**Critical Illness Factors Associated With Long-Term Mortality and Health Related**

**Quality of Life Morbidity Following Community-Acquired Pediatric Septic Shock**

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**eTable 1. Admission Demographics by Survey and Vital Status at Month 3**

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| --- |
| **Patient Characteristic** | **HRQL Survey Status, Month 3** |  | **Subject Vital Status, Month 3** |  |
|  | Overall(N = 389) | Completed(N = 203) | Incomplete (N = 186) | P-value | Alive(N = 346) | Dead(N = 43) | P-value |
|  Age (years) |   |   |   |  0.6582 |   |   |  0.0802 |
|  Median |  6.4 |  6.2 |  6.5 |   |  6.7 |  4.1 |   |
|  [Q1, Q3] |  [1.7, 13.0] |  [1.6, 12.7] |  [1.7, 13.1] |   |  [1.8, 13.1] |  [1.0, 10.7] |   |
|  Sex |   |   |   |  0.1853 |   |   |  0.5173 |
|  Male |  211 (54.2%) |  117 (57.6%) |  94 (50.5%) |   |  190 (54.9%) |  21 (48.8%) |   |
|  Female |  178 (45.8%) |  86 (42.4%) |  92 (49.5%) |   |  156 (45.1%) |  22 (51.2%) |   |
|  Ethnicity |   |   |   |  0.0523 |   |   |  0.0723 |
|  Unknown or Not Reported |  5 (1.3%) |  1 (0.5%) |  4 (2.2%) |   |  2 (0.6%) |  3 (7.0%) |   |
|  Hispanic or Latino |  88 (22.6%) |  38 (18.7%) |  50 (26.9%) |   |  74 (21.4%) |  14 (32.6%) |   |
|  Not Hispanic or Latino |  296 (76.1%) |  164 (80.8%) |  132 (71.0%) |   |  270 (78.0%) |  26 (60.5%) |   |
|  Race |   |   |   |  0.2033 |   |   |  0.0903 |
|  Unknown or not reported |  31 (8.0%) |  18 (8.9%) |  13 (7.0%) |   |  27 (7.8%) |  4 (9.3%) |   |
|  White |  234 (60.2%) |  130 (64.0%) |  104 (55.9%) |   |  211 (61.0%) |  23 (53.5%) |   |
|  Black or African American |  80 (20.6%) |  37 (18.2%) |  43 (23.1%) |   |  73 (21.1%) |  7 (16.3%) |   |
|  Multiracial |  13 (3.3%) |  6 (3.0%) |  7 (3.8%) |   |  9 (2.6%) |  4 (9.3%) |   |
|  Other |  31 (8.0%) |  12 (5.9%) |  19 (10.2%) |   |  26 (7.5%) |  5 (11.6%) |   |
|  Medical complexity algorithm category1 |   |   |   |  0.0114 |   |   |  0.7264 |
|  Missing PHIS |  1 (0.3%) |  0 (0.0%) |  1 (0.5%) |   |  1 (0.3%) |  0 (0.0%) |   |
|  No chronic comorbid conditions |  189 (48.6%) |  85 (41.9%) |  104 (55.9%) |   |  168 (48.6%) |  21 (48.8%) |   |
|  Chronic comorbid conditions (non-complex) |  20 (5.1%) |  14 (6.9%) |  6 (3.2%) |   |  20 (5.8%) |  0 (0.0%) |   |
|  Chronic comorbid conditions (complex) |  179 (46.0%) |  104 (51.2%) |  75 (40.3%) |   |  157 (45.4%) |  22 (51.2%) |   |
|  |
| Abbreviations: PICU, pediatric intensive care unit; HRQL, health-related quality of life; PHIS, Pediatric Health Information System1Medical Complexity Algorithm category was determined using ICD9 and ICD10 diagnostic codes up to three years prior to the sepsis index admission. If no diagnostic codes were identified, subjects were assumed to have no chronic, comorbid conditions. Missing PHIS counts are not included in the p-value calculations.2Wilcoxon rank-sum test3Fisher’s exact test4Cochran-Armitage test for trend |

