

Supplemental Information

SUPPLEMENTARY TABLE 5 Detailed Characteristics of the 838 Children Admitted to a PICU With Confirmed or Probable 2009 H1N1 in the United States (May 1, 2009, to April 15, 2010)

| Characteristic | <i>n</i> (%) |
|--------------------------------------|--------------|
| Gender | |
| Male | 485 (57.9) |
| Female | 353 (42.1) |
| Age group ^a | |
| <6 mo | 71 (8.5) |
| 6–23 mo | 113 (13.5) |
| 2–4 y | 131 (15.6) |
| 5–12 y | 336 (40.1) |
| 13–17 y | 157 (18.7) |
| 18–20 y | 30 (3.6) |
| Ethnicity ^b | |
| Hispanic or Latino | 229 (27.3) |
| Non-Hispanic or Latino | 525 (62.6) |
| Not reported | 84 (10.0) |
| Race ^b | |
| White | 458 (54.7) |
| Black | 168 (20.0) |
| Asian, Hawaiian, or Pacific Islander | 45 (5.4) |
| Native American | 8 (1.0) |
| Other or not reported | 159 (19.0) |
| Underlying health conditions | |
| Previously healthy (none) | 251 (30.0) |
| ≥1 underlying condition | 587 (70.0) |
| Chronic respiratory | 356 (42.5) |
| Asthma | 258 (30.8) |
| On controller medications | 155 (18.5) |
| Bronchopulmonary dysplasia | 36 (4.3) |
| Other chronic lung disease | 116 (13.8) |
| Chronic ventilator support | 27 (3.2) |
| ≤12 h/d | 14 (1.7) |
| >12 h/d | 13 (1.6) |
| Tracheostomy | 62 (7.4) |
| Neurologic or neuromuscular | 263 (31.4) |
| Seizure disorder | 139 (16.6) |
| Cerebral palsy | 70 (8.4) |
| Developmental delay | 199 (23.7) |
| Spina bifida | 4 (0.5) |
| Cerebrovascular disease | 2 (0.2) |
| Other neurologic disease | 76 (9.1) |
| Cardiovascular | 80 (9.5) |
| Congenital heart disease | 58 (6.9) |
| Valvular heart disease | 6 (0.7) |
| Congestive heart failure | 6 (0.7) |
| Hypertension | 17 (2.0) |
| Arrhythmia | 5 (0.6) |
| Peripheral vascular disease | 1 (0.1) |

SUPPLEMENTARY TABLE 5 Continued

| Characteristic | n (%) |
|--|------------|
| Gastrointestinal or hepatic | 80 (9.5) |
| Gastrointestinal disease | 79 (9.4) |
| Cirrhosis | 4 (0.5) |
| Metabolic | 37 (4.4) |
| Diabetes | 24 (2.9) |
| Other metabolic condition (ACIP) | 15 (1.8) |
| Immune compromise | 33 (3.9) |
| Current/active metastatic solid cancer | 6 (0.7) |
| Current/active hematologic malignancy | 9 (1.1) |
| Other immunosuppression (ie, BMT) | 18 (2.1) |
| Renal | 10 (1.2) |
| Chronic renal insufficiency | 7 (0.8) |
| Renal failure requiring dialysis | 4 (0.5) |
| Hemoglobinopathy | 22 (2.6) |
| Other chronic condition | 126 (15) |
| Medication use before admission | |
| Statins | 4 (0.5) |
| Corticosteroids ^b | 73 (8.7) |
| Nonsteroidal immunosuppressive agents | 27 (3.2) |
| ACE inhibitors | 14 (1.7) |
| Anti-influenza agents | 49 (5.8) |
| Clinical features on presentation | |
| Fever | 664 (79.2) |
| Cough | 608 (72.6) |
| Shortness of breath | 452 (53.9) |
| Vomiting | 250 (29.8) |
| Rhinorrhea | 214 (25.5) |
| Wheezing | 184 (22.0) |
| Fatigue | 174 (20.8) |
| Diarrhea | 100 (11.9) |
| Seizures | 83 (9.9) |
| Sore throat | 74 (8.8) |
| Nausea | 63 (7.5) |
| Altered awareness | 60 (7.2) |
| Headache | 56 (6.7) |
| Myalgias | 53 (6.3) |
| Chills | 23 (2.7) |

ACIP indicates Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention; BMT, bone marrow transplant; ACE, angiotensin-converting enzyme.

^a The median age of the patients was 6 years (range: 6 days to 20 years).

^b Race or ethnic group was reported in the clinical chart.

