

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Clinical signs on the first day of antibiotics stratified by hospital

| | Academic Medical Center 1 N=3814 | | Academic Medical Center 2 N=5827 | | Community Hospital 1 N=1161 | | Community Hospital 2 N=1471 | |
|--|-------------------------------------|---------------|-------------------------------------|---------------|--------------------------------|---------------|--------------------------------|---------------|
| | HAP N=1031 | CAP N=2783 | HAP N=1380 | CAP N=4447 | HAP N=129 | CAP N=1069 | HAP N=193 | CAP N=1278 |
| Frequency of normal clinical signs on first day of antibiotics, N (%) | | | | | | | | |
| Maximum temperature >36 and <38° C | 722 (70.0) | 2194 (78.8) | 972 (70.4) | 3546 (79.7) | 102 (79.1) | 859 (83.2) | 139 (72.0) | 900 (70.4) |
| Median daily respiratory rate <22 breaths/minute | 793 (76.9) | 2234 (80.3) | 1161 (84.1) | 3862 (86.9) | 115 (89.2) | 842 (81.6) | 113 (58.6) | 841 (65.8) |
| White blood cell count >4,000 and <12,000 cells/mm ³ | 471 (45.7) | 1513 (54.4) | 667 (48.3) | 2395 (53.9) | 75 (58.1) | 650 (63.0) | 113 (58.6) | 695 (54.4) |
| Not on supplemental oxygen | 543 (52.7) | 1443 (51.9) | 730 (52.9) | 2363 (53.1) | 86 (66.7) | 568 (55.0) | 109 (56.5) | 654 (51.2) |
| Oxygen saturation ≥95% without supplemental oxygen | 377 (36.6) | 1120 (40.2) | 465 (33.7) | 1752 (39.4) | 49 (38.0) | 404 (39.2) | 64 (33.2) | 441 (34.5) |
| Median respiratory rate <22 breaths/min and oxygen saturation ≥95% without supplemental oxygen | 337 (32.7) | 1040 (37.4) | 446 (32.3) | 1709 (38.4) | 49 (38.0) | 377 (36.5) | 45 (23.3) | 380 (29.7) |
| All signs normal | 125 (12.1) | 489 (17.6) | 189 (13.7) | 866 (19.5) | 30 (23.3) | 230 (22.3) | 26 (13.5) | 194 (15.2) |
| Days until clinical signs normal for patients with abnormal sign(s) on the first day of antibiotics | | | | | | | | |
| Temperature, Mean (SD) | 1.9 (1.6) | 1.8 (1.6) | 2.1 (2.2) | 1.6 (1.3) | 1.6 (0.9) | 1.3 (0.7) | 1.7 (1.6) | 1.5 (0.9) |
| Temperature, Median (IQR) | 1 (1-2) | 1 (1-2) | 1 (1-2) | 1 (1-2) | 1 (1-2) | 1 (1-1) | 1 (1-2) | 1 (1-2) |
| White blood cell count, Mean (SD) | 6.1 (7.0) | 4.1 (4.8) | 5.6 (6.5) | 3.8 (4.2) | 4.0 (4.0) | 2.8 (2.5) | 3.5 (2.9) | 2.7 (2.7) |
| White blood cell count, Median (IQR) | 3 (2-7) | 2 (1-5) | 3 (2-7) | 2 (1-4) | 2 (1-6) | 2 (1-3) | 3 (1-5) | 2 (1-3) |
| Median respiratory rate, Mean (SD) | 2.6 (3.5) | 2.2 (2.5) | 2.6 (2.7) | 1.9 (1.7) | 2.2 (1.7) | 1.6 (1.5) | 2.6 (1.9) | 2.7 (2.4) |
| Median respiratory rate, Median (IQR) | 1 (1-3) | 1 (1-2) | 2 (1-3) | 1 (1-2) | 2 (1-3) | 1 (1-2) | 2 (1-3) | 2 (1-3) |
| Off supplemental oxygen, Mean (SD) | 3.9 (4.6) | 4.5 (4.2) | 3.9 (4.0) | 4.3 (4.4) | 3.4 (2.8) | 3.3 (3.2) | 3.4 (2.5) | 3.4 (2.9) |
| Off supplemental oxygen, Median (IQR) | 2 (1-5) | 3 (2-6) | 3 (1-5) | 3 (1-6) | 3 (1-5) | 2 (1-4) | 3 (2-5) | 3 (1-4) |
| Off supplemental oxygen and saturation ≥95%, Mean (SD) | 6.4 (9.6) | 5.0 (6.1) | 5.9 (7.8) | 4.8 (5.7) | 3.2 (3.0) | 3.3 (3.2) | 3.7 (3.5) | 3.4 (3.2) |
| Off supplemental oxygen and saturation ≥95%, Median (IQR) | 3 (1-8) | 3 (1-6) | 3 (2-7) | 3 (1-6) | 2 (1-4) | 2 (1-4) | 3 (2-5) | 2 (1-4) |
| Median resp rate <22 and oxygen saturation ≥95%, Mean (SD) | 5.0 (5.5) | 3.7 (4.4) | 4.9 (5.5) | 3.7 (4.6) | 4.2 (3.8) | 2.9 (2.1) | 4.2 (6.8) | 2.5 (3.4) |
| Median resp rate <22 and oxygen saturation ≥95%, Median (IQR) | 3 (2-6) | 3 (1-4) | 3 (1-6) | 2 (1-5) | 3 (2-5) | 2 (1-4) | 2 (1-4) | 2 (1-3) |
| All signs normal, Mean (SD) | 7.9 (10.1) | 5.6 (6.5) | 7.3 (8.3) | 5.3 (5.9) | 4.4 (4.3) | 3.7 (3.4) | 4.3 (3.9) | 3.9 (3.3) |
| All signs normal, Median (IQR) | 5 (2-10) | 3 (2-7) | 4 (2-9) | 3 (2-7) | 3 (2-6) | 3 (2-5) | 3 (2-6) | 3 (2-5) |