**eTable 2. Critical Illness Variables by HRQL Survey and Vital Status at Month 3**

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| --- |
| **Illness Severity Measure** | **HRQL Survey Completion at Month 3** |  | **Subject Vital Status at Month 3** |  |
|   | Completed(N = 203) | Incomplete (N = 186) | P-value | Alive(N = 346) | Dead(N = 43) | P-value |
|  **ADMISSION DATA** |   |   |   |   |   |   |
|  PRISM-IV1 |  11.0 [6.0, 16.0] |  11.0 [6.0, 19.0] |  0.4606 |  11.0 [6.0, 16.0] |  13.0 [9.0, 22.0] |  0.0106 |
|  PELOD-2, Day 0 |  8.0 [5.0, 11.0] |  9.0 [6.0, 11.0] |  0.0746 |  8.0 [5.0, 11.0] |  10.0 [7.0, 14.0] |  0.0056 |
|  PELOD-2, First Day2 |  8.0 [6.0, 11.0] |  9.0 [7.0, 12.0] |  0.0056 |  8.0 [6.0, 11.0] |  12.0 [9.0, 15.0] |  <0.0016 |
|  Immunocompromised |  32 (15.8%) |  36 (19.4%) |  0.4237 |  58 (16.8%) |  10 (23.3%) |  0.2907 |
|  PedsQLTM Baseline |   |   |   |  80.6 [67.4, 92.4] |  70.7 [61.9, 85.7] |  0.1086 |
|  FSII-R Baseline |   |   |   |  71.4 [60.7, 85.2] |  67.9 [50.0, 77.7] |  0.4636 |
|  **HOSPITAL DATA** |   |   |   |   |   |   |
|  PedsQLTM CFB at Day 7 |   |   |   |  -17.1 [-41.0, -1.5] |  -10.6 [-42.4, 0.7] |  0.5656 |
|  FSII-R CFB at Day 7 |   |   |   |  -10.7 [-33.8, 3.6] |  -10.7 [-32.1, -7.1] |  0.4666 |
|  PedsQLTM CFB at Day 28 |   |   |   |  -11.1 [-29.2, 5.4] |  10.9 [-29.3, 11.1] |  0.5086 |
|  FSII-R CFB at Day 28 |   |   |   |  0.0 [-10.7, 10.7] |  -28.6 [-28.6, 21.4] |  0.5356 |
|  Sum of PELOD in PICU |  52.0 [29.0, 83.0] |  68.0 [34.0, 105.0] |  0.0056 |  52.5 [30.0, 88.0] |  102.0 [69.0, 179.0] |  <0.0016 |
|  PRBC first transfer (relative to Day 0) |  1.0 [0.0, 3.0] |  1.0 [0.0, 2.0] |  0.9326 |  1.0 [0.0, 3.0] |  1.0 [0.0, 1.5] |  0.0786 |
|  Hospital length of stay (days) |  16.1 [9.7, 25.8] |  15.4 [8.8, 26.8] |  0.6746 |  15.8 [9.5, 25.6] |  15.4 [6.9, 31.9] |  0.5326 |
|  PICU length of stay (days) |  9.1 [5.2, 14.9] |  9.9 [5.8, 17.2] |  0.2586 |  9.1 [5.6, 15.1] |  11.0 [4.9, 20.9] |  0.2316 |
|  Highest VIS in PICU |  10.0 [5.2, 20.0] |  10.0 [5.0, 23.0] |  0.6066 |  10.0 [5.0, 20.0] |  20.0 [8.0, 45.0] |  <0.0016 |
|  Sum of VIS in PICU |  29.0 [11.0, 61.0] |  40.0 [11.2, 101.0] |  0.0596 |  30.0 [10.0, 64.0] |  124.0 [17.1, 259.0] |  <0.0016 |
|  Mechanical ventilator days |  8.0 [4.0, 12.0] |  8.0 [5.0, 15.0] |  0.2326 |  8.0 [4.0, 12.0] |  11.0 [6.0, 21.0] |  00.0206 |
|  Renal replacement therapy in PICU |  14 (6.9%) |  24 (12.9%) |  0.0597 |  24 (6.9%) |  14 (32.6%) |  <0.0017 |
|  ECLS in PICU |  7 (3.4%) |  20 (10.8%) |  0.0057 |  15 (4.3%) |  12 (27.9%) |  <0.0017 |
|  FSS CFB at Day 7 (>0 implies worsening)3 |  4.0 [0.0, 9.0] |  4.0 [0.0, 12.0] |  0.5046 |  3.0 [0.0, 9.0] |  13.0 [5.0, 17.5] |  <0.0016 |
|  POPC CFB at Day 7 (>0 implies worsening)3 |  1.0 [0.0, 2.0] |  1.0 [0.0, 2.0] |  0.0336 |  1.0 [0.0, 2.0] |  2.0 [1.0, 3.0] |  <0.0016 |
|  PCPC CFB at Day 7 (>0 implies worsening)3 |  0.0 [0.0, 1.0] |  0.0 [0.0, 2.5] |  0.0306 |  0.0 [0.0, 1.0] |  2.0 [1.0, 4.0] |  <0.0016 |
|  FSS CFB at Day 28 (>0 implies worsening)3 |  0.0 [0.0, 2.0] |  0.0 [0.0, 3.0] |  0.3696 |  0.0 [0.0, 2.0] |  5.5 [2.0, 14.0] |  <0.0016 |
|  POPC CFB at Day 28 (>0 implies worsening)3 |  0.0 [0.0, 1.0] |  0.0 [0.0, 2.0] |  0.0016 |  0.0 [0.0, 1.0] |  3.0 [1.0, 4.0] |  <0.0016 |
|  PCPC CFB at Day 28 (>0 implies worsening)3 |  0.0 [0.0, 0.0] |  0.0 [0.0, 1.0] |  <.0016 |  0.0 [0.0, 0.0] |  3.0 [1.0, 5.0] |  <0.0016 |
|  FSS outcome at Day 284 |   |   |  0.1597 |   |   |  <0.0017 |
|  Good |  164 (80.8%) |  116 (62.4%) |   |  274 (79.2%) |  6 (14.0%) |   |
|  Poor |  39 (19.2%) |  40 (21.5%) |   |  67 (19.4%) |  12 (27.9%) |   |
|  Unknown |  0 (0.0%) |  30 (16.1%) |   |  5 (1.4%) |  25 (58.1%) |   |
|  PCPC outcome at Day 285 |   |   |  <.0017 |   |   |  <0.0017 |
|  Good |  185 (91.1%) |  135 (72.6%) |   |  310 (89.6%) |  10 (23.3%) |   |
|  Poor |  18 (8.9%) |  46 (24.7%) |   |  32 (9.2%) |  32 (74.4%) |   |
|  Unknown |  0 (0.0%) |  5 (2.7%) |   |  4 (1.2%) |  1 (2.3%) |   |
|  POPC outcome at Day 285 |   |   |  <.0017 |   |   |  <0.0017 |
|  Good |  174 (85.7%) |  125 (67.2%) |   |  289 (83.5%) |  10 (23.3%) |   |
|  Poor |  29 (14.3%) |  56 (30.1%) |   |  53 (15.3%) |  32 (74.4%) |   |
|  Unknown |  0 (0.0%) |  5 (2.7%) |   |  4 (1.2%) |  1 (2.3%) |   |
|  Anisocoria or absence of pupillary response |  21 (10.3%) |  41 (22.0%) |  0.0027 |  38 (11.0%) |  24 (55.8%) |  <0.0017 |
|  Pathologic breathing pattern |  19 (9.4%) |  26 (14.0%) |  0.2047 |  31 (9.0%) |  14 (32.6%) |  <0.0017 |
|  Stereotypic posturing or flaccid posture |  20 (9.9%) |  21 (11.3%) |  0.7417 |  29 (8.4%) |  12 (27.9%) |  <0.0017 |
|  Seizure activity and or abnormal EEG |  41 (20.2%) |  46 (24.7%) |  0.3307 |  68 (19.7%) |  19 (44.2%) |  <0.0017 |
|  New anoxic-ischemic injury on CT/MRI imaging |  10 (4.9%) |  15 (8.1%) |  0.2217 |  14 (4.0%) |  11 (25.6%) |  <0.0017 |
|  Treatment for increased intracranial pressure |  4 (2.0%) |  12 (6.5%) |  0.0387 |  11 (3.2%) |  5 (11.6%) |  0.0237 |
|  Neurologic injury suspected by care provider |  21 (10.3%) |  40 (21.5%) |  0.0037 |  40 (11.6%) |  21 (48.8%) |  <0.0017 |
|  Autonomic storming |  3 (1.5%) |  7 (3.8%) |  0.2047 |  7 (2.0%) |  3 (7.0%) |  0.0877 |
|  Cardiopulmonary arrest or chest compressions |  11 (5.4%) |  26 (14.0%) |  0.0057 |  18 (5.2%) |  19 (44.2%) |  <0.0017 |
|  Any neurologic insult/event |  79 (38.9%) |  90 (48.4%) |  0.0667 |  134 (38.7%) |  35 (81.4%) |  <0.0017 |
|  |

Abbreviations: HRQL, health-related quality of life; PRISM-IV, Pediatric Risk of Mortality score, Version IV; PELOD-2, Pediatric Logistic Organ Dysfunction score, version 2; PedsQLTM, Pediatric Quality of Life inventory; FSII-R, Stein-Jessop Functional Status Scale; PRBC, packed red blood cells; CFB, change from baseline; PICU, pediatric intensive care unit; VIS, Vasoactive-Inotropic Score; ECLS, extracorporeal life support; FSS, Functional Status Scale; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category

1Collected during a modified 6 hour period of 2 hours prior to PICU admission through 4 hours post PICU admission

2Fist day was defined as the day of admission if admission time occurred before 1200 pm or the following day if admission time occurred after 1200 pm

3CFB at Day 7 and Day 28 for PCPC, POPC, and FSS reflect days post PICU admission or hospital discharge whichever occurred first.

4Poor FSS outcome was defined as a score increase of 3 or more from baseline to day 28 or hospital discharge, which ever occurred first.

5Poor PCPC and POPC outcomes were defined as an increase of at least one point from baseline and a score >3 at 28 days or hospital discharge, whichever occurred first.

