Annals of Internal Medicine ORIGINAL RESEARCH

Excess Antibiotic Treatment Duration and Adverse Events in Patients Hospitalized With Pneumonia

A Multihospital Cohort Study

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Background: Randomized trials demonstrate no benefit from antibiotic treatment exceeding the shortest effective duration.

Objective: To examine predictors and outcomes associated with excess duration of antibiotic treatment.

Design: Retrospective cohort study.

Setting: 43 hospitals in the Michigan Hospital Medicine Safety Consortium.

Patients: 6481 general care medical patients with pneumonia.

Measurements: The primary outcome was the rate of excess antibiotic treatment duration (excess days per 30-day period). Excess days were calculated by subtracting each patient's shortest effective (expected) treatment duration (based on time to clinical stability, pathogen, and pneumonia classification [community-acquired vs. health care–associated]) from the actual duration. Negative binomial generalized estimating equations (GEEs) were used to calculate rate ratios to assess predictors of 30-day rates of excess duration. Patient outcomes, assessed at 30 days via the medical record and telephone calls, were evaluated using logit GEEs that adjusted for patient characteristics and probability of treatment.

Results: Two thirds (67.8% [4391 of 6481]) of patients received excess antibiotic therapy. Antibiotics prescribed at discharge accounted for 93.2% of excess duration. Patients who had respiratory cultures or nonculture diagnostic testing, had a longer stay, received a high-risk antibiotic in the prior 90 days, had community-acquired pneumonia, or did not have a total antibiotic treatment duration documented at discharge were more likely to receive excess treatment. Excess treatment was not associated with lower rates of any adverse outcomes, including death, readmission, emergency department visit, or *Clostridioides difficile* infection. Each excess day of treatment was associated with a 5% increase in the odds of antibiotic-associated adverse events reported by patients after discharge.

Limitation: Retrospective design; not all patients could be contacted to report 30-day outcomes.

Conclusion: Patients hospitalized with pneumonia often receive excess antibiotic therapy. Excess antibiotic treatment was associated with patient-reported adverse events. Future interventions should focus on whether reducing excess treatment and improving documentation at discharge improves outcomes.

Primary Funding Source: Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships program.

Ann Intern Med. 2019;171:153-163. doi:10.7326/M18-3640 **Annals.org**
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This article was published at Annals.org on 9 July 2019.

Pneumonia is the most common reason for inpatient antibiotic use and overuse (1). Historically, providers prescribed long durations of antibiotic therapy for pneumonia because of concerns that short courses could lead to disease relapse or progression (2, 3). However, recent studies, including multiple randomized controlled trials and systematic reviews, have demonstrated that shorter antibiotic therapy is safe and equally effective for most patients with pneumonia (4–9). Conversely, longer treatment places patients at risk for antibiotic-associated adverse events, *Clostridioides difficile* infection, and multidrug-resistant organisms (10–12).

To minimize harm, antibiotic stewardship guidelines recommend that hospitals "implement interventions to reduce antibiotic therapy to the shortest effective duration" (13–15). However, patients often receive excess antibiotic therapy. We used data from an ongoing cohort study of medical patients hospitalized with community-acquired pneumonia (CAP) or health care–associated pneumonia (HCAP) in 43 hospitals across Michigan to quantify excess antibiotic treatment duration, determine factors associated with it, and evaluate its relationship with outcomes.

Methods

The Michigan Hospital Medicine Safety Consortium

The Michigan Hospital Medicine Safety Consortium (HMS) is a statewide multi-institutional collaborative quality initiative sponsored by Blue Cross Blue Shield of Michigan and Blue Care Network. Its goal is to improve the quality of care for hospitalized medical patients who are at risk for adverse events. Participation in HMS is voluntary, and hospitals that join collect and share data to improve patient care and outcomes (16, 17). Of the 92 non–critical access, nonfederal hospitals in Michigan, 43 (47%) participate in HMS and share data on antibiotic use.

See also:

Editorial comment 210

In 2017, HMS began an initiative to improve antibiotic use in patients hospitalized with pneumonia. Since inception, HMS has provided hospitals with education on best practices for antibiotic prescribing and hospital-specific feedback on antibiotic use. The consortium's data collection and quality assurance procedures have been previously described (18). Briefly, trained abstractors consecutively screen patients 30 days after discharge and include the first patient who meets inclusion criteria on each day. Data are collected retrospectively from 90 days before admission until 30 days after discharge or until follow-up is terminated by a major complication (such as death). Data are collected from medical records by using a standardized data dictionary and operations manual. Patients are contacted for additional outcome data by telephone follow-up with a standardized script.

Inclusion and Exclusion Criteria

Patients were eligible for inclusion if they were adult medical patients receiving general care who were discharged between January 2017 and April 2018 with community-onset pneumonia, including CAP or HCAP (the latter involving nursing home residence, hospitalization within 90 days, intravenous chemotherapy, home wound care or infusion therapy, or long-term hemodialysis) (19). To improve specificity of pneumonia diagnostic criteria (20), patients were included only if they had all of the following: a discharge diagnostic code for pneumonia (20), symptoms and radiographs consistent with pneumonia (21), receipt of at least 4 days of antibiotic treatment (to exclude brief empