Online-Only Supplementary Text

Grouping of antibiotics

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| --- | --- | --- |
| **Antibiotic** | **Chemical class** | **Functional class** |
| Amikacin | Aminoglycoside | Anti-pseudomonal |
| Amoxicillin | Penicillin | CA - Narrow |
| Amoxicillin/clavulanic acid | Penicillin | CA - Broad |
| Ampicillin | Penicillin | CA - Narrow |
| Ampicillin/sulbactam | Penicillin | CA - Broad |
| Azithromycin | Macrolide | Atypical |
| Cefazolin | Cephalosporin-1st/2nd gen. | MSSA |
| Cefdinir | Cephalosporin-3rd/4th gen. | CA - Broad |
| Cefepime | Cephalosporin-3rd/4th gen. | Anti-pseudomonal |
| Cefotaxime | Cephalosporin-3rd/4th gen. | CA - Broad |
| Cefoxitin | Cephalosporin-1st/2nd gen. | MSSA |
| Ceftazadine | Cephalosporin-3rd/4th gen. | Anti-pseudomonal |
| Ceftriaxone | Cephalosporin-3rd/4th gen. | CA - Broad |
| Cefuroxime | Cephalosporin-1st/2nd gen. | MSSA |
| Ciprofloxacin | Fluoroquinolone | Anti-pseudomonal |
| Clindamycin | Other | MRSA |
| Gentamicin | Aminoglycoside | Anti-pseudomonal |
| Levofloxacin | Fluoroquinolone | MRSA |
| Linezolid | Other | MRSA |
| Meropenem | Carbapenem | Anti-pseudomonal |
| Nafcillin | Penicillin | MSSA |
| Oxacillin | Penicillin | MSSA |
| Penicillin | Penicillin | CA - Narrow |
| Piperacillin/tazobactam | Penicillin | Anti-pseudomonal |
| Tobramycin | Aminoglycoside | Anti-pseudomonal |
| Trimethoprim/sulfamethoxazole | Other | MRSA |
| Vancomycin | Glycopeptide | MRSA |

Data Source

Data for this study were obtained from the Pediatric Health Information System (PHIS), an administrative database that contains inpatient, emergency department, ambulatory surgery and observation encounter-level data from over 45 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children’s Hospital Association (Overland Park, KS). Data quality and reliability are assured through a joint effort between the Children’s Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, MI). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data including demographics, diagnoses, and procedures. Nearly all of these hospitals also submit resource utilization data (e.g. pharmaceuticals, imaging, and laboratory) into the PHIS database. Data are de-identified at the time of data submission, and are subjected to a number of reliability and validity checks before being included in the database.

Supplemental Table 1. Multivariate models including children <2mo at hospital admission (n = 1058)

|  |  |  |
| --- | --- | --- |
| Variable | Duration of MV | Length of Stay |
| Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| Intercept | 7.23 (6.12, 8.33) | <0.001 | 13.84 (12.19, 15.48) | <0.001 |
| Antibiotics on first 2 days of MV vs. not | -1.29 (-2.00, -0.58) | <0.001 | -2.40 (-3.61, -1.19) | <0.001 |
| Admit age | 0.40 (-0.10, 0.90) | 0.117 | 0.20 (-0.65, 1.06) | 0.643 |
| Race - African-American vs. Caucasian | 0.80 (0.06, 1.53) | 0.034 | 1.56 (0.31, 2.82) | 0.015 |
|  - Other vs. Caucasian | 0.29 (-0.37, 0.95) | 0.387 | 1.08 (-0.03, 2.19) | 0.056 |
| Female vs. male | 0.18 (-0.32, 0.68) | 0.487 | 0.07 (-0.79, 0.93) | 0.872 |
| Vasoactive medication on day1 MV vs. not | 0.88 (0.13, 1.63) | 0.022 | 0.93 (-0.35, 2.21) | 0.155 |
| No private insurance vs. private insurance | 0.87 (0.30, 1.45) | 0.003 | 1.67 (0.69, 2.65) | <0.001 |