6Wilcoxon rank-sum test

7Fisher’s exact test

**eTable 3. Admission Demographics By Outcomes at Month 3**

 **Persistent, Severe HRQL Deterioration Poor Outcome**

 **No**

**(N = 176) Yes**

**(N = 27) P-value No**

**(N = 176) Yes**

**(N = 70) P-value**

 **Age (years) 5.0 [1.5, 12.2] 10.7 [4.9, 14.5] 0.0192 5.0 [1.5, 12.2] 7.2 [1.3, 12.9] 0.5812**

 **Female 78 (44.3%) 8 (29.6%) 0.2093 78 (44.3%) 30 (42.9%) 0.8873**

 **Ethnicity 0.6033 0.0563**

 **Hispanic or Latino 32 (18.2%) 6 (22.2%) 32 (18.2%) 20 (28.6%)**

 **Not Hispanic or Latino 143 (81.3%) 21 (77.8%) 143 (81.3%) 47 (67.1%)**

 **Unknown or Not Reported 1 (0.6%) 0 (0.0%) 1 (0.6%) 3 (4.3%)**

 **Race 0.7273 0.2693**

 **White 115 (65.3%) 15 (55.6%) 115 (65.3%) 38 (54.3%)**

 **Black or African American 31 (17.6%) 6 (22.2%) 31 (17.6%) 13 (18.6%)**

 **Multiracial 5 (2.8%) 1 (3.7%) 5 (2.8%) 5 (7.1%)**

 **Other 11 (6.3%) 1 (3.7%) 11 (6.3%) 6 (8.6%)**

 **Unknown or not reported 14 (8.0%) 4 (14.8%) 14 (8.0%) 8 (11.4%)**

 **Medical complexity algorithm category1 0.0404 0.0884**

 **No chronic comorbid conditions 68 (38.6%) 17 (63.0%) 68 (38.6%) 38 (54.3%)**

 **Chronic comorbid conditions (non-complex) 14 (8.0%) 0 (0.0%) 14 (8.0%) 0 (0.0%)**

 **Chronic comorbid conditions (complex) 94 (53.4%) 10 (37.0%) 94 (53.4%) 32 (45.7%)**

**1 Medical complexity algorithm category using diagnosis codes up to three years prior to the LAPSE index admission. If no diagnosis codes were found, subjects are assumed to have no chronic comorbid conditions.**

**2 Wilcoxon rank-sum test.**

**3 Fisher's exact test.**

**4 Cochran-Armitage test for trend.**

|  |
| --- |
| **Patient Characteristic**  | **PSD-HRQL**  |  | **Death or PSD-HRQL** |  |
|   | No(N = 176) | Yes(N = 27) | P-value | No(N = 176) | Yes(N = 70) | P-value |
|  Age (years) |  5.0 [1.5, 12.2] |  10.7 [4.9, 14.5] |  0.0192 |  5.0 [1.5, 12.2] |  7.2 [1.3, 12.9] |  0.5812 |
|  Female |  78 (44.3%) |  8 (29.6%) |  0.2093 |  78 (44.3%) |  30 (42.9%) |  0.8873 |
|  Ethnicity |   |   |  0.6033 |   |   |  0.0563 |
|  Hispanic or Latino |  32 (18.2%) |  6 (22.2%) |   |  32 (18.2%) |  20 (28.6%) |   |
|  Not Hispanic or Latino |  143 (81.3%) |  21 (77.8%) |   |  143 (81.3%) |  47 (67.1%) |   |
|  Unknown or Not Reported |  1 (0.6%) |  0 (0.0%) |   |  1 (0.6%) |  3 (4.3%) |   |
|  Race |   |   |  0.7273 |   |   |  0.2693 |
|  White |  115 (65.3%) |  15 (55.6%) |   |  115 (65.3%) |  38 (54.3%) |   |
|  Black or African American |  31 (17.6%) |  6 (22.2%) |   |  31 (17.6%) |  13 (18.6%) |   |
|  Multiracial |  5 (2.8%) |  1 (3.7%) |   |  5 (2.8%) |  5 (7.1%) |   |
|  Other |  11 (6.3%) |  1 (3.7%) |   |  11 (6.3%) |  6 (8.6%) |   |
|  Unknown or not reported |  14 (8.0%) |  4 (14.8%) |   |  14 (8.0%) |  8 (11.4%) |   |
|  Medical complexity algorithm category1 |   |   |  0.0404 |   |   |  0.0884 |
|  No chronic comorbid conditions |  68 (38.6%) |  17 (63.0%) |   |  68 (38.6%) |  38 (54.3%) |   |
|  Chronic comorbid conditions (non-complex) |  14 (8.0%) |  0 (0.0%) |   |  14 (8.0%) |  0 (0.0%) |   |
|  Chronic comorbid conditions (complex) |  94 (53.4%) |  10 (37.0%) |   |  94 (53.4%) |  32 (45.7%) |   |
|  |

Abbreviations: PICU, intensive care unit; HRQL, health-related quality of life; PSD, persistent, severe deterioration defined as PedsQLTM or FSII-R assessment at Month 3 > 25% below baseline value; Poor outcome was defined as death or PSD HRQL.

1Medical Complexity Algorithm category was determined using ICD9 and ICD10 diagnostic codes up to three years prior to the sepsis index admission. If no diagnostic codes were identified, subjects were assumed to have no chronic, comorbid conditions.