eTable 2. Duration of antibiotics relative to clinical signs stratified by hospital

| | Academic Medical Center 1 N=3814 | | Academic Medical Center 2 N=5827 | | Community Hospital 1 N=1161 | | Community Hospital 2 N=1471 | |
|---|-------------------------------------|---------------|-------------------------------------|---------------|--------------------------------|---------------|--------------------------------|---------------|
| | HAP N=1031 | CAP N=2783 | HAP N=1380 | CAP N=4447 | HAP N=129 | CAP N=1032 | HAP N=193 | CAP N=1296 |
| Total duration of treatment | | | | | | | | |
| All patients, Mean (SD) | 7.0 (6.2) | 5.8 (5.7) | 7.1 (8.3) | 5.8 (5.8) | 5.3 (3.1) | 5.1 (6.3) | 4.8 (3.6) | 4.7 (3.6) |
| All patients, Median (IQR) | 6 (3-9) | 5 (2-8) | 6 (3-8) | 5 (2-7) | 5 (3-7) | 4 (1-7) | 4 (2-7) | 5 (2-6) |
| Patients with normal signs first day of antibiotics, Mean (SD) | 5.3 (4.3) | 4.9 (5.1) | 5.9 (7.3) | 4.8 (6.1) | 5.2 (3.0) | 4.0 (7.0) | 4.4 (3.2) | 3.9 (4.2) |
| Patients with normal signs first day of antibiotics, Median (IQR) | 5 (2-7) | 4 (1-6) | 5 (2-7) | 4 (1-6) | 5 (3-7) | 2 (1-5) | 4 (2-6) | 3 (1-5) |
| Patients with abnormal signs first day of antibiotics, Mean (SD) | 7.2 (6.4) | 6.1 (5.8) | 7.2 (8.4) | 6.0 (5.7) | 5.3 (3.1) | 5.4 (6.1) | 4.8 (3.7) | 4.8 (3.5) |
| Patients with abnormal signs first day of antibiotics, Median (IQR) | 6 (3-9) | 5 (2-8) | 6 (3-8) | 5 (2-8) | 5 (3-7) | 5 (2-7) | 5 (2-7) | 5 (2-6) |
| Duration of treatment after all signs normal | | | | | | | | |
| All patients, Mean (SD) | 3.3 (5.4) | 2.5 (4.3) | 3.2 (7.1) | 2.6 (4.7) | 3.0 (3.7) | 2.8 (5.9) | 2.2 (3.8) | 2.0 (3.0) |
| All patients, Median (IQR) | 0 (0-5) | 1 (0-4) | 1 (0-5) | 1 (0-4) | 2 (0-5) | 1 (0-4) | 0 (0-4) | 1 (0-3) |
| Patients with abnormal signs first day of antibiotics, Mean (SD) | 2.5 (4.3) | 2.3 (4.3) | 2.5 (6.9) | 2.3 (4.4) | 2.0 (2.9) | 2.6 (5.7) | 1.7 (2.8) | 1.8 (2.7) |
| Patients with abnormal signs first day of antibiotics, Median (IQR) | 0 (0-4) | 0 (0-4) | 1 (0-4) | 1 (0-4) | 0 (0-4) | 1 (0-4) | 0 (0-3) | 0 (0-3) |
| Counts of patients with extended courses of antibiotics | | | | | | | | |
| ≥3 days antibiotics beyond last day of abnormal signs, Count (%) | 410 (39.8) | 939 (33.7) | 519 (37.6) | 1590 (35.8) | 58 (45.0) | 373 (36.1) | 63 (32.6) | 420 (32.9) |
| ≥5 days antibiotics beyond last day of abnormal signs, Count (%) | 285 (27.6) | 587 (21.1) | 351 (25.4) | 902 (20.3) | 38 (29.5) | 206 (20.0) | 34 (17.6) | 192 (15.0) |