^c More than 20 mg/day prednisone equivalent for adults and >0.3 mg/kg per day for patients younger than 18 years for any duration within 6 months of ICU admission.

SUPPLEMENTARY TABLE 6 Detailed Characteristics of Bacterial Organisms Identified From Lower Respiratory Specimens of Patients With 2009 H1N1 Collected Within 72 Hours of PICU Admission

| Bacterial Organisms | n (%) |
|---|----------|
| MRSA | 34 (4.1) |
| Methicillin-susceptible <i>S aureus</i> | 37 (4.4) |
| <i>Pseudomonas</i> (all species) | 30 (3.6) |
| <i>Streptococcus pneumoniae</i> | 15 (1.8) |
| <i>Moraxella catarrhalis</i> | 14 (1.7) |
| <i>Haemophilus influenzae</i> | 13 (1.6) |
| <i>Streptococcus pyogenes</i> | 7 (0.8) |
| Other bacteria | 54 (6.4) |
| <i>Acinetobacter</i> species | 2 (0.2) |
| <i>Alcaligenes faecalis</i> | 1 (0.1) |
| <i>Bordetella pertussis</i> | 2 (0.2) |
| <i>Burkholderia cepacia</i> | 1 (0.1) |
| <i>Enterobacter</i> species | 11 (1.3) |
| <i>Escherichia coli</i> | 3 (0.4) |
| <i>Klebsiella pneumoniae</i> | 2 (0.2) |
| <i>Morganella morganii</i> | 1 (0.1) |
| <i>Mycoplasma</i> | 1 (0.1) |
| <i>Prevotella</i> species | 1 (0.1) |
| <i>Proteus mirabilis</i> | 1 (0.1) |
| <i>Serratia marcescens</i> | 6 (0.7) |
| <i>Stenotrophomonas maltophilia</i> | 4 (0.5) |
| Other <i>Streptococcus</i> species | 8 (1.0) |
| Other Gram-positive cocci (not speciated) | 14 (1.7) |
| Other Gram-positive rods (not speciated) | 1 (0.1) |
| Other Gram-negative rods (not speciated) | 8 (1.0) |
| Other Gram-negative cocci (not speciated) | 10 (1.2) |

Some patients had polymicrobial culture-confirmed infections.

SUPPLEMENTARY TABLE 7 Characteristics of Patients With pH1N1-Associated Encephalitis During PICU Course

| Age ^a | Comorbidity | Clinical Presentation | Seizure in ICU | Mechanical Ventilation | Length of Hospital Stay, d | Outcome | Discharge Location |
|------------------|--------------------------------|---|----------------|----------------------------|----------------------------|----------|--------------------|
| Infant | Previously healthy | Respiratory failure | Yes | Invasive (ETT)/noninvasive | 4 | Survived | Home |
| Preschool | Previously healthy | Suspected CNS infection, respiratory failure | No | Invasive (ETT) | 2 | Survived | Home |
| Preschool | Previously healthy | Suspected CNS infection, seizure | Yes | None | 12 | Survived | Home |
| Preschool | Seizure disorder | Respiratory failure, Inc seizures | No | Invasive (ETT) | 28 | Died | — |
| Preschool | Previously healthy | Suspected CNS infection, alternative location | No | Invasive (ETT) | 1 | Died | — |
| Preschool | Previously healthy | Respiratory failure, cardiac arrest | No | Invasive (ETT) | 30 | Survived | Rehab hospital |
| Child | Previously healthy | Suspected CNS infection, alternative location | Yes | Invasive (ETT) | 31 | Survived | Rehab hospital |
| Child | Previously healthy | Suspected CNS infection, seizures | Yes | None | 2 | Survived | Home |
| Child | Immune compromised, asthma, CP | Suspected CNS infection | No | Invasive (ETT) | 8 | Died | — |
| Child | Seizure disorder | Respiratory failure, Inc seizures | Yes | Invasive (ETT) | 1 | Died | — |
| Adolescent | Previously healthy | Suspected CNS infection, respiratory failure | No | Invasive (ETT) | 3 | Survived | Home |
| Adolescent | Previously healthy | Suspected CNS infection | Yes | None | 6 | Survived | Home |
| Adolescent | Seizure disorder | Suspected CNS infection, seizure | Yes | Noninvasive | 28 | Survived | Rehab hospital |
| Adolescent | Type 1 diabetes | Suspected CNS infection | No | Invasive (ETT) | 4 | Survived | Home |

Diagnosis of encephalitis was made by MRI, high cerebrospinal fluid protein level, or clinical diagnosis by neurologist at study hospital. CNS indicates central nervous system; ETT, endotracheal tube; CP, cerebral palsy.

