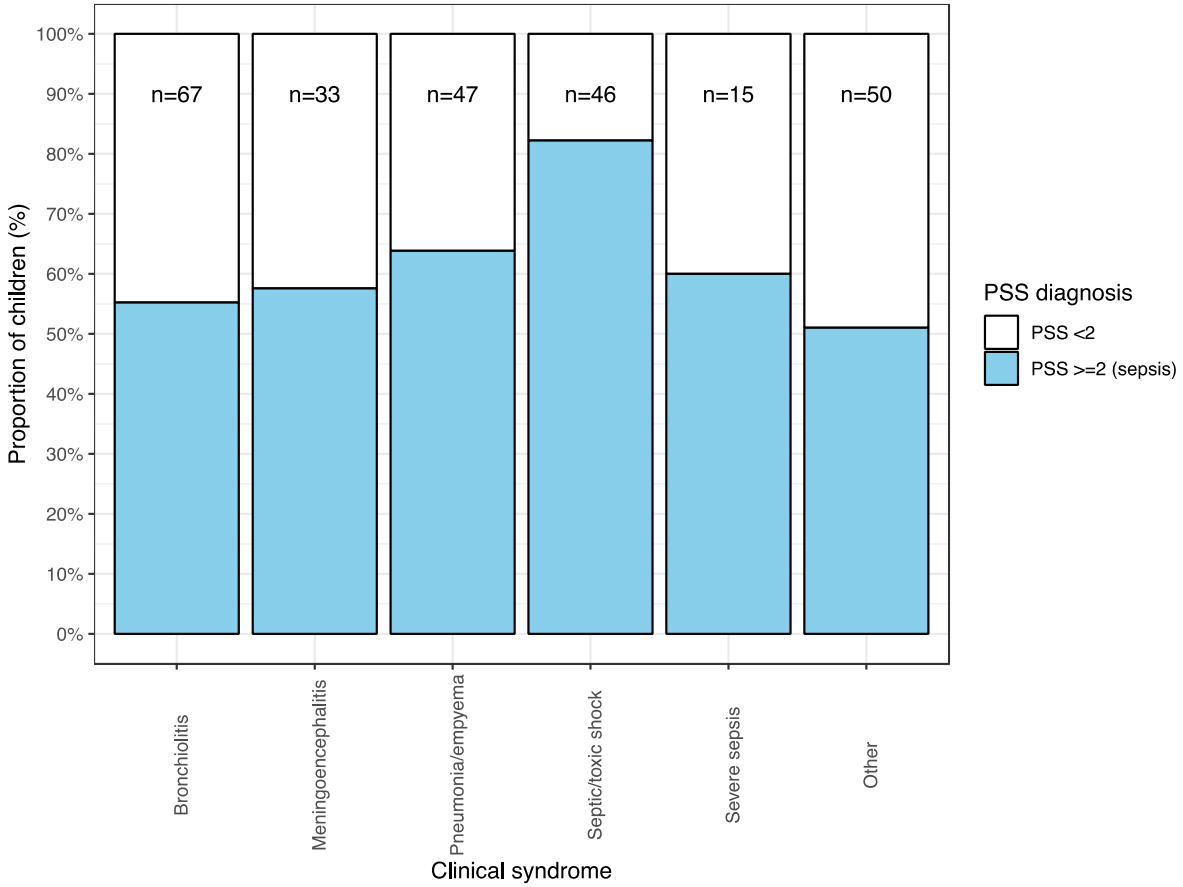
