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Ultrashort course antibiotics for suspected pneumonia with preserved oxygenation

Michael Klompas, MD, MPH[1,2], **Caroline McKenna, MPH**[1], **Aileen Ochoa, MPH**[1], **Wenjing Ji, PhD**[3], **Tom Chen, ScD**[1], **Jessica Young, PhD**[1,4], **Chanu Rhee, MD, MPH**[1,2] **CDC Prevention Epicenters**

[1]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, USA

[2]Department of Medicine, Brigham and Women's Hospital, Boston, USA

[3]Department of Pharmacy Administration and Clinical Pharmacy, School of Pharmacy, Xi'an Jiaotong University, Xi'an, Shaanxi, China

[4]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, USA

Abstract

Background: Suspected pneumonia is the most common indication for antibiotics in hospitalized patients but frequently overdiagnosed. We explored whether normal oxygenation could be used as an indicator to support early discontinuation of antibiotics.

Methods: We retrospectively identified all patients started on antibiotics for pneumonia in 4 hospitals with oxygen saturations ≥95% on ambient air, May 2017-February 2021. We propensity-matched patients treated 1-2 days vs 5-8 days and compared hospital mortality and time-to-discharge using subdistribution hazard ratios (SHRs). Secondary outcomes included readmissions, 30-day mortality, *C.difficile* infections, hospital-free days, and antibiotic-free days.

Results: Amongst 39,752 patients treated for possible pneumonia, 10,012 had median oxygen saturations ≥95% without supplemental oxygen. Of these, 2,871 were treated 1-2 days and 2,891 for 5-8 days; 4,478 patients were propensity-matched. Patients treated 1-2 vs 5-8 days had similar hospital mortality (2.1% vs 2.8%, SHR 0.75, 95% CI 0.51-1.09) but less time-to-discharge (6.1 vs 6.6 days, SHR 1.13, 95% CI 1.07-1.19) and more 30-day hospital-free days (23.1 vs 22.7, mean difference 0.44, 95% CI 0.09-0.78). There were no significant differences in 30-day readmissions (16.0% vs 15.8%, OR 1.01, 95% CI 0.86-1.19), 30-day mortality (4.6% vs 5.1%, OR 0.91, 95% CI 0.69-1.19), or 90-day *C.difficile* infections (1.3% vs 0.8%, OR 1.67, 95% CI 0.94-2.99).

Conclusions: One quarter of hospitalized patients treated for pneumonia had oxygenation saturations ≥95% on ambient air. Outcomes were similar with 1-2 vs 5-8 days of antibiotics.

Corresponding author: Michael Klompas, Department of Population Medicine, Harvard Medical School & Harvard Pilgrim Health Care Institute, 401 Park Drive, Suite 401 East, Boston, MA 02215, USA, 617-867-4991, mklompas@bwh.harvard.edu. Alternate author: Chanu Rhee, Department of Population Medicine, Harvard Medical School & Harvard Pilgrim Health Care Institute, 401 Park Drive, Suite 401 East, Boston, MA 02215, USA, 617-867-4211, crhee@bwh.harvard.edu.

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Normal oxygenation levels may help identify candidates for early antibiotic discontinuation. Prospective trials are warranted.

Summary:

Amongst 39,752 hospitalized patients treated for possible pneumonia, 10,012 had oxygen saturations ≥95% on ambient air. Outcomes were similar with 1-2 days versus 5-8 days of antibiotics. Normal oxygenation may be an indicator that antibiotics can be stopped early.

Keywords

pneumonia; antibiotic stewardship; oxygenation; quality improvement

Suspected respiratory tract infections are the most common indication for antibiotics in hospitalized patients.[1-4] A substantial fraction of antibiotics prescribed for possible pneumonia, however, may be unnecessary.[5] Expert reviews, computed tomography audits, and autopsy series suggest that 30-50% of hospitalized patients diagnosed with pneumonia do not in fact have pneumonia.[6-12] One of the main drivers of antibiotic overprescribing is the subjectivity and lack of specificity of the core clinical signs and symptoms used to diagnose pneumonia. Shortness of breath, changes in sputum production, and radiographic opacities are all common but non-specific findings in hospitalized patients.[13, 14] Clinicians are wary of missing the diagnosis of pneumonia, however, and therefore tend to err on the side of prescribing even if the diagnosis is uncertain. Better strategies are needed to help clinicians at the bedside determine if antibiotics are warranted or not, and if started, whether to continue them or stop.