^a Age ranges: neonate, ≤ 30 days; infant >30 days to <1 year; toddler, 1 to ≤ 2 years; preschool, 3 to ≤ 5 years; child, 6 to ≤ 12 years; adolescent, 13 to ≤ 17 years; and adult, 18 to ≤ 21 years.

SUPPLEMENTARY TABLE 8 Children With a Clinical Diagnosis of pH1N1-Associated Myocarditis as the Primary Reason Underlying PICU Admission

| Age ^a | Comorbidities | Clinical Presentation | Thrombocytopenia ^b | Neutropenia ^c | Highest Troponin, ng/mL/CPK Level, U/L | Echo | LVEF, % | ECMO (d) | Length of Hospital Stay, d | Outcome |
|------------------|------------------------|------------------------------|-------------------------------|--------------------------|--|------|---------|----------|----------------------------|----------|
| Toddler | Previously healthy | Shock requiring vasopressors | No | No | NA/NA | No | — | No | 18 | Survived |
| Child | Seizure disorder | Cardiac arrest | No | No | 15.5 (I)/NA | Yes | 15 | Yes (7) | 21 | Survived |
| Adolescent | Previously healthy | Lower respiratory infection | NA | NA | 71.6 (I)/2455 | Yes | 55 | No | 5 | Survived |
| Adolescent | Previously healthy | Respiratory failure, shock | Yes | No | 3.7 (I)/405 | Yes | 16 | Yes (14) | >90 | Survived |
| Adolescent | Hematologic malignancy | Lower respiratory infection | Yes | Yes | NA/NA | Yes | 14 | Yes (15) | 17 | Died |
| Adolescent | Previously healthy | Lower respiratory infection | Yes | No | 1.2 (I)/1748 | Yes | Unknown | No | 1 | Died |

CPK indicates creatine phosphokinase; Echo, echocardiography; LVEF, left ventricular ejection fraction; NA, not applicable/not obtained; (I), troponin I; (T), troponin T.

^a Age ranges: toddler, 1 to ≤ 2 years; child, 6 to ≤ 12 years; and adolescent, 13 to ≤ 17 years.

^b Closest to ICU admission ± 2 days: $<150 \times 10^9/\text{mL}$.

^c Closest to ICU admission ± 2 days: <500 cells per mL.

SUPPLEMENTARY TABLE 9 Demographic Factors, Chronic Health Conditions, Clinical Conditions, and Secondary Infections Tested in Multivariable Analyses

| Parameter | RR (95% CI) | <i>P</i> |
|---|----------------|----------|
| Overall cohort (<i>N</i> = 838) | | |
| Female gender | 1.9 (1.2–3.0) | .003 |
| Age 5–20 vs 0–4 y | 1.2 (0.8–2.0) | .4 |
| Neurologic condition | 1.8 (1.1–2.7) | .01 |
| Immune compromise | 2.2 (1.1–4.5) | .02 |
| Metabolic disorder | 1.9 (0.9–4.0) | .08 |
| Encephalitis diagnosed | 3.4 (1.6–7.5) | .002 |
| Myocarditis diagnosed | 3.8 (1.2–12.0) | .03 |
| MRSA coinfection (lung) within ≤72 h | 3.3 (1.7–6.4) | .0005 |
| Previously healthy only (<i>N</i> = 251) | | |
| Female gender | 1.2 (0.5–2.6) | .8 |
| Age 5–20 vs 0–4 y | 1.5 (0.6–3.9) | .4 |
| Encephalitis diagnosed | 2.3 (0.3–14.9) | .4 |
| Myocarditis diagnosed | 5.1 (0.9–30.0) | .07 |
| MRSA coinfection (lung) within ≤72 h | 8.0 (3.9–20.6) | <.0001 |

Patients with the factor were compared to patients without the factor for those patients for whom the factor was reported. The multivariate analysis excluded catheter-related bloodstream infection.