eTable 3. Clinical signs on the first day of antibiotics (primary analysis vs sensitivity analyses restricted to patients with discharge diagnosis codes for pneumonia and patients with negative blood and sputum cultures)

| | All Patients | | Patients with Discharge Codes for Pneumonia | | Patients with Negative Blood and Sputum Cultures | |
|--|---------------------------------------|--|---|--|--|--|
| | Hospital-Acquired Pneumonia (N=2,733) | Community-Acquired Pneumonia (N=9,540) | Hospital-Acquired Pneumonia (N=530) | Community-Acquired Pneumonia (N=3,228) | Hospital-Acquired Pneumonia (N=582) | Community-Acquired Pneumonia (N=1,994) |
| Frequency of normal signs on the first day of antibiotics | | | | | | |
| Maximum temperature >36 and <38° C | 1935 (70.8) | 7499 (78.6) | 367 (69.3) | 2374 (73.5) | 298 (51.2) | 1333 (66.9) |
| Median daily respiratory rate ≤22 breaths/minute | 2182 (79.8) | 7779 (81.5) | 449 (84.7) | 2596 (80.4) | 434 (74.6) | 1520 (76.2) |
| Maximum WBC count >4,000 and <12,000 cells/mm ³ | 1326 (48.5) | 5253 (55.1) | 261 (49.3) | 1646 (51.0) | 259 (44.5) | 928 (46.5) |
| Not on supplemental oxygen | 1468 (53.7) | 5028 (52.7) | 298 (56.2) | 1686 (52.2) | 255 (43.8) | 892 (44.7) |
| Oxygen saturation ≥95% without supplemental oxygen | 955 (34.9) | 3717 (39.0) | 197 (37.2) | 1217 (37.7) | 153 (26.3) | 614 (30.8) |
| Median respiratory rate <22 breaths/minute and oxygen saturation ≥95% without supplemental oxygen | 877 (32.1) | 3506 (36.8) | 191 (36.0) | 1150 (35.6) | 134 (23.0) | 565 (28.3) |
| All signs normal | 370 (13.5) | 1779 (18.7) | 84 (15.9) | 526 (16.3) | 41 (7.0) | 196 (9.8) |
| | | | | | | |
| Days until clinical signs normal for patients with abnormal sign(s) on the first day of antibiotics | | | | | | |
| Temperature, Mean (SD) | 2.0 (1.9) | 1.6 (1.3) | 2.3 (2.6) | 1.6 (1.2) | 2.2 (2.0) | 1.7 (1.3) |
| Temperature, Median (IQR) | 1 (1-2) | 1 (1-2) | 1 (1-3) | 1 (1-2) | 1 (1-3) | 1 (1-2) |
| White blood cell count, Mean (SD) | 5.7 (6.5) | 3.7 (4.1) | 5.2 (5.8) | 3.3 (3.2) | 6.1 (7.7) | 4.3 (4.5) |
| White blood cell count, Median (IQR) | 3 (2-7) | 2 (1-4) | 3 (2-6) | 2 (1-4) | 3 (2-7) | 3 (1-5) |
| Median respiratory rate, Mean (SD) | 2.6 (3.0) | 2.2 (2.2) | 2.7 (3.1) | 2.2 (2.0) | 2.5 (2.2) | 2.6 (2.4) |
| Median respiratory rate, Median (IQR) | 2 (1-3) | 1 (1-3) | 2 (1-3) | 1 (1-3) | 2 (1-3) | 2 (1-3) |
| Off supplemental oxygen, Mean (SD) | 3.8 (4.1) | 4.1 (4.1) | 4.1 (4.1) | 4.0 (3.7) | 3.3 (3.7) | 4.4 (4.6) |
| Off supplemental oxygen, Median (IQR) | 2 (1-5) | 3 (1-6) | 2 (1-5) | 3 (1-6) | 2 (1-4) | 3 (1-6) |
| Off supplemental oxygen and saturation ≥95%, Mean (SD) | 5.8 (8.2) | 4.5 (5.4) | 4.9 (5.8) | 4.4 (5.0) | 7.5 (10.8) | 5.6 (6.5) |
| Off supplemental oxygen and saturation ≥95% Median (IQR) | 3 (1-7) | 3 (1-6) | 3 (1-6) | 3 (1-6) | 4 (2-9) | 4 (2-7) |
| Median resp rate <22 and O ₂ saturation ≥95%, Mean (SD) | 4.9 (5.5) | 3.5 (4.3) | 4.4 (5.5) | 3.1 (3.1) | 4.9 (5.5) | 3.5 (3.2) |
| Median resp rate <22 and O ₂ saturation ≥95%, Median (IQR) | 3 (1-6) | 2 (1-4) | 3 (1-5) | 2 (1-4) | 4 (1-6) | 3 (1-5) |
| All signs normal, Mean (SD) | 7.2 (8.8) | 5.0 (5.7) | 6.1 (6.4) | 4.8 (5.1) | 9.1 (11.4) | 6.2 (6.5) |
| All signs normal, Median (IQR) | 4 (2-9) | 3 (2-6) | 4 (2-8) | 3 (2-6) | 5 (3-11) | 4 (2-8) |

eTable 4. Duration of antibiotics relative to clinical signs (primary analysis vs sensitivity analysis restricted to patients with discharge diagnosis codes for pneumonia and patients with negative blood and sputum cultures)