One very simple and sensitive (albeit non-specific) sign that may differentiate between true and serious respiratory infections versus non-infectious mimicking conditions or very mild pneumonias is oxygen saturation. Pneumonia, by definition, involves invasion of the lung parenchyma. The absence of impaired gas exchange therefore makes severe pneumonia unlikely. Indeed, there is a strong and consistent association between the magnitude of impaired oxygenation in patients with possible pneumonia and their risk for death and other poor outcomes.[15-18] Conversely, oxygen saturations ≥95% are associated with a lower probability of true infection [18] and oxygen saturations >92% have been associated with minimal marginal risk for death or hospitalization amongst outpatients treated for pneumonia.[19]

Focusing on oxygenation levels to inform the decision to start or continue antibiotics could have a large potential effect on antibiotic utilization. Up to one third of hospitalized patients treated for pneumonia have oxygen saturations ≥95% without supplemental oxygen.[10, 20, 21] There are very few studies, however, on the safety of stopping antibiotics in this population.[22] We therefore undertook a retrospective analysis of outcomes amongst hospitalized patients with oxygen saturations ≥95% without supplemental oxygen who were treated for possible pneumonia with very short courses of antibiotics (1-2 days) versus propensity-matched patients treated with more conventional courses (5-8 days).

Methods:

We identified all patients age ≥18 years admitted to four hospitals in eastern Massachusetts between May 2017 and February 2021 who were treated with antibiotics with a stated indication of pneumonia. Study hospitals included two large tertiary referral hospitals (Brigham and Women's Hospital, Massachusetts General Hospital) and two community hospitals (Faulkner Hospital, Newton Wellesley Hospital). Granular clinical data were extracted from an Enterprise Data Warehouse populated by the electronic health record system shared by all study hospitals (Epic Systems, Verona, WI) including demographics, diagnosis codes, locations, services, vital signs, laboratory values, medications, and antibiotic indications. Providers are required to specify an indication whenever new antibiotics are ordered for inpatients. This is done within the antibiotic order screen in the electronic health record by selecting from a structured list of options that includes pneumonia. Providers can also enter a free text indication. Validation studies suggest that the indications specified by clinicians accurately reflect their working diagnoses at the time of prescription as specified in their concurrent clinical notes.[10, 23]

We limited the population to patients with median daily oxygen saturation levels of ≥95% without supplemental oxygen on both the first and second calendar days of antibiotics. Median oxygen saturation levels were calculated using all recorded values on a calendar day. We excluded patients with positive blood cultures (other than common skin contaminants), missing vital signs on the first day of antibiotics, or discharge diagnosis codes for empyema, cystic fibrosis, or bronchiectasis (E84, J85, J86) since standard of care for these conditions includes longer antibiotic courses. If a patient was admitted more than once during the study period then a single admission was selected at random. Missing laboratory values were imputed from the closest measured value within 2 days before or after the first day of antibiotics but if no measurements were available then missing values were imputed as normal.

We compared outcomes for patients treated with 1-2 days of antibiotics versus those treated with 5-8 days of antibiotics by propensity-matching those treated for 1-2 days to those treated 5-8 days using a caliper of 0.1 times the standard deviation of the estimated logit propensity score.[24] Post-discharge antibiotics were included when calculating duration of antibiotics. We chose these two intervals (1-2 days and 5-8 days) to provide clear separation in treatment durations between groups and because we hypothesized clinical equipoise amongst clinicians on whether patients with normal oxygenation levels have pneumonia or not: we reasoned that clinicians who stopped antibiotics within 1-2 days likely decided against pneumonia whereas those who treated for 5-8 days opted in favor of pneumonia. We recognize, however, that clinicians may be more likely to stop antibiotics if evidence for pneumonia is more equivocal. We therefore propensity matched patients treated 1-2 days to patients treated 5-8 days using an extensive array of granular clinical parameters including demographics, comorbidities, vital signs, laboratory values, culture orders, respiratory viral studies, and baseline medications. We also limited the analysis to patients who survived at least 5 days counting from the first day of antibiotics in order to assure that antibiotic courses of less than 5 days were due to clinical choice, not early death, and thus mitigate survivor bias in favor of those treated with longer courses.

Propensity scores for treatment interval were calculated by stratifying patients by hospital and then within each hospital using patient's demographics (age, race, sex), clinical service on the first day of antibiotics (medicine, neurology, obstetrics, oncology, surgery, cardiology, cardiac surgery), presence in an intensive care unit on the first day of antibiotics, comorbidities (congestive heart failure, renal failure, liver disease, metastatic cancer, solid tumor, diabetes, cerebrovascular disease, pulmonary circulation disorder), vital signs on the first day of antibiotics (maximum temperature, median respiratory rate, maximum heart rate, minimum systolic blood pressure), laboratory values on the first of antibiotics (maximum white blood cell count, minimum hematocrit, minimum platelets, maximum creatinine, minimum sodium, maximum glucose, maximum alanine aminotransferase, maximum bilirubin, maximum albumin, maximum international normalized ratio), vasopressor use on the first day of antibiotics, antibiotic exposure for other indications between admission and the first day of antibiotics for pneumonia, number of days from admission until first day of antibiotics, whether blood cultures were obtained, whether a sputum culture was obtained, whether sputum cultures were positive for potentially pathogenic organisms (i.e. organisms other than coagulase-negative Staphylococci, Enterococcus, and Candida), and whether any assays for respiratory viruses were positive (including SARS-CoV-2, influenza, respiratory syncytial virus, parainfluenza, rhinovirus, human metapneumovirus, and adenovirus). Patients' comorbidities were derived using the methods of Charlson and Elixhauser.[25, 26] We used the median respiratory rate rather than the minimum or maximum given that this parameter is prone to wide fluctuation over the course of a day depending on patients' activities and clinical interventions.

We compared hospital death, hospital discharge 30-day mortality, 30-day readmission, and 90-day positive *Clostridioides difficile* counting from the first day of antibiotics using sample proportions, and total antibiotic days, total antibiotic-free days alive, and total hospital-free days alive within 30 days of the first day of antibiotics using sample means. We calculated P-values for comparisons in the total and matched cohorts using two-sample t-tests.

We further estimated measures of association for short vs conventional treatment groups amongst propensity-matched patients using Fine and Gray regression for propensity-score matched data [27] to estimate subdistribution hazard ratios for hospital death and discharge, logistic regression to estimate odds ratios for 30-day mortality, 30-day readmission and 90-day positive *Clostridioides difficile* toxin assays. We used linear regression to estimate mean differences for total antibiotic days, total antibiotic-free days alive, and total hospital-free days alive within 30-days of the first day of antibiotics. We generated 95% confidence intervals for odds ratios and mean differences using cluster-robust standard errors to account for the paired nature of the data.

We performed sensitivity analyses limited to patients with community acquired pneumonia (first day of antibiotics on hospital day 1-2), hospital-acquired pneumonia (first day of antibiotics on hospital day ≥3), patients in whom sputum cultures were obtained, patients with positive sputum cultures, and patients with discharge diagnosis codes for pneumonia (J13-J18). We also did a sensitivity analysis in which we matched patients using their clinical parameters from the second day of antibiotics since decision making regarding

duration of antibiotics may have been made on the basis of patients' clinical parameters on the second day of treatment. All calculations were performed using R version 4.03. The study was approved by the Mass General Brigham Institutional Review Board.