SUPPLEMENTARY TABLE 10 Characteristics of Previously Healthy Patients With pH1N1 and *Staphylococcus aureus* Coinfection of the Lung

| Age ^a | Infection, Source | Clinical Presentation | Shock Requiring Vasopressors ^b | Thrombocytopenia ^c | Neutropenia ^d | Time to Appropriate Antibiotics ^e | Lowest P/F Ratio | Ventilation/ECMO | Hospital Stay, d | Outcome |
|------------------|-------------------|--|---|-------------------------------|--------------------------|--|------------------|------------------|------------------|----------|
| Infant | MSSA, ET | LRTI, shock, respiratory failure | Yes | NA | NA | 13 h after ICU admit | 215 | MV | 32 | Survived |
| Infant | MSSA, ET | Respiratory failure | Yes | No | No | 9 h after ICU admit | 262 | MV | 66 | Survived |
| Infant | MSSA, ET | LRTI, shock, respiratory failure | Yes | Yes | Yes | 15 h before ICU admit | 68 | MV/ECMO | 20 | Died |
| Toddler | MSSA, ET | LRTI, respiratory failure | No | No | No | 5 h before ICU admit | NA | MV | 3 | Survived |
| Child | MSSA, ET | LRTI, shock, respiratory failure | Yes | Yes | Yes | 3 h before ICU admit | 93 | MV/ECMO | 29 | Died |
| Child | MSSA, ET | Respiratory failure, shock | Yes | No | No | 30 min before ICU admit | 182 | MV | 22 | Survived |
| Child | MSSA, ET | Respiratory failure, shock | Yes | Yes | No | 4.5 h before ICU admit | 113 | MV | 59 | Survived |
| Child | MSSA, ET | LRTI, respiratory failure | Yes | No | No | 4 h after ICU admit | 73 | MV | 22 | Survived |
| Adolescent | MSSA, ET | Respiratory failure | No | Yes | No | Unknown | 126 | MV | 28 | Survived |
| Adolescent | MSSA, ET | LRTI, respiratory failure | Yes | No | No | 4 h before ICU admit | 106 | MV | 27 | Survived |
| Adolescent | MSSA, ET | LRTI, shock, respiratory failure | Yes | Yes | No | 15 h before ICU admit | 83 | MV | 34 | Survived |
| Infant | MRSA, ET | Cardiac arrest, respiratory failure | Yes | No | No | None, comfort measures only | 243 | MV | 10 | Died |
| Toddler | MRSA, ET | Respiratory failure | No | No | No | 10 d after ICU admit | 377 | MV | 20 | Survived |
| Toddler | MRSA, empyema | LRTI | No | No | No | 3 h before ICU admit | NA | None | 12 | Survived |
| Toddler | MRSA, ET | Suspected CNS infection, respiratory failure | No | No | No | 1.5 h before ICU admit | 230 | MV | 2 | Died |
| Preschool | MRSA, ET | LRTI, shock, respiratory failure | Yes | NA | NA | 2 h after ICU admit | 97 | MV/ECMO | 20 | Died |
| Preschool | MRSA, ET | LRTI, respiratory failure | No | No | No | 6 h after ICU admit | 76 | MV | 22 | Survived |
| Child | MRSA, ET | LRTI, respiratory failure | Yes | No | NA | At ICU admit | 53 | MV/ECMO | 44 | Survived |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | No | Yes | At ICU admit | 83 | MV/ECMO | 35 | Died |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | Yes | Yes | 45 min after ICU admit | 74 | MV/ECMO | 24 | Survived |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | No | Yes | 3 h after ICU admit | 144 | MV | 11 | Survived |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | Yes | Yes | 1 h before ICU admit | 149 | MV | 15 | Survived |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | Yes | NA | 1.5 h before ICU admit | 40 | MV/ECMO | 124 | Died |
| Child | MRSA, ET | LRTI, shock, respiratory failure | Yes | Yes | No | 1 h before ICU admit | 237 | MV | 20 | Survived |
| Adolescent | MRSA, ET | Respiratory failure, shock | Yes | Yes | Yes | 12 h before ICU admit | 77 | MV | 53 | Survived |
| Adolescent | MRSA, ET | LRTI, shock, respiratory failure | Yes | No | Yes | 2 h after ICU admit | 41 | MV/ECMO | 13 | Died |

P/F, PaO₂/FiO₂; MSSA, methicillin-susceptible *S aureus*; ETI, endotracheal tube; LRTI, lower respiratory tract infection; NA, not applicable/not obtained; MV, mechanical ventilation; empyema, empyema fluid; CNS, central nervous system.

^aAge ranges: toddler, 1 to ≤2 years; child, 6 to ≤12 years; and adolescent, 13 to ≤17 years.

^bDuring hospitalization, any intravenous dopamine at >5 μg/kg per minute or any norepinephrine, epinephrine, or phenylephrine.

^cClosest to ICU admission ± 2 days: <150 × 10⁹/mL.

^dClosest to ICU admission ± 2 days: <1500 cells per mL.

^eAny penicillin, cephalosporin, linezolid, or vancomycin for methicillin-susceptible *S aureus*; vancomycin or linezolid for MRSA.