MV, mechanical ventilation

Supplemental Table 2. Multivariate models including children ≥2mo at hospital admission (n = 1049)

|  |  |  |
| --- | --- | --- |
| Variable | Duration of MV | Length of Stay |
| Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| Intercept | 7.87 (6.87, 8.88) | <0.001 | 14.01 (12.40, 15.63) | <0.001 |
| Antibiotics on first 2 days of MV vs. not | -1.24 (-1.87, -0.61) | 0.001 | -1.70 (-2.82, -0.57) | 0.003 |
| Admit age | -0.07 (-0.12, -0.02) | 0.003 | -0.13 (-0.22, -0.05) | 0.003 |
| Race - African-American vs. Caucasian | 0.68 (0.00-1.35) | 0.0499 | 1.81 (0.61, 3.02) | 0.003 |
|  - Other vs. Caucasian | 0.15 (-0.48, 0.79) | 0.632 | 0.36 (-0.76, 1.49) | 0.525 |
| Female vs. male | 0.26 (-0.24, 0.75) | 0.313 | 0.77 (-0.12, 1.65) | 0.091 |
| Vasoactive medication on day1 MV vs. not | 1.23 (0.44, 2.02) | 0.002 | 2.16 (0.75, 3.58) | 0.003 |
| No private insurance vs. private insurance | 0.62 (0.05, 1.19) | 0.032 | 1.35 (0.33, 2.36) | 0.009 |

MV, mechanical ventilation

Supplemental Table 3. Multivariate models including children with non-RSV disease

|  |  |  |
| --- | --- | --- |
| Variable | Duration of MV | Length of Stay |
| Estimate (95% CI) | p-value | Estimate (95% CI) | p-value |
| Intercept | 7.43 (6.73, 8.12) | <0.001 | 13.50 (12.45, 14.55) | <0.001 |
| Antibiotics on first 2 days of MV vs. not | -1.01 (-1.41, -0.62) | <0.001 | -1.57 (-2.28, -0.87) | <0.001 |
| Admit age | -0.10 (-0.13, -0.07) | <0.001 | -0.19 (-0.24, -0.13) | <0.001 |
| Race - African-American vs. Caucasian | 0.26 (-0.14, 0.66) | 0.208 | 1.14 (0.43, 1.86) | 0.002 |
|  - Other vs. Caucasian | -0.02 (-0.40, 0.37) | 0.935 | 0.30 (-0.38, 0.98) | 0.391 |
| Female vs. male | 0.24 (-0.06, 0.53) | 0.112 | 0.47 (-0.06, 0.99) | 0.084 |
| Vasoactive medication on day1 MV vs. not | 0.90 (0.45, 1.35) | <0.001 | 1.41 (0.60, 2.21) | <0.001 |
| No private insurance vs. private insurance | 0.64 (0.30, 0.98) | <0.001 | 1.31 (0.70, 1.92) | <0.001 |

MV, mechanical ventilation

Note: In order to adjust for institutional variation, each center’s difference from the overall average proportion of early antibiotic administration (i.e. center usage rate minus overall usage rate for children with RSV or non-RSV disease) was included in the mixed-effect models as a random effect.

Supplemental Figure 1



1a

1b



1c

Antibiotics prescribed during the first two days of antibiotic therapy. Bars represent the percentage of subjects prescribed that specific antibiotic or individual antibiotic class. Solid bars represent early antibiotic group. Striped bars represent late antibiotic group. Asterisks denote statistically significant differences between groups (p < 0.001 by Fisher’s exact test). Individual antibiotics prescribed ≤5 times in the dataset are not shown in Supplementary Figure 1a. In 1b and 1c, the stacked horizontal bars show the percentage of subjects prescribed each unique combination of antibiotic classes (e.g. just CA-Broad, just MRSA, both CA-Broad and MRSA, etc.). These combinations were mutually exclusive and each subject is only included in a single category. In 1b and 1c, both the individual bars and the stacked bars use the same colors to represent the same antibiotic class (e.g. blue represents CA-Broad, etc.).

CA, community acquired. MRSA = methicillin-resistant *Staphylococcal aureus*, MSSA = methicillin-sensitive *Staphylococcal aureus.*

Supplemental Figure 2



Early antibiotic usage by PHIS hospital among children <2mo. Black bars show the percentage of subjects prescribed early antibiotics at each hospital. White boxes show the number of subjects included from each center (right y-axis)

Supplemental Figure 3



Early antibiotic usage by PHIS hospital among children ≥2mo. Black bars show the percentage of subjects prescribed early antibiotics at each hospital. White boxes show the number of subjects included from each center (right y-axis)