Results

There were 39,752 patients started on antibiotics with a stated indication of pneumonia during the study period. Of these, 10,012 had a median oxygen saturation of ≥95% without supplemental oxygen on the first and second days of antibiotics. After applying the study exclusion criteria and limiting to patients treated for 1-2 or 5-8 days there were 5,762 patients remaining (2,871 treated for 1-2 days and 2,891 treated for 5-8 days). After propensity matching, 4,478 patients were included in the primary analysis (2,239 in each group). Characteristics of patients before and after propensity matching are shown in Table 1. Within the propensity matched set, average age was 66 years, 55% were male, 68% were white, 73% were on an internal medicine service, 23% had cancer, 28% had diabetes, 26% had renal failure, and 26% had congestive heart failure. Antibiotics for pneumonia were started within the first 2 days of hospitalization in 3466/4478 (77%) and on hospital day 3 or later in in the remainder. Standardized differences between patients treated for 1-2 days versus those treated for 5-8 days were <0.1 on all patient characteristics after propensity matching.[28]

Outcomes

Absolute outcomes for both the total cohort and the propensity-matched subset are shown in Table 2 and measures of association for propensity-matched patients treated with 1-2 vs 5-8 days of antibiotics are shown in Table 3. There were no statistically significant differences in hospital mortality (2.1% vs 2.8%, subdistribution hazard ratio 0.75, 95% CI 0.51-1.09) but the subdistribution hazard ratio for time to discharge alive was significantly higher for patients treated with 1-2 days of antibiotics (i.e. they were discharged sooner, mean days to discharge 6.1 vs 6.6, subdistribution hazard ratio 1.13, 95% CI 1.07-1.19) and they had slightly more 30-day hospital-free days (23.1 vs 22.7, mean difference 0.44, 95% CI 0.09-0.78). There were no significant differences in 30-day readmissions (16.0% vs 15.8%, odds ratio 1.01, 95% CI 0.86-1.19), 30-day mortality (4.6% vs 5.1%, odds ratio 0.91, 95% CI 0.69-1.19), or 90-day *C. difficile* infections (1.3% vs 0.8%, odds ratio 1.67, 95% CI 0.94-2.99). However, patients treated for 1-2 days had 4.4 more antibiotic-free days alive (25.9 vs 21.5, mean difference 95% CI 4.08-4.69) compared to those treated with 5-8 days of antibiotics.

Subgroup analyses

Measures of association were largely consistent in all subgroup analyses (Table 3). Short courses were associated with higher hazards for hospital discharge (i.e. less time to discharge) amongst patients treated for community acquired pneumonia, those in whom sputum cultures were obtained, and patients with discharge diagnosis codes for pneumonia, but were not significant for those with hospital-acquired pneumonia. There were no significant differences in hospital deaths, readmissions, 30-day deaths, hospital-free days, or *C. difficile* infections between short versus conventional courses in any of the subgroups.

Antibiotic-free days were significantly higher for patients treated with 1-2 days of antibiotics in all subgroups. When patients were propensity matched using clinical parameters from the second day of antibiotics rather than from the first day of antibiotics results were consistent with the primary analysis.

Discussion

In this large propensity-matched analysis we did not detect any statistically significant differences in mortality or readmissions amongst patients treated for possible pneumonia who had oxygen saturations ≥95% without supplemental oxygen regardless of whether they were treated with 1-2 days of antibiotics versus 5-8 days of antibiotics. Our findings suggest that deliberate review of oxygenation levels may be a practical strategy to help clinicians identify patients on antibiotics for possible pneumonia who are promising candidates for early discontinuation of antibiotics.

The lack of apparent benefit of conventional antibiotic course durations for patients with possible pneumonia but preserved oxygenation likely reflects a combination of factors. Some patients may not have had pneumonia at all, a frequent phenomenon in the hospitalized population given the non-specific nature of the clinical symptoms, signs, laboratory tests, and radiographs used to diagnose pneumonia.[6-11] Other patients may have had pneumonia but with a viral rather than a bacterial etiology. One third to one half of community-acquired pneumonias in hospitalized patients and one fifth of hospital-acquired pneumonias are attributable to viruses.[29-31] A further set of patients may indeed have had bacterial pneumonia but mild cases with minimal parenchymal invasion and / or very good physiologic reserves as suggested by their preserved oxygenation levels such that they were able to recover with very brief treatment courses.