2Wilcoxon rank-sum test

3Fisher’s exact test

4Cochran-Armitage test for trend

**eTable 4. Univariable Analyses With Mortality at Month 3 as Outcome**

|  |
| --- |
|  **Patient Characteristic** | **Month 3 Mortality** |
|   | % Missing | Overall(N = 389) | Dead(N = 43) | Alive(N = 346) | Odds ratio(95% CI) | P-value |
|  **Age (years)** |  0% |  6.4 [1.7, 13.0] |  4.1 [1.0, 10.7] |  6.7 [1.8, 13.1] |  0.95 (0.89, 1.01) |  0.079 |
|  **Sex** |  0% |   |   |   |   |  0.452 |
|  Male |   |  211 (54.2%) |  21 (48.8%) |  190 (54.9%) |  0.78 (0.41, 1.48) |   |
|  Female |   |  178 (45.8%) |  22 (51.2%) |  156 (45.1%) |  Reference |   |
|  **Ethnicity** |  1% |   |   |   |   |  0.066 |
|  Unknown or Not Reported |   |  5 (1.3%) |  3 (7.0%) |  2 (0.6%) |   |   |
|  Hispanic or Latino |   |  88 (22.6%) |  14 (32.6%) |  74 (21.4%) |  1.96 (0.95, 3.90) |   |
|  Not Hispanic or Latino |   |  296 (76.1%) |  26 (60.5%) |  270 (78.0%) |  Reference |   |
|  **Race** |  8% |   |   |   |   |  0.156 |
|  Unknown or not reported |   |  31 (8.0%) |  4 (9.3%) |  27 (7.8%) |   |   |
|  White |   |  234 (60.2%) |  23 (53.5%) |  211 (61.0%) |  Reference |   |
|  Black or African American |   |  80 (20.6%) |  7 (16.3%) |  73 (21.1%) |  0.88 (0.34, 2.04) |   |
|  Multiracial |   |  13 (3.3%) |  4 (9.3%) |  9 (2.6%) |  4.08 (1.04, 13.63) |   |
|  Other |   |  31 (8.0%) |  5 (11.6%) |  26 (7.5%) |  1.76 (0.56, 4.73) |   |
|  **Medical complexity algorithm category** |  0% |   |   |   |   |  0.484 |
|  Missing PHIS |   |  1 (0.3%) |  0 (0.0%) |  1 (0.3%) |   |   |
|  None/Non-complex |   |  209 (53.7%) |  21 (48.8%) |  188 (54.3%) |  Reference |   |
|  Complex |   |  179 (46.0%) |  22 (51.2%) |  157 (45.4%) |  1.25 (0.66, 2.38) |   |
|  **PRISM** |  0% |  11.0 [6.0, 17.0] |  13.0 [9.0, 22.0] |  11.0 [6.0, 16.0] |  1.05 (1.01, 1.08) |  0.018 |
|  **PELOD, First Day** |  0% |  9.0 [6.0, 11.0] |  12.0 [9.0, 15.0] |  8.0 [6.0, 11.0] |  1.23 (1.14, 1.34) |  <0.001 |
|  **Immunocompromised** |  0% |   |   |   |   |  0.307 |
|  No |   |  321 (82.5%) |  33 (76.7%) |  288 (83.2%) |  Reference |   |
|  Yes |   |  68 (17.5%) |  10 (23.3%) |  58 (16.8%) |  1.50 (0.67, 3.13) |   |
|  **Sum of PELOD in PICU** |  0% |  57.0 [32.0, 94.0] |  102.0 [69.0, 179.0] |  52.5 [30.0, 88.0] |  1.01 (1.01, 1.01) |  <0.001 |
|  **PRBC first transfusion** |  51% |  1.0 [0.0, 2.0] |  1.0 [0.0, 1.5] |  1.0 [0.0, 3.0] |  0.86 (0.69, 1.00) |  0.058 |
|  **Hospital length of stay (days)** |  0% |  15.7 [9.2, 26.0] |  15.4 [6.9, 31.9] |  15.8 [9.5, 25.6] |  1.00 (0.98, 1.01) |  0.677 |
|  **PICU length of stay (days)** |  0% |  9.4 [5.6, 15.4] |  11.0 [4.9, 20.9] |  9.1 [5.6, 15.1] |  1.01 (0.99, 1.02) |  0.306 |
|  **Highest VIS in PICU** |  0% |  10.0 [5.0, 21.0] |  20.0 [8.0, 45.0] |  10.0 [5.0, 20.0] |  1.03 (1.01, 1.04) |  <0.001 |
|  **Sum of VIS in PICU** |  0% |  31.0 [11.0, 75.0] |  124.0 [17.1, 259.0] |  30.0 [10.0, 64.0] |  1.01 (1.00, 1.01) |  <0.001 |
|  **Mechanical ventilator days** |  0% |  8.0 [4.0, 13.0] |  11.0 [6.0, 21.0] |  8.0 [4.0, 12.0] |  1.05 (1.01, 1.09) |  0.012 |
|  **Renal replacement therapy in PICU** |  0% |   |   |   |   |  <0.001 |
|  No |   |  351 (90.2%) |  29 (67.4%) |  322 (93.1%) |  Reference |   |
|  Yes |   |  38 (9.8%) |  14 (32.6%) |  24 (6.9%) |  6.48 (2.98, 13.80) |   |
|  **ECMO in PICU** |  0% |   |   |   |   |  <0.001 |
|  No |   |  362 (93.1%) |  31 (72.1%) |  331 (95.7%) |  Reference |   |
|  Yes |   |  27 (6.9%) |  12 (27.9%) |  15 (4.3%) |  8.54 (3.63, 19.89) |   |
|  **FSS CFB at Day 7 (>0 implies worsening)** |  4% |  4.0 [0.0, 10.0] |  13.0 [5.0, 17.5] |  3.0 [0.0, 9.0] |  1.13 (1.08, 1.19) |  <0.001 |
|  **PCPC CFB at Day 7 (>0 implies worsening)** |  1% |  0.0 [0.0, 2.0] |  2.0 [1.0, 4.0] |  0.0 [0.0, 1.0] |  2.03 (1.63, 2.55) |  <0.001 |
|  **POPC CFB at Day 7 (>0 implies worsening)** |  1% |  1.0 [0.0, 2.0] |  2.0 [1.0, 3.0] |  1.0 [0.0, 2.0] |  1.78 (1.42, 2.25) |  <0.001 |
|  **Anisocoria or absence of pupillary response** |  0% |   |   |   |   |  <0.001 |
|  No |   |  327 (84.1%) |  19 (44.2%) |  308 (89.0%) |  Reference |   |
|  Yes |   |  62 (15.9%) |  24 (55.8%) |  38 (11.0%) |  10.24 (5.17, 20.66) |   |
|  **Pathologic breathing pattern** |  0% |   |   |   |   |  <0.001 |
|  No |   |  344 (88.4%) |  29 (67.4%) |  315 (91.0%) |  Reference |   |
|  Yes |   |  45 (11.6%) |  14 (32.6%) |  31 (9.0%) |  4.91 (2.31, 10.16) |   |
|  **Stereotypic posturing or flaccid posture** |  0% |   |   |   |   |  <0.001 |
|  No |   |  348 (89.5%) |  31 (72.1%) |  317 (91.6%) |  Reference |   |
|  Yes |   |  41 (10.5%) |  12 (27.9%) |  29 (8.4%) |  4.23 (1.91, 8.98) |   |
|  **Seizure activity and or abnormal EEG** |  0% |   |   |   |   |  <0.001 |
|  No |   |  302 (77.6%) |  24 (55.8%) |  278 (80.3%) |  Reference |   |
|  Yes |   |  87 (22.4%) |  19 (44.2%) |  68 (19.7%) |  3.24 (1.66, 6.24) |   |
|  **New anoxic-ischemic injury on CT/MRI imaging** |  0% |   |   |   |   |  <0.001 |
|  No |   |  364 (93.6%) |  32 (74.4%) |  332 (96.0%) |  Reference |   |
|  Yes |   |  25 (6.4%) |  11 (25.6%) |  14 (4.0%) |  8.15 (3.37, 19.45) |   |
|  **Treatment for increased intracranial pressure** |  0% |   |   |   |   |  0.025 |
|  No |   |  373 (95.9%) |  38 (88.4%) |  335 (96.8%) |  Reference |   |
|  Yes |   |  16 (4.1%) |  5 (11.6%) |  11 (3.2%) |  4.01 (1.21, 11.66) |   |
|  **Neurologic injury suspected by care provider** |  0% |   |   |   |   |  <0.001 |
|  No |   |  328 (84.3%) |  22 (51.2%) |  306 (88.4%) |  Reference |   |
|  Yes |   |  61 (15.7%) |  21 (48.8%) |  40 (11.6%) |  7.30 (3.69, 14.53) |   |
|  **Autonomic storming** |  0% |   |   |   |   |  0.098 |
|  No |   |  379 (97.4%) |  40 (93.0%) |  339 (98.0%) |  Reference |   |
|  Yes |   |  10 (2.6%) |  3 (7.0%) |  7 (2.0%) |  3.63 (0.76, 13.64) |   |
|  **Cardiopulmonary arrest or chest compressions** |  0% |   |   |   |   |  <0.001 |
|  No |   |  352 (90.5%) |  24 (55.8%) |  328 (94.8%) |  Reference |   |
|  Yes |   |  37 (9.5%) |  19 (44.2%) |  18 (5.2%) |  14.43 (6.73, 31.43) |   |
|  **Any neurologic insult** |  0% |   |   |   |   |  <0.001 |
|  No |   |  220 (56.6%) |  8 (18.6%) |  212 (61.3%) |  Reference |   |
|  Yes |   |  169 (43.4%) |  35 (81.4%) |  134 (38.7%) |  6.92 (3.27, 16.46) |   |
| Abbreviations: PSD HRQL, persistent, severe deterioration (> 25% below baseline) in health-related quality of life; PRISM-IV, Pediatric Risk of Mortality score, version IV; PELOD-2, Pediatric Logistic Organ Dysfunction score, version 2; PRBC, packed red blood cells; CFB, change from baseline; PICU, pediatric intensive care unit; VIS, Vasoactive-Inotropic Score; EEG, electroencephalogram; CT/MRI, computerized tomography/magnetic resonance imaging; FSS, Functional Status Scale; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category. PRBC first transfusion is relative to Day 0. Results are based on univariable models. |