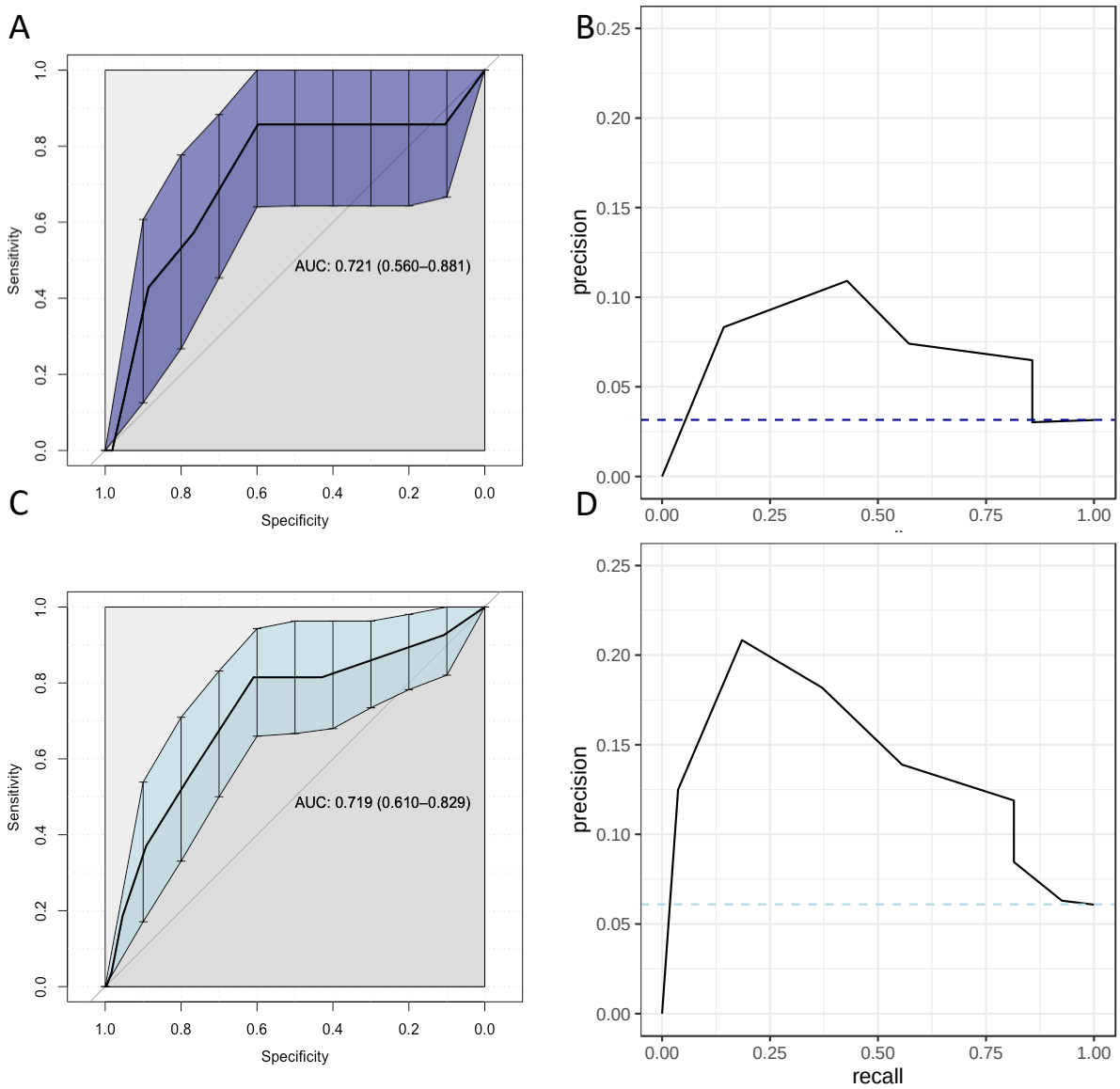