| | All Patients | | Patients with Discharge Codes for Pneumonia | | Patients with Negative Sputum and Blood Cultures | |
|---|---------------------------------------|--|---|--|--|--|
| | Hospital-Acquired Pneumonia (N=2,733) | Community-Acquired Pneumonia (N=9,540) | Hospital-Acquired Pneumonia (N=530) | Community-Acquired Pneumonia (N=3,228) | Hospital-Acquired Pneumonia (N=582) | Community-Acquired Pneumonia (N=1,994) |
| Total duration of treatment in days | | | | | | |
| All patients, Mean (SD) | 6.8 (7.2) | 5.6 (5.6) | 7.5 (5.4) | 6.4 (5.3) | 8.0 (7.1) | 7.3 (5.6) |
| All patients, Median (IQR) | 5 (3-8) | 5 (2-7) | 7 (4-9) | 6 (3-8) | 7 (4-9) | 6 (4-9) |
| Patients with normal signs on first day of antibiotics, Mean (SD) | 6.2 (9.6) | 4.7 (5.6) | 6.1 (4.7) | 5.3 (5.4) | 6.9 (5.1) | 6.0 (4.8) |
| Patients with normal signs on first day of antibiotics, Median (IQR) | 5 (3-7) | 4 (1-6) | 5 (3-8) | 5 (2-7) | 6 (4-8) | 5 (2-8) |
| Patients with abnormal signs on first day of antibiotics, Mean (SD) | 6.9 (6.4) | 5.9 (5.6) | 7.8 (5.5) | 6.6 (5.3) | 8.0 (7.2) | 7.4 (5.7) |
| Patients with abnormal signs on first day of antibiotics, Median (IQR) | 6 (3-8) | 5 (2-7) | 7 (5-9) | 6 (3-8) | 7 (4-10) | 7 (4-9) |
| | | | | | | |
| Duration of treatment beyond the last day of abnormal signs | | | | | | |
| All patients, Mean (SD) | 3.2 (6.2) | 2.5 (4.5) | 3.7 (5.0) | 3.1 (4.4) | 2.8 (4.7) | 3.0 (4.6) |
| All patients, Median (IQR) | 1 (0-5) | 1 (0-4) | 2 (0-5) | 2 (0-5) | 0 (0-4) | 1 (0-4) |
| Patients with abnormal signs on first day of antibiotics, Mean (SD) | 2.4 (5.7) | 2.3 (4.3) | 3.0 (4.2) | 2.9 (4.4) | 2.6 (4.6) | 2.8 (4.5) |
| Patients with abnormal signs on first day of antibiotics, Median (IQR) | 0 (0-4) | 0 (0-4) | 2 (0-5) | 2 (0-4) | 0 (0-4) | 1 (0-4) |
| | | | | | | |
| Counts of patients with extended courses of antibiotics | | | | | | |
| ≥3 days of antibiotics beyond the last day of abnormal signs, Count (%) | 1050 (38.4) | 3322 (34.8) | 259 (48.9) | 1436 (44.5) | 219 (37.6) | 784 (39.3) |
| ≥5 days of antibiotics beyond the last day of abnormal signs, Count (%) | 708 (25.9) | 1887 (19.8) | 168 (31.7) | 844 (26.2) | 129 (22.2) | 485 (24.3) |

eTable 5. Clinical signs on the first day of antibiotics in immunocompetent vs immunocompromised patients

| | Immunocompetent Patients | | Immunocompromised Patients | |