**eTable 5. Univariable Analyses With PSD-HRQL at Month 3 as Outcome**

|  |
| --- |
|  **Patient Characteristic** | **Persistent, Severe HRQL Deterioration at Month 3** |
|   | % Missing | Overall(N = 203) | No(N = 176) | Yes(N = 27) | Odds ratio(95% CI) | P-value |
|  **Age (years)** |  0% |  6.2 [1.6, 12.7] |  5.0 [1.5, 12.2] |  10.7 [4.9, 14.5] |  1.09 (1.02, 1.18) |  0.014 |
|  **Sex** |  0% |   |   |   |   |  0.144 |
|  Male |   |  117 (57.6%) |  98 (55.7%) |  19 (70.4%) |  1.89 (0.81, 4.79) |   |
|  Female |   |  86 (42.4%) |  78 (44.3%) |  8 (29.6%) |  Reference |   |
|  **Ethnicity** |  0% |   |   |   |   |  0.632 |
|  Unknown or Not Reported |   |  1 (0.5%) |  1 (0.6%) |  0 (0.0%) |   |   |
|  Hispanic or Latino |   |  38 (18.7%) |  32 (18.2%) |  6 (22.2%) |  1.28 (0.44, 3.26) |   |
|  Not Hispanic or Latino |   |  164 (80.8%) |  143 (81.3%) |  21 (77.8%) |  Reference |   |
|  **Race** |  9% |   |   |   |   |  0.839 |
|  Unknown or not reported |   |  18 (8.9%) |  14 (8.0%) |  4 (14.8%) |   |   |
|  White |   |  130 (64.0%) |  115 (65.3%) |  15 (55.6%) |  Reference |   |
|  Black or African American |   |  37 (18.2%) |  31 (17.6%) |  6 (22.2%) |  1.48 (0.50, 3.99) |   |
|  Multiracial |   |  6 (3.0%) |  5 (2.8%) |  1 (3.7%) |  1.53 (0.08, 10.39) |   |
|  Other |   |  12 (5.9%) |  11 (6.3%) |  1 (3.7%) |  0.70 (0.04, 3.99) |   |
|  **Medical complexity algorithm category** |  0% |   |   |   |   |  0.112 |
|  None/Non-complex |   |  99 (48.8%) |  82 (46.6%) |  17 (63.0%) |  Reference |   |
|  Complex |   |  104 (51.2%) |  94 (53.4%) |  10 (37.0%) |  0.51 (0.22, 1.17) |   |
|  **PRISM** |  0% |  11.0 [6.0, 16.0] |  11.0 [6.0, 16.0] |  11.0 [6.0, 19.0] |  1.04 (0.99, 1.09) |  0.111 |
|  **PELOD, First Day** |  0% |  8.0 [6.0, 11.0] |  8.0 [6.0, 10.0] |  9.0 [6.0, 14.0] |  1.14 (1.02, 1.27) |  0.021 |
|  **Immunocompromised** |  0% |   |   |   |   |  0.459 |
|  No |   |  171 (84.2%) |  147 (83.5%) |  24 (88.9%) |  Reference |   |
|  Yes |   |  32 (15.8%) |  29 (16.5%) |  3 (11.1%) |  0.63 (0.14, 1.97) |   |
|  **Sum of PELOD in PICU** |  0% |  52.0 [29.0, 83.0] |  45.5 [27.0, 74.5] |  72.0 [52.0, 178.0] |  1.01 (1.01, 1.02) |  <0.001 |
|  **PRBC first transfusion**  |  53% |  1.0 [0.0, 3.0] |  1.0 [0.0, 2.5] |  1.0 [0.0, 5.0] |  1.01 (0.86, 1.14) |  0.858 |
|  **Hospital length of stay (days)** |  0% |  16.1 [9.7, 25.8] |  15.0 [9.2, 23.8] |  28.0 [19.8, 57.9] |  1.01 (1.00, 1.02) |  0.012 |
|  **PICU length of stay (days)** |  0% |  9.1 [5.2, 14.9] |  8.1 [4.9, 13.8] |  14.5 [8.7, 25.4] |  1.04 (1.02, 1.06) |  <0.001 |
|  **Highest VIS in PICU** |  0% |  10.0 [5.2, 20.0] |  10.0 [5.0, 20.0] |  13.0 [8.0, 25.0] |  1.02 (1.00, 1.04) |  0.029 |
|  **Sum of VIS in PICU** |  0% |  29.0 [11.0, 61.0] |  25.0 [8.0, 57.0] |  43.0 [27.0, 130.0] |  1.01 (1.00, 1.01) |  0.004 |
|  **Mechanical ventilator days** |  0% |  8.0 [4.0, 12.0] |  7.0 [4.0, 11.5] |  10.0 [7.0, 24.0] |  1.07 (1.02, 1.12) |  0.005 |
|  **Renal replacement therapy in PICU** |  0% |   |   |   |   |  0.117 |
|  No |   |  189 (93.1%) |  166 (94.3%) |  23 (85.2%) |  Reference |   |
|  Yes |   |  14 (6.9%) |  10 (5.7%) |  4 (14.8%) |  2.89 (0.74, 9.44) |   |
|  **Extracorporeal life support** |  0% |   |   |   |   |  0.279 |
|  No |   |  196 (96.6%) |  171 (97.2%) |  25 (92.6%) |  Reference |   |
|  Yes |   |  7 (3.4%) |  5 (2.8%) |  2 (7.4%) |  2.74 (0.38, 13.46) |   |
|  **FSS CFB at Day 7 (>0 implies worsening)** |  1% |  4.0 [0.0, 9.0] |  3.0 [0.0, 8.0] |  7.5 [4.0, 14.0] |  1.13 (1.05, 1.21) |  <0.001 |
|  **PCPC CFB at Day 7 (>0 implies worsening)** |  0% |  0.0 [0.0, 1.0] |  0.0 [0.0, 1.0] |  1.0 [0.0, 2.0] |  1.48 (1.05, 2.06) |  0.027 |
|  **POPC CFB at Day 7 (>0 implies worsening)** |  0% |  1.0 [0.0, 2.0] |  0.0 [0.0, 1.0] |  1.0 [0.0, 3.0] |  1.63 (1.19, 2.26) |  0.003 |
|  **Anisocoria or absence of pupillary response** |  0% |   |   |   |   |  0.165 |
|  No |   |  182 (89.7%) |  160 (90.9%) |  22 (81.5%) |  Reference |   |
|  Yes |   |  21 (10.3%) |  16 (9.1%) |  5 (18.5%) |  2.27 (0.69, 6.48) |   |
|  **Pathologic breathing pattern** |  0% |   |   |   |   |  0.743 |
|  No |   |  184 (90.6%) |  160 (90.9%) |  24 (88.9%) |  Reference |   |
|  Yes |   |  19 (9.4%) |  16 (9.1%) |  3 (11.1%) |  1.25 (0.28, 4.11) |   |
|  **Stereotypic posturing or flaccid posture** |  0% |   |   |   |   |  0.816 |
|  No |   |  183 (90.1%) |  159 (90.3%) |  24 (88.9%) |  Reference |   |
|  Yes |   |  20 (9.9%) |  17 (9.7%) |  3 (11.1%) |  1.17 (0.26, 3.82) |   |
|  **Seizure activity and or abnormal EEG** |  0% |   |   |   |   |  0.440 |
|  No |   |  162 (79.8%) |  139 (79.0%) |  23 (85.2%) |  Reference |   |
|  Yes |   |  41 (20.2%) |  37 (21.0%) |  4 (14.8%) |  0.65 (0.18, 1.83) |   |
|  **New anoxic-ischemic injury on CT/MRI imaging** |  0% |   |   |   |   |  0.156 |
|  No |   |  193 (95.1%) |  169 (96.0%) |  24 (88.9%) |  Reference |   |
|  Yes |   |  10 (4.9%) |  7 (4.0%) |  3 (11.1%) |  3.02 (0.62, 11.68) |   |
|  **Treatment for increased intracranial pressure** |  0% |   |   |   |   |  0.074 |
|  No |   |  199 (98.0%) |  174 (98.9%) |  25 (92.6%) |  Reference |   |
|  Yes |   |  4 (2.0%) |  2 (1.1%) |  2 (7.4%) |  6.96 (0.81, 60.13) |   |
|  **Neurologic injury suspected by care provider** |  0% |   |   |   |   |  0.049 |
|  No |   |  182 (89.7%) |  161 (91.5%) |  21 (77.8%) |  Reference |   |
|  Yes |   |  21 (10.3%) |  15 (8.5%) |  6 (22.2%) |  3.07 (1.00, 8.49) |   |
|  **Autonomic storming** |  0% |   |   |   |   |  0.031 |
|  No |   |  200 (98.5%) |  175 (99.4%) |  25 (92.6%) |  Reference |   |
|  Yes |   |  3 (1.5%) |  1 (0.6%) |  2 (7.4%) |  14.00 (1.30, 307.58) |   |
|  **Cardiopulmonary arrest or chest compressions** |  0% |   |   |   |   |  0.639 |
|  No |   |  192 (94.6%) |  167 (94.9%) |  25 (92.6%) |  Reference |   |
|  Yes |   |  11 (5.4%) |  9 (5.1%) |  2 (7.4%) |  1.48 (0.22, 6.19) |   |
|  **Any neurologic sign/event** |  0% |   |   |   |   |  0.295 |
|  No |   |  124 (61.1%) |  110 (62.5%) |  14 (51.9%) |  Reference |   |
|  Yes |   |  79 (38.9%) |  66 (37.5%) |  13 (48.1%) |  1.55 (0.68, 3.51) |   |
|  |