Our results are compatible with the growing literature demonstrating the safety of brief antibiotic courses for community acquired pneumonia. Two randomized trials comparing the safety of 3 versus 8 days of antibiotics for patients hospitalized with moderate to severe pneumonia reported no differences in outcomes between groups.[32, 33] A third trial reported a similar finding amongst ventilated patients with pulmonary infiltrates and low clinical pulmonary infection scores who were randomized to stopping antibiotics after 3 days versus usual care.[22] Our study builds upon these trials by demonstrating the generalizability of these findings to real-world populations without the enrollment exclusion criteria applied in these trials, the potential utility of using oxygenation levels to identify candidates for early discontinuation of antibiotics, and the potential safety of stopping antibiotics after less than three days amongst the subset of patients with suspected pneumonia but preserved oxygenation levels.

Limitations of our study include the observational design and thus the possibility of unmeasured confounding by indication. Clinicians may have been more likely to stop antibiotics early in patients who appeared to be more stable or in whom other information emerged that pointed to a non-bacterial or non-infectious process. We attempted to control for confounding by indication, however, by propensity-matching patients using an extensive array of clinically detailed variables including patients' demographics, comorbidities, vital

signs, laboratory values, bacterial and viral testing, and prior treatments. Despite the large number and granularity of the clinical parameters included in our propensity scores we were able to achieve a close match without a large loss in sample size. Indeed, it is notable that even before matching, patients were almost perfectly divided into short course and conventional course groups with small standardized differences for the majority of patient characteristics. This suggests there is some degree of clinical equipoise at the bedside as to whether patients with possible pneumonia but preserved oxygen saturations need antibiotics or not. Nonetheless, the finding that patients treated with shorter courses may have been discharged sooner may be due to residual confounding.

Other limitations of our study include our focus on four hospitals from a single region of one country. This may limit generalizability. It is also possible that treating clinicians misspecified indications for some patients leading to contamination of the study sample with patients without pneumonia. Prior validation studies, however, have suggested that the indications provided by clinicians when they prescribe antibiotics accurately reflect their clinical impressions at the time of specification.[10, 23] In addition, results were consistent in the sensitivity analyses restricted to patients with a higher probability of having true pneumonia, namely those with positive sputum cultures and those with discharge diagnosis codes for pneumonia. Post-discharge antibiotic durations were calculated from discharge prescriptions but may not reflect what patients took if patients failed to fill prescriptions, stopped their courses early, or received extensions from their providers. Finally, propensity score matching does not accommodate time-varying confounders that are affected by past treatment; for example, some residual bias in our estimates is possible if time-updated lab measures or vital signs suggesting disease progression affected clinicians' decisions to stop or continue antibiotics and were also, themselves, affected by past antibiotic decisions.[34] Our findings were consistent on a sensitivity analysis where we used patients' clinical parameters on the second day of treatment rather than the first but bias may still occur even when such measures are included in the propensity score model. Emerging causal inference methods can better accommodate these more complex data interactions and are a promising route for future observational studies of time-varying treatment strategies.[35]

In summary, we found no evidence of harm and possible benefit with 1-2 versus 5-8 days of antibiotics to treat possible pneumonia in patients who had oxygen saturations ≥95% on ambient air. This analysis suggests a potentially powerful strategy to help clinicians to easily identify a subset of patients with possible pneumonia in whom early discontinuation of antibiotics may be safe. The potential population that could benefit from this strategy is large. Our study and others suggest that a quarter to a third of hospitalized patients treated for possible pneumonia may fall into this category.[10, 20, 21] Early discontinuation of antibiotics started for possible pneumonia in hospitalized patients with normal oxygenation merits testing in a prospective randomized trial to confirm or refute the feasibility, safety, and utility of this strategy for reducing unnecessary antibiotic use.

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Table 1.