|--|---------------------------------------|--|-------------------------------------|--|
| | Hospital-Acquired Pneumonia (N=2,004) | Community-Acquired Pneumonia (N=7,745) | Hospital-Acquired Pneumonia (N=729) | Community-Acquired Pneumonia (N=1,795) |
| Frequency of normal signs on the first day of antibiotics | | | | |
| Daily maximum temperature >36 and <38° C | 1480 (73.9) | 6174 (79.7) | 455 (62.4) | 1325 (73.8) |
| Median daily respiratory rate ≤22 breaths/minute | 1585 (79.1) | 6257 (80.8) | 597 (81.9) | 1522 (84.8) |
| Daily maximum WBC count >4,000 and <12,000 cells/mm ³ | 1056 (52.7) | 4446 (57.4) | 270 (37.0) | 807 (45.0) |
| Not on supplemental oxygen | 1041 (52.0) | 4053 (52.3) | 427 (58.6) | 975 (54.3) |
| Oxygen saturation ≥95% without supplemental oxygen | 658 (32.8) | 2977 (38.4) | 297 (40.7) | 740 (41.2) |
| Median respiratory rate <22 breaths/minute and oxygen saturation ≥95% without supplemental oxygen | 593 (29.6) | 2789 (36.0) | 284 (39.0) | 717 (39.9) |
| All signs normal | 297 (14.8) | 1525 (19.7) | 73 (10.0) | 254 (14.2) |
| Days until clinical signs normal for patients with abnormal sign(s) on the first day of antibiotics | | | | |
| Temperature, Mean (SD) | 1.8 (1.6) | 1.5 (1.2) | 2.3 (2.4) | 2.0 (1.6) |
| Temperature, Median (IQR) | 1 (1-2) | 1 (1-2) | 1 (1-3) | 1 (1-2) |
| White blood cell count, Mean (SD) | 4.9 (5.4) | 3.2 (3.4) | 7.3 (8.1) | 5.3 (5.6) |
| White blood cell count, Median (IQR) | 3 (1-6) | 2 (1-4) | 4 (2-9) | 3 (2-7) |
| Median respiratory rate, Mean (SD) | 2.6 (3.1) | 2.1 (2.2) | 2.8 (2.7) | 2.3 (2.1) |
| Median respiratory rate, Median (IQR) | 2 (1-3) | 1 (1-2) | 2 (1-3) | 2 (1-3) |
| Off supplemental oxygen, Mean (SD) | 3.6 (4.0) | 4.0 (4.0) | 4.5 (4.4) | 5.0 (4.5) |
| Off supplemental oxygen, Median (IQR) | 2 (1-5) | 3 (1-5) | 3 (1-6) | 4 (2-7) |
| Off supplemental oxygen and saturation ≥95%, Mean (SD) | 5.8 (8.5) | 4.3 (5.2) | 5.9 (7.2) | 5.6 (6.1) |
| Off supplemental oxygen and saturation ≥95%, Median (IQR) | 3 (1-7) | 3 (1-5) | 3 (2-8) | 4 (2-7) |
| Median resp rate <22 and oxygen saturation ≥95%, Mean (SD) | 4.4 (4.9) | 3.2 (3.8) | 6.0 (6.5) | 4.5 (5.6) |
| Median resp rate <22 and oxygen saturation ≥95%, Median (IQR) | 3 (1-5) | 2 (1-4) | 4 (2-8) | 3 (2-5) |
| All signs normal, Mean (SD) | 6.8 (8.5) | 4.6 (5.1) | 8.3 (9.3) | 6.7 (7.1) |
| All signs normal, Median (IQR) | 4 (2-8) | 3 (2-6) | 5 (2-11) | 5 (2-8) |