Abbreviations: PSD-HRQL, persistent, serious deterioration (> 25% below baseline) in health-related quality of life; PRISM, Pediatric Risk of Mortality score, version IV; PELOD, Pediatric Logistic Organ Dysfunction score, version 2; PRBC, packed red blood cells; CFB, change from baseline; PICU, pediatric intensive care unit; VIS, Vasoactive-Inotropic Score; EEG, electroencephalogram; CT/MRI, computerized tomography/magnetic resonance imaging; FSS, Functional Status Scale; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category. PRBC first transfusion is relative to Day 0. Results are based on univariable models.

**eTable 6. Univariable Analyses With Mortality or PSD-HRQL at Month 3 as Outcome**

|  |
| --- |
|  **Patient Characteristic** | **Mortality or PSD-HRQL at Month 3** |
|   | % Missing | Overall(N = 246) | No(N = 176) | Yes(N = 70) | Odds Ratio(95% CI) | P-value |
|  **Age (years)** |  0% |  5.4 [1.5, 12.3] |  5.0 [1.5, 12.2] |  7.2 [1.3, 12.9] |  1.02 (0.97, 1.07) |  0.486 |
|  **Sex** |  0% |   |   |   |   |  0.835 |
|  Male |   |  138 (56.1%) |  98 (55.7%) |  40 (57.1%) |  1.06 (0.61, 1.87) |   |
|  Female |   |  108 (43.9%) |  78 (44.3%) |  30 (42.9%) |  Reference |   |
|  **Ethnicity** |  2% |   |   |   |   |  0.055 |
|  Unknown or Not Reported |   |  4 (1.6%) |  1 (0.6%) |  3 (4.3%) |   |   |
|  Hispanic or Latino |   |  52 (21.1%) |  32 (18.2%) |  20 (28.6%) |  1.90 (0.98, 3.62) |   |
|  Not Hispanic or Latino |   |  190 (77.2%) |  143 (81.3%) |  47 (67.1%) |  Reference |   |
|  **Race** |  9% |   |   |   |   |  0.334 |
|  Unknown or not reported |   |  22 (8.9%) |  14 (8.0%) |  8 (11.4%) |   |   |
|  White |   |  153 (62.2%) |  115 (65.3%) |  38 (54.3%) |  Reference |   |
|  Black or African American |   |  44 (17.9%) |  31 (17.6%) |  13 (18.6%) |  1.27 (0.59, 2.63) |   |
|  Multiracial |   |  10 (4.1%) |  5 (2.8%) |  5 (7.1%) |  3.03 (0.80, 11.43) |   |
|  Other |   |  17 (6.9%) |  11 (6.3%) |  6 (8.6%) |  1.65 (0.54, 4.65) |   |
|  **Medical complexity algorithm category** |  0% |   |   |   |   |  0.276 |
|  None/Non-complex |   |  120 (48.8%) |  82 (46.6%) |  38 (54.3%) |  Reference |   |
|  Complex |   |  126 (51.2%) |  94 (53.4%) |  32 (45.7%) |  0.73 (0.42, 1.28) |   |
|  **PRISM-IV** |  0% |  11.0 [6.0, 17.0] |  11.0 [6.0, 16.0] |  12.0 [7.0, 21.0] |  1.05 (1.02, 1.09) |  0.005 |
|  **PELOD-2, First Day** |  0% |  9.0 [6.0, 12.0] |  8.0 [6.0, 10.0] |  11.0 [7.0, 14.0] |  1.21 (1.12, 1.32) |  <0.001 |
|  **Immunocompromised** |  0% |   |   |   |   |  0.696 |
|  No |   |  204 (82.9%) |  147 (83.5%) |  57 (81.4%) |  Reference |   |
|  Yes |   |  42 (17.1%) |  29 (16.5%) |  13 (18.6%) |  1.16 (0.55, 2.34) |   |
|  **Sum of PELOD-2 in PICU** |  0% |  57.5 [31.0, 96.0] |  45.5 [27.0, 74.5] |  91.5 [57.0, 178.0] |  1.01 (1.01, 1.02) |  <0.001 |
|  **PRBC first transfusion** |  48% |  1.0 [0.0, 2.0] |  1.0 [0.0, 2.5] |  1.0 [0.0, 2.0] |  0.96 (0.84, 1.06) |  0.423 |
|  **Hospital length of stay (days)** |  0% |  16.0 [9.2, 26.7] |  15.0 [9.2, 23.8] |  21.3 [9.5, 47.9] |  1.01 (1.00, 1.02) |  0.069 |
|  **PICU length of stay (days)** |  0% |  9.3 [5.2, 15.1] |  8.1 [4.9, 13.8] |  12.7 [7.9, 24.2] |  1.03 (1.01, 1.05) |  <0.001 |
|  **Highest VIS in PICU** |  0% |  12.0 [6.0, 23.0] |  10.0 [5.0, 20.0] |  18.8 [8.0, 30.0] |  1.03 (1.01, 1.04) |  <0.001 |
|  **Sum of VIS in PICU** |  0% |  32.3 [12.8, 93.5] |  25.0 [8.0, 57.0] |  85.5 [25.0, 226.5] |  1.01 (1.00, 1.01) |  <0.001 |
|  **Mechanical ventilator days** |  0% |  8.0 [4.0, 13.0] |  7.0 [4.0, 11.5] |  10.5 [6.0, 21.0] |  1.06 (1.03, 1.10) |  <0.001 |
|  **Renal replacement therapy**  |  0% |   |   |   |   |  <0.001 |
|  No |   |  218 (88.6%) |  166 (94.3%) |  52 (74.3%) |  Reference |   |