Characteristics of hospitalized patients treated with 1-2 days vs 5-8 days of antibiotics for possible pneumonia who had oxygen saturations ≥95% on ambient air

	Total Cohort			Propensity-matched cohort		
	1-2 Days of Antibiotics (N=2,871)	5-8 Days of Antibiotics (N=2,891)	Std Diff	1-2 Days of Antibiotics (N=2,239)	5-8 Days of Antibiotics (N=2,239)	Std Diff
Demographics						
Age (mean, SD)	66.1 (18.2)	64.9 (18.5)	.07	65.4 (18.3)	65.5 (18.5)	.01
Male sex	1543 (53.7%)	1584 (54.8%)	.02	1220 (54.5%)	1202 (53.7%)	.02
Race/Ethnicity						
White	1925 (67.0%)	2008 (69.5%)	.05	1511 (67.5%)	1514 (67.6%)	.01
Black	400 (13.9%)	386 (13.4%)	.02	312 (13.9%)	312 (13.9%)	.01
Hispanic	60 (2.1%)	48 (1.7%)	.03	42 (1.9%)	39 (1.7%)	.01
Asian	134 (4.7%)	131 (4.5%)	.01	99 (4.4%)	113 (5.0%)	.01
Other/Missing	352 (12.3%)	318 (11.0%)	.04	275 (12.3%)	261 (11.7%)	.01
Hospital						
Tertiary hospital 1	822 (29%)	796 (28%)	.02	633 (28.3%)	633 (28.3%)	.00
Tertiary hospital 2	1301 (45%)	1411 (49%)	.08	1084 (48.4%)	1084 (48.4%)	.00
Community hospital 1	384 (13%)	295 (10%)	.09	244 (10.9%)	244 (10.9%)	.00
Community hospital 2	364 (13%)	389 (14%)	.03	278 (12.4%)	278 (12.4%)	.00
Clinical Service[1]						
Cardiac surgery	8 (0.3%)	11 (0.4%)	.02	7 (0.3%)	6 (0.3%)	.02
Cardiology	92 (3.2%)	61 (2.1%)	.07	53 (2.4%)	58 (2.6%)	.01
Emergency	51 (1.8%)	57 (2.0%)	.02	47 (2.1%)	48 (2.1%)	.02
Gynecology	3 (0.1%)	5 (0.2%)	.03	3 (0.1%)	2 (0.1%)	.00
Medicine	2165 (75.8%)	2029 (70.3%)	.12	1662 (74.2%)	1626 (72.6%)	.04
Neurology	86 (3.0%)	94 (3.3%)	.02	67 (3.0%)	72 (3.2%)	.00
Obstetrics	9 (0.3%)	8 (0.3%)	.00	5 (0.2%)	7 (0.3%)	.01
Oncology	274 (9.6%)	398 (13.8%)	.13	253 (11.3%)	268 (12.0%)	.04
Surgery	127 (4.4%)	182 (6.3%)	.09	109 (4.9%)	124 (5.6%)	.02
Comorbidities						
Congestive heart failure	807 (28.1%)	666 (23.0%)	.02	582 (26.0%)	569 (25.4%)	.03
Renal failure	759 (26.4%)	734 (25.4%)	.03	589 (26.3%)	590 (26.4%)	.04
Liver disease	228 (7.9%)	285 (9.9%)	.12	196 (8.8%)	199 (8.9%)	.01
Cancer	577 (20.1%)	713 (24.6%)	.03	501 (22.4%)	525 (23.4%)	.03
Diabetes	854 (29.7%)	791 (27.4%)	.12	640 (28.6%)	629 (28.1%)	.02
Neurological disease	425 (14.8%)	439 (15.2%)	.02	325 (14.5%)	318 (14.2%)	.01
Elixhauser score (mean, SD)	10.8 (11.7)	11.9 (12.2)	.09	11.0 (12.0)	11.4 (12.1)	.03
Clinical characteristics						