Figure 3. Receiver operating characteristic (ROC) curves and precision-recall curves (PRC) for Phoenix Sepsis Scores in children with suspected/confirmed infection status at time of transport. A. ROC curve for Phoenix Sepsis Score: Prediction of mortality. B. ROC curve for Phoenix Sepsis Scores: Prediction of mortality or ventilation ≥30 days from time of transport. C. Precision-recall curve for Phoenix Sepsis Score: Prediction of mortality (horizontal dark blue line indicates proportional mortality). D. Precision-recall curve for Phoenix Sepsis Score: Prediction of mortality or ventilation ≥30 days from time of transport (horizontal light blue line indicates proportional mortality or ventilation ≥30 days).



SUPPLEMENTAL DIGITAL CONTENT

Table 1. Components of the Phoenix Sepsis Score.

Variables	0 Points	1 Point	2 Points	3 Points
Respiratory, 0-3 points				
	PaO2:FIO2 ≥400 or SpO2:FIO2 ≥292b	PaO2:FIO2 <400 on any respiratory support or SpO2:FIO2 <292 on any respiratory support	PaO2:FIO2 100-200 and IMV or SpO2:FIO2 148-220 and IMVb	PaO2:FIO2<100 and IMV or SpO2:FIO2 <148 and IMV
Cardiovascular, 0-6 points				
		1 Point each (up to 3)	2 Points each (up to 6)	
	No vasoactive medications	1 Vasoactive medication	≥2 Vasoactive medications	
	Lactate <5 mmol/L	Lactate 5-10.9 mmol/L	Lactate ≥11 mmol/L	
Age based				
	Mean arterial pressure, mmHg			
<1mo	>30	17-30	<17	
1to11mo	>38	25-38	<25	
1to<2y	>43	31-43	<31	
2to<5y	>44	32-44	<32	
5to<12y	>48	36-48	<36	
12to17y	>51	38-51	<38	
Coagulation (0-2 points)				
		1 Point each (maximum 2 points)		
	Platelets ≥100 × 103/μL	Platelets <100 × 103/μL		
	International normalized ratio ≤1.3 D-dimer ≤2 mg/L FEU	International normalized ratio >1.3 D-dimer >2 mg/L FEU		
	Fibrinogen ≥100 mg/dL	Fibrinogen <100 mg/dL		
Neurological (0-2 points)				
	Glasgow Coma Scale score >10; pupils reactive	Glasgow Coma Scale score ≤10	Fixed pupils bilaterally	
Phoenix sepsis criteria				
Sepsis	Suspected infection and Phoenix Sepsis Score ≥2 points			
Septic shock	Sepsis with ≥1 cardiovascular point(s)			

Table 2. Data availability for the variables used in the calculation of the Phoenix Sepsis Score in children with presumed infection (n=444).

Variable	Available (%)	Not available (%)
Respiratory		
PaO2:FiO2 ratio	287 (64.6)	157 (35.4)
SpO2:FiO2 ratio	282 (63.5)	162 (36.5)
Cardiovascular		
Vasoactive medications	444 (100.0)	0 (0.0)
Serum lactate	403 (90.8)	41 (9.2)
Mean arterial blood pressure	421 (94.8)	23 (5.2)
Coagulation		
Platelet count	249 (56.1)	195 (43.9)
International normalised ratio	0 (0.0)	444 (100.0)
D-dimer	0 (0.0)	444 (100.0)
Fibrinogen	0 (0.0)	444 (100.0)
Neurological		
Glasgow coma scale	343 (77.3)	101 (22.7)
Pupillary reaction	388 (87.4)	56 (12.6)

Table 3. Phoenix sepsis scores and organ-specific subscores by sepsis diagnosis based on PSS criteria in children with suspected/confirmed infection.

	All	PSS ≥2 (n=260)	PSS<2 (n=184)
Total Score			
Median score, IQR	2 (1,3)		
0	47 (10.6)	0	47 (25.5)
1	137 (30.9)	0	137 (74.5)
2	75 (16.9)	75 (28.8)	0
3	77 (17.3)	77 (29.6)	0
4	53 (11.9)	53 (20.4)	0
5	31 (7.0)	31 (11.9)	0
>5	24 (5.4)	24 (9.3)	0
Respiratory subscore			
Median score, IQR	1 (0,2)		
0	95 (21.4)	24 (9.2)	71 (38.6)
1	61 (13.7)	39 (15.0)	22 (11.9)
2	70 (15.8)	70 (26.9)	0
3	62 (13.9)	62 (23.9)	0
Missing	156 (35.1)	65 (25.0)	91 (49.5)
Cardiovascular subscore			
Median score, IQR	0 (0,2)		
0	255 (57.4)	83 (31.9)	172 (93.5)
1	71 (16.0)	59 (22.7)	12 (6.5)
2	78 (17.6)	78 (30.0)	0
3	34 (7.7)	34 (13.1)	0
4	4 (0.9)	4 (1.5)	0
5	1 (0.2)	1 (0.4)	0
6	1 (0.2)	1 (0.4)	0
Coagulation score			
Median score, IQR	0 (0,0)		
0	237 (53.4)	138 (53.1)	99 (53.8)
1	12 (2.7)	10 (3.6)	2 (1.1)
Missing	195 (43.9)	112 (43.1)	83 (45.1)
Neurological score			
Median score, IQR	1 (0,1)		
0	171 (38.5)	88 (33.8)	83 (45.1)
1	268 (60.4)	167 (64.2)	101 (54.9)
2	5 (1.1)	5 (1.9)	0 (0.0)

Figure 1. Strengthening the reporting of observational studies in epidemiology (STROBE) flowchart for study recruitment.