|  Yes |   |  28 (11.4%) |  10 (5.7%) |  18 (25.7%) |  5.75 (2.54, 13.68) |   |
|  **Extracorporeal life support** |  0% |   |   |   |   |  <0.001 |
|  No |   |  227 (92.3%) |  171 (97.2%) |  56 (80.0%) |  Reference |   |
|  Yes |   |  19 (7.7%) |  5 (2.8%) |  14 (20.0%) |  8.55 (3.12, 27.42) |   |
|  **FSS CFB at Day 7 (>0 implies worsening)** |  5% |  5.0 [0.0, 10.0] |  3.0 [0.0, 8.0] |  10.5 [4.0, 16.0] |  1.15 (1.10, 1.22) |  <0.001 |
|  **PCPC CFB at Day 7 (>0 implies worsening)** |  0% |  1.0 [0.0, 2.0] |  0.0 [0.0, 1.0] |  2.0 [0.0, 3.0] |  1.98 (1.59, 2.52) |  <0.001 |
|  **POPC CFB at Day 7 (>0 implies worsening)** |  0% |  1.0 [0.0, 2.0] |  0.0 [0.0, 1.0] |  2.0 [1.0, 3.0] |  1.80 (1.45, 2.25) |  <0.001 |
|  **Anisocoria or absence of pupillary response** |  0% |   |   |   |   |  <0.001 |
|  No |   |  201 (81.7%) |  160 (90.9%) |  41 (58.6%) |  Reference |   |
|  Yes |   |  45 (18.3%) |  16 (9.1%) |  29 (41.4%) |  7.07 (3.56, 14.53) |   |
|  **Pathologic breathing pattern** |  0% |   |   |   |   |  0.003 |
|  No |   |  213 (86.6%) |  160 (90.9%) |  53 (75.7%) |  Reference |   |
|  Yes |   |  33 (13.4%) |  16 (9.1%) |  17 (24.3%) |  3.21 (1.51, 6.85) |   |
|  **Stereotypic posturing or flaccid posture** |  0% |   |   |   |   |  0.017 |
|  No |   |  214 (87.0%) |  159 (90.3%) |  55 (78.6%) |  Reference |   |
|  Yes |   |  32 (13.0%) |  17 (9.7%) |  15 (21.4%) |  2.55 (1.18, 5.46) |   |
|  **Seizure activity and or abnormal EEG** |  0% |   |   |   |   |  0.056 |
|  No |   |  186 (75.6%) |  139 (79.0%) |  47 (67.1%) |  Reference |   |
|  Yes |   |  60 (24.4%) |  37 (21.0%) |  23 (32.9%) |  1.84 (0.99, 3.40) |   |
|  **New anoxic-ischemic injury on CT/MRI imaging** |  0% |   |   |   |   |  <0.001 |
|  No |   |  225 (91.5%) |  169 (96.0%) |  56 (80.0%) |  Reference |   |
|  Yes |   |  21 (8.5%) |  7 (4.0%) |  14 (20.0%) |  6.04 (2.39, 16.63) |   |
|  **Treatment for increased intracranial pressure** |  0% |   |   |   |   |  0.002 |
|  No |   |  237 (96.3%) |  174 (98.9%) |  63 (90.0%) |  Reference |   |
|  Yes |   |  9 (3.7%) |  2 (1.1%) |  7 (10.0%) |  9.67 (2.27, 66.03) |   |
|  **Neurologic injury suspected by care provider** |  0% |   |   |   |   |  <0.001 |
|  No |   |  204 (82.9%) |  161 (91.5%) |  43 (61.4%) |  Reference |   |
|  Yes |   |  42 (17.1%) |  15 (8.5%) |  27 (38.6%) |  6.74 (3.34, 14.08) |   |
|  **Autonomic storming** |  0% |   |   |   |   |  0.005 |
|  No |   |  240 (97.6%) |  175 (99.4%) |  65 (92.9%) |  Reference |   |
|  Yes |   |  6 (2.4%) |  1 (0.6%) |  5 (7.1%) |  13.46 (2.12, 260.36) |   |
|  **Cardiopulmonary arrest or chest compressions** |  0% |   |   |   |   |  <0.001 |
|  No |   |  216 (87.8%) |  167 (94.9%) |  49 (70.0%) |  Reference |   |
|  Yes |   |  30 (12.2%) |  9 (5.1%) |  21 (30.0%) |  7.95 (3.52, 19.34) |   |
|  **Any neurologic sign/event** |  0% |   |   |   |   |  <0.001 |
|  No |   |  132 (53.7%) |  110 (62.5%) |  22 (31.4%) |  Reference |   |
|  Yes |   |  114 (46.3%) |  66 (37.5%) |  48 (68.6%) |  3.64 (2.04, 6.65) |   |
|  |
|  |

Abbreviations: PSD-HRQL, persistent, serious deterioration of health-related quality of life > 25% below baseline; PRISM-IV, Pediatric Risk of Mortality score, version IV; PELOD-2, Pediatric Logistic Organ Dysfunction score, version 2; PRBC, packed red blood cells; CFB, change from baseline; PICU, pediatric intensive care unit; VIS, Vasoactive-Inotropic Score; EEG, electroencephalogram; CT/MRI, computerized tomography/magnetic resonance imaging; FSS, Functional Status Scale; PCPC, Pediatric Cerebral Performance Category; POPC, Pediatric Overall Performance Category. Poor outcome is defined as death or PedsQLTM or FSII-R assessment at Month 3 > 25% below baseline value. PRBC first transfusion is relative to Day 0. Results are based on univariable models.