	Total Cohort			Propensity-matched cohort		
	1-2 Days of Antibiotics (N=2,871)	5-8 Days of Antibiotics (N=2,891)	Std Diff	1-2 Days of Antibiotics (N=2,239)	5-8 Days of Antibiotics (N=2,239)	Std Diff
Antibiotic exposure before pneumonia[2]	297 (10.3%)	460 (15.9%)	.17	272 (12.1%)	296 (13.2%)	.02
Intensive care exposure before pneumonia[2]	134 (4.7%)	251 (8.7%)	.16	119 (5.3%)	135 (6.0%)	.03
Hospital days before pneumonia[2] (mean, SD)	1.3 (4.4)	2.2 (6.0)	.06	1.5 (4.1)	1.7 (4.4)	.05
Blood cultures drawn	1370 (47.7%)	1718 (59.4%)	.24	1166 (52.1%)	1187 (53.0%)	.01
Sputum cultures obtained	397 (13.8%)	681 (23.6%)	.25	380 (17.0%)	380 (17.0%)	.02
Sputum cultures positive	92 (3.2%)	176 (6.1%)	.14	88 (3.9%)	97 (4.3%)	.02
Gram positives	40 (1.4%)	88 (3.0%)	.11	40 (1.8%)	42 (1.9%)	.03
Enteric gram negatives	35 (1.2%)	73 (2.5%)	.10	34 (1.5%)	41 (1.8%)	.00
Non-fermenters	23 (0.8%)	28 (1.0%)	.02	19 (0.8%)	22 (1.0%)	.01
Positive respiratory viral assay	262 (9.1)	199 (6.9)	.08	183 (8.2)	165 (7.4)	.03
Vital signs						
Maximum temperature (mean, SD)	99.2 (1.3)	99.6 (1.5)	.29	99.3 (1.4)	99.3 (1.4)	.00
Median respiratory rate (mean, SD)	19.3 (2.7)	19.5 (2.8)	.07	19.4 (2.7)	19.3 (2.6)	.04
Maximum heart rate (mean, SD)	98.4 (20.9)	101.6 (20.8)	.15	99.7 (21.3)	99.6 (20.5)	.01
Median systolic blood pressure	130.3 (21.6)	127.5 (21.1)	.13	128.8 (20.7)	128.8 (21.5)	.00
Vasopressors first day of pneumonia	29 (1.0%)	50 (1.7%)	.16	26 (1.2%)	28 (1.3%)	.02
Laboratory values						
White blood cell count (mean, SD)	9.7 (6.8)	10.8 (6.8)	.16	10.0 (5.8)	10.3 (5.7)	.05
Hemoglobin (mean, SD)	11.5 (2.3)	11.1 (2.3)	.04	11.3 (2.4)	11.3 (2.2)	.00
Hematocrit (mean, SD)	34.9 (6.7)	33.8 (6.4)	.17	34.4 (6.7)	34.3 (6.3)	.02
Platelets (mean, SD)	233.1 (111.2)	231.4 (130.4)	.01	233.6 (115.9)	232.9 (114.2)	.01
Creatinine (mean, SD)	1.4 (1.7)	1.3 (1.3)	.07	1.4 (1.6)	1.3 (1.4)	.07
Sodium (mean, SD)	137.3 (4.7)	137.0 (4.9)	.06	137.2 (4.9)	137.1 (4.8)	.02
Alanine aminotransferase (mean, SD)	32.5 (61.3)	33.7 (81.8)	.02	33.3 (65.1)	31.8 (47.2)	.03
Bilirubin (mean, SD)	0.7 (1.2)	0.8 (2.2)	.06	0.7 (1.3)	0.7 (1.3)	.00
Albumin (mean, SD)	3.7 (0.6)	3.6 (0.6)	.17	3.7 (0.6)	3.7 (0.6)	.00
International Normalized Ratio (mean, SD)	1.2 (0.7)	1.3 (0.8)	.13	1.2 (0.7)	1.2 (0.7)	.00
Glucose (mean, SD)	148.7 (83.6)	153.8 (89.9)	.06	150.9 (87.8)	149.9 (81.4)	.01

[1] Clinical service on hospital day 2

[2] Exposures measured prior to the first day of antibiotics with a stated indication of pneumonia

[3] Excluding common skin contaminants

Table 2.