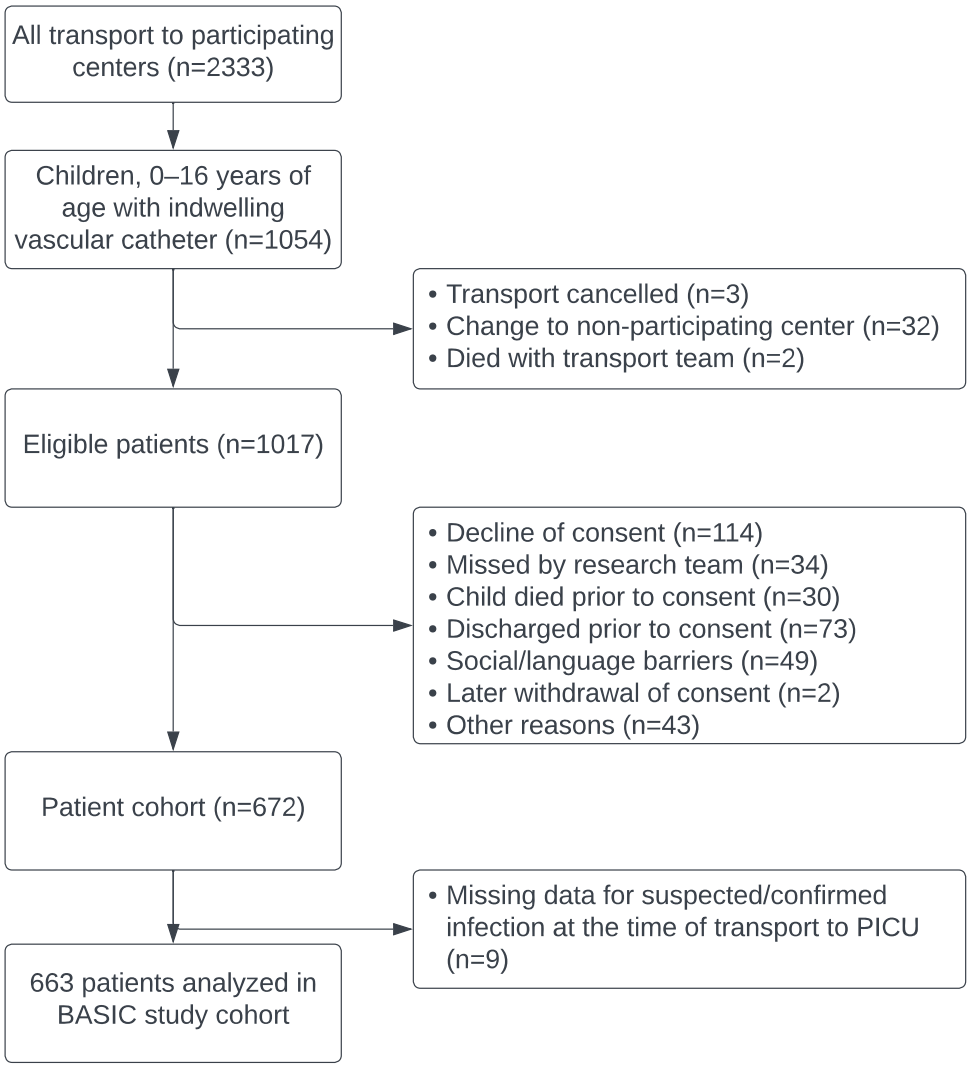


Figure 2. Positive predictive values (PPV, %) for levels of Phoenix sepsis score. A. PPV for prediction of mortality within 30 days of transport by Phoenix Sepsis Score (dashed lines show 95% CI about the PPV). D. PPV for prediction of mortality or ventilation ≥30 days from time of transport by Phoenix Sepsis Score (dashed lines show 95% CI about the PPV).