**eTable 7. Statistically Equivalent Models for Mortality by Month 3**

|  |
| --- |
| (Candidate Models 1-5) |
| Variable | **Model 1** ∆ BIC = 0.0  | **Model 2** ∆ BIC = 0.5  | **Model 3**∆ BIC = 0.6 | **Model 4**∆ BIC = 0.7 | **Model 5**∆ BIC = 0.9 |
| Odds ratio(95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value |
| Sum of VIS in PICU | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 | 1.01 (1.00, 1.01) | <0.001 | 1.01 (1.00, 1.01) | <0.001 |
| Anisocoria or absence of pupillary response |  | 0.004 |  | 0.005 |  | <0.001 |  | 0.003 |  | 0.007 |
|  No | Reference |  | Reference |  | Reference |  | Reference |  | Reference |  |
|  Yes  | 4.29 (1.64, 10.99) |  | 4.10 (1.55, 10.64) |  | 5.26 (2.06, 13.20) |  | 4.43 (1.69, 11.37) |  | 3.86 (1.46, 10.02) |  |
| Stereotypic posturing or flaccid posture |  | 0.011 |  | 0.012 |  |  |  |  |  | 0.017 |
|  No | Reference |  | Reference |  |  |  |  |  | Reference |  |
|  Yes | 4.39 (1.43, 12.70) |  | 4.47 (1.43, 13.16) |  |  |  |  |  | 4.06 (1.30, 11.88) |  |
| Cardiopulmonary arrest or chest compressions |  |  |  | 0.021 |  |  |  |  |  |  |
|  No |  |  | Reference |  |  |  |  |  |  |  |
|  Yes |  |  | 4.20 (1.25, 12.98) |  |  |  |  |  |  |  |
| Pathologic breathing pattern |  |  |  |  |  |  |  | 0.017 |  | 0.026 |
|  No |  |  |  |  |  |  | Reference |  | Reference |  |
|  Yes |  |  |  |  |  |  | 3.79 (1.29, 10.52) |  | 3.49 (1.17, 9.80) |  |
| Neurologic injury suspected by care provider |  |  |  |  |  |  |  |  |  |  |
|  No |  |  |  |  |  |  |  |  |  |  |
|  Yes |  |  |  |  |  |  |  |  |  |  |

|  |
| --- |
| (Candidate Models 6-10) |
| Variable | **Model 6**∆ BIC = 0.9 | **Model 7**∆ BIC = 1.1 | **Model 8** ∆ BIC = 1.3 | **Model 9**∆ BIC = 1.4 | **Model 10**∆ BIC = 1.9 |
| Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value |
| Sum of VIS in PICU | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 | 1.01(1.00, 1.01) | <0.001 |
| Anisocoria or absence of pupillary response |  | 0.012 |  | 0.002 |  |  |  |  |  | 0.005 |
|  No | Reference |  | Reference |  |  |  |  |  | Reference |  |
|  Yes  | 3.62 (1.34, 9.57) |  | 4.82 (1.84, 12.33) |  |  |  |  |  | 4.13 (1.54, 10.76) |  |
| Stereotypic posturing or flaccid posture |  |  |  |  |  |  |  |  |  |  |
|  No |  |  |  |  |  |  |  |  |  |  |
|  Yes |  |  |  |  |  |  |  |  |  |  |
| Cardiopulmonary arrest or chest compressions |  |  |  | 0.021 |  |  |  |  |  | 0.031 |
|  No |  |  | Reference |  |  |  |  |  | Reference |  |
|  Yes |  |  | 4.17 (1.26, 12.74) |  |  |  |  |  | 3.79 (1.14, 11.73) |  |
| Pathologic breathing pattern |  |  |  |  |  | 0.015 |  |  |  | 0.025 |
|  No |  |  |  |  | Reference |  |  |  | Reference |  |
|  Yes |  |  |  |  | 4.02 (1.34, 11.29) |  |  |  | 3.52 (1.18, 9.92) |  |
| Neurologic injury suspected by care provider |  |  |  |  |  | 0.004 |  | 0.001 |  |  |
|  No | Reference | 0.019 |  |  | Reference |  | Reference |  |  |  |
|  Yes | 3.44 (1.23, 9.37) |  |  |  | 4.53 (1.65, 12.00) |  | 5.20 (1.98, 13.32) |  |  |  |

Abbreviations: BIC, Bayesian Information Criterion; VIS, Vasoactive-Inotropic Score; PICU, pediatric intensive care unit.

**eTable 8. Statistically Equivalent Models for PSD-HRQL at Month 3**

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|  |
| **Variable** | **Model 1**∆ BIC = 0.0 | **Model 2**∆ BIC = 0.7 | **Model 3**∆ BIC =1.7 | **Model 4**∆ BIC =1.7 |
| Odds ratio(95% CI) | P-Value | Odds ratio(95% CI) | P-Value | Odds ratio(95% CI) | P-Value | Odds ratio(95% CI) | P-Value |
| **Age (years)** | 1.13 (1.04, 1.23) | 0.003 | 1.15 (1.06, 1.25) | <.001 | 1.13 (1.04, 1.23) | 0.002 | 1.13 (1.04, 1.23) | 0.002 |
| **∑ Daily PICU PELOD-2**  | 1.01 (1.01, 1.02) | <.001 | 1.01 (1.00, 1.02) | 0.002 | 1.01 (1.01, 1.02) | <.001 | 1.01 (1.01, 1.02) | <0.001 |
| **POPC CFB** **at Day 7**  | -------- | -------- | 1.53 (1.04, 2.28) | 0.031 | -------- | -------- |  |  |
| **PMCA** **Category** |  |  |  |  |  | 0.058 |  |  |
| None/ Non-complex |  |  |  |  | Reference |  |  |  |
|  Complex |  |  |  |  | 0.41 (0.15, 1.03) |  |  |  |
| **Neurologic** **Sign/Event** |  |  |  |  |  |  |  | 0.058 |
|  No | -------- | -------- | -------- | -------- |  |  | Reference |  |
|  Yes | -------- | -------- | -------- | -------- |  |  | 3.40 (0.96, 11.10) |  |

Abbreviations: PSD-HRQL, persistent, severe deterioration of health related quality of life > 25% below baseline assessed at Month 3. BIC, Bayesian Information Criterion; PELOD-2, Pediatric Logistic Organ Dysfunction Score, version 2; POPC, Pediatric Overall Performance Category; CFB, change from baseline; PMCA, Pediatric Medical Complexity Algorithm.

Modeling is based on the 201 complete records in which all potential predictors and the outcome are not missing.

**eTable 9. Statistically Equivalent Models for Mortality or PSD-HRQL at Month 3**

|  |  |
| --- | --- |
|  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Model 1∆ BIC = 0.0  | Model 2∆ BIC = 1.7  | Model 3 ∆ BIC = 1.8  |
|  | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value | Odds ratio (95% CI) | P- Value |
| ∑ Daily PICU PELOD-2 | 1.01 (1.01, 1.02) | <0.001 | 1.01 (1.01, 1.02) | <0.001 | 1.03 (1.02, 1.04) | <0.001 |
| Highest VIS in PICU | 1.02 (1.01, 1.04) |  0.003 | -------- | -------- | -------- | -------- |
| Suspected Neurologic Injury |  | <0.001 | -------- | <0.001  | -------- | 0.001 |
|  No | Reference |  | Reference | -------- | Reference | -------- |
|  Yes | 5.04 (2.15, 12.01) |  | 4.93 (2.10, 11.74) | -------- | 4.32 (1.80, 10.45) | -------- |
| ∑ VIS Scores in PICU | -------- | -------- | 1.00 (1.00, 1.01) | 0.008 | -------- | -------- |
| Mechanical Ventilation Days | -------- | -------- | -------- | -------- | 0.88 (0.80, 0.97) | 0.009 |

Abbreviations: PSD-HRQL persistent, severe deterioration in health-related quality of life > 25% below baseline assessed at Month 3; BIC, Bayesian Information Criterion; PICU, pediatric intensive care unit; PELOD-2, Pediatric Logistic Organ Dysfunction Score, version 2; VIS, Vasoactive-Inotropic Score

Modeling is based on the 229 complete records in which all potential predictors and the outcome are non-missing.