Comparative outcomes amongst hospitalized patients treated with 1-2 days vs 5-8 days of antibiotics for possible pneumonia who had oxygen saturations ≥95% on ambient air

	Total Cohort			Propensity-matched cohort		
	1-2 Days of Antibiotics (N=2,871)	**5-8 Days of Antibiotics (N=2,891)**	**P**	**1-2 Days of Antibiotics (N=2,239)**	**5-8 Days of Antibiotics (N=2,239)**	**P**
Antibiotic days[1] (mean, SD)	1.31 (0.5)	6.3 (1.1)	<.001	1.3 (0.5)	6.2 (1.1)	<.001
Antibiotic-free days[2] (mean, SD)	26.1 (5.7)	21.5 (4.9)	<.001	25.9 (5.9)	21.5 (4.8)	<.001
Hospital days until discharge[3] (mean, SD)	6.1 (7.5)	7.0 (7.9)	<.001	6.1 (7.7)	6.6 (7.1)	.04
Hospital days, total (mean, SD)	7.4 (9.2)	9.2 (11.2)	<.001	7.6 (9.3)	8.3 (9.0)	.01
Hospital-free days[2] (mean, SD)	23.2 (6.0)	22.4 (6.2)	<.001	23.1 (6.1)	22.7 (5.9)	.02
Hospital Death (count, %)	58 (2.0%)	87 (3.0%)	.02	47 (2.1%)	63 (2.8%)	.15
30-day mortality (count, %)	127 (4.4%)	161 (5.6%)	.05	104 (4.6%)	114 (5.1%)	.53
30-day readmissions (count, %)	438 (15.3%)	453 (15.7%)	.69	358 (16.0%)	354 (15.8%)	.90
C. difficile toxin positive within 90 days (count, %)	33 (1.1%)	24 (0.8%)	.27	30 (1.3%)	18 (0.8%)	.11

[1] Includes both inpatient antibiotics and discharge antibiotics

[2] Within 30 days of the first day of antibiotics

[3] Measured from the first day of antibiotics for pneumonia

Table 3.

Overall and subgroup outcome comparisons of patients treated with very short courses (1-2 days) matched to patients treated with conventional courses (5-8 days) of antibiotics for possible pneumonia with oxygen saturations ≥95% on ambient air.

	Measure Of Association	All patients (N=4,478)	Community Acquired pneumonia (N=3,466)	Hospital Acquired Pneumonia (N=746)	Sputum Cultures Obtained (N=712)	Discharge Diagnosis Code for Pneumonia (N=1,104)
In-Hospital Death	Subdistribution Hazard Ratio	0.75 (0.51, 1.09)	0.76 (0.47-1.23)	1.08 (0.53-2.21)	0.83 (0.25-2.74)	1.61 (0.72-3.57)
Hospital discharge	Subdistribution Hazard Ratio	1.13 (1.07, 1.19)	1.14 (1.07-1.21)	1.09 (0.95-1.25)	1.14 (1.00-1.31)	1.11 (1.00-1.23)
Readmission within 30 days	Odds Ratio	1.01 (0.86, 1.19)	1.04 (0.86-1.25)	1.09 (0.76-1.58)	0.79 (0.51-1.21)	0.96 (0.68-1.34)
30-day Deaths	Odds Ratio	0.91 (0.69, 1.19)	0.84 (0.60-1.18)	1.38 (0.81-2.36)	1.00 (0.45-2.22)	1.09 (0.61-1.95)
Hospital-free days	Mean Difference	0.44 (0.09, 0.78)	0.38 (0.00, 0.76)	0.57 (−0.49, 1.62)	0.49 (−0.33, 1.32)	0.48 (−0.22, 1.18)
C. difficile within 90 days	Odds Ratio	1.67 (0.94, 2.99)	1.42 (0.67-2.99)	3.07 (0.97-9.70)	2.01 (0.36-11.15)	1.51 (0.42-5.40)
Antibiotic days	Mean Difference	−4.92 (−4.97, −4.87)	−4.90 (−4.96, −4.85)	−4.94 (−5.07, −4.81)	−4.87 (−5.00, −4.74)	−4.84 (−4.94, −4.74)
Antibiotic-free days	Mean Difference	4.38 (4.08, 4.69)	4.58 (4.26, 4.90)	2.24 (1.23, 3.25)	3.44 (2.69, 4.18)	3.25 (2.69, 3.81)