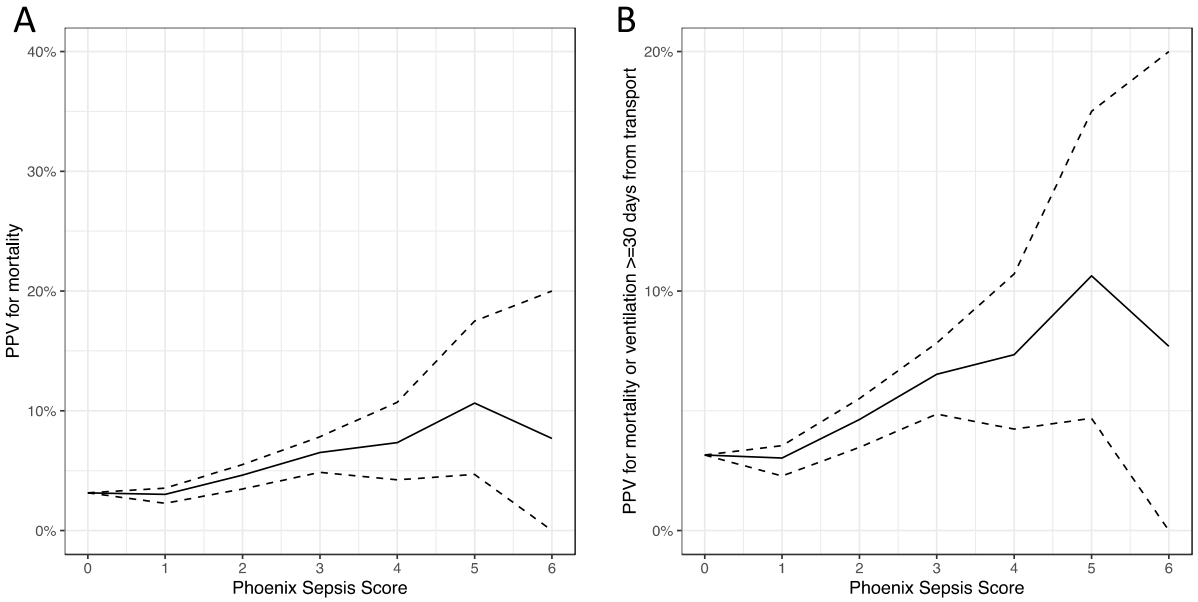
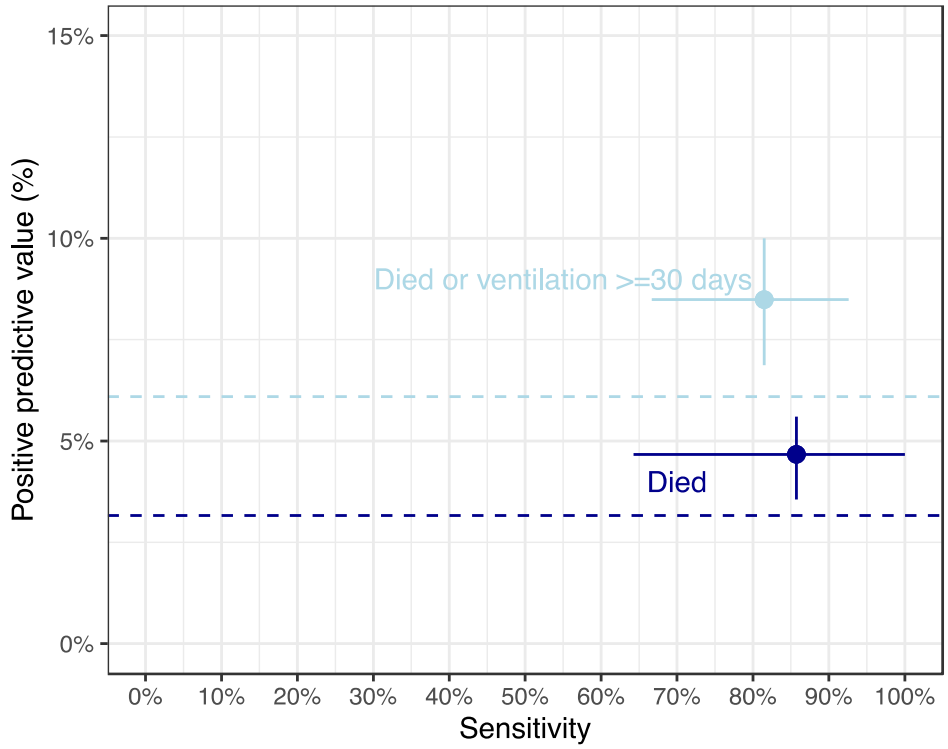


Figure S3. Positive predictive values (PPV) and sensitivity for mortality (dark blue) or mortality or ventilation ≥30 days (light blue), with 95% CI for both PPV and sensitivity, for a Phoenix Sepsis Score of 2 in children with suspected/confirmed infection status at time of transport. The horizontal lines represent proportional mortality (dark blue) or mortality or ventilation ≥30 days from time of transport (light blue).



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