eTable 6. Duration of antibiotics relative to clinical signs in immunocompetent vs immunocompromised patients

| | Immunocompetent Patients | | Immunocompromised Patients | |
|---|---------------------------------------|--|-------------------------------------|--|
| | Hospital-Acquired Pneumonia (N=2,004) | Community-Acquired Pneumonia (N=7,745) | Hospital-Acquired Pneumonia (N=729) | Community-Acquired Pneumonia (N=1,795) |
| Total duration of treatment in days | | | | |
| All patients, Mean (SD) | 6.2 (6.3) | 5.2 (5.1) | 8.4 (9.0) | 7.4 (7.1) |
| All patients, Median (IQR) | 5 (3-8) | 5 (2-7) | 6 (3-10) | 6 (3-9) |
| Patients with normal signs on first day of antibiotics, Mean (SD) | 5.1 (4.3) | 4.2 (5.1) | 7.3 (9.9) | 6.9 (8.6) |
| Patients with normal signs on first day of antibiotics, Median (IQR) | 5 (2-7) | 3 (1-6) | 6 (3-8) | 5 (2-8) |
| Patients with abnormal signs on first day of antibiotics, Mean (SD) | 6.4 (6.5) | 5.4 (5.1) | 8.5 (8.8) | 7.4 (6.8) |
| Patients with abnormal signs on first day of antibiotics, Median (IQR) | 5 (3-8) | 5 (2-7) | 7 (3-10) | 6 (3-9) |
| | | | | |
| Duration of treatment beyond the last day of abnormal signs | | | | |
| All patients, Mean (SD) | 3.0 (6.1) | 2.4 (4.4) | 3.6 (6.3) | 2.9 (5.1) |
| All patients, Median (IQR) | 1 (0-5) | 1 (0-4) | 0 (0-5) | 1 (0-4) |
| Patients with abnormal signs on first day of antibiotics, Mean (SD) | 2.2 (5.6) | 2.2 (4.3) | 3.0 (5.9) | 2.7 (4.5) |
| Patients with abnormal signs on first day of antibiotics, Median (IQR) | 0 (0-4) | 0 (0-3) | 0 (0-4) | 0 (0-4) |
| | | | | |
| Counts of patients with extended courses of antibiotics | | | | |
| ≥3 days of antibiotics beyond the last day of abnormal signs, Count (%) | 771 (38.5) | 2672 (34.5) | 279 (38.3) | 650 (36.2) |
| ≥5 days of antibiotics beyond the last day of abnormal signs, Count (%) | 612 (30.5) | 1684 (21.7) | 200 (27.4) | 434 (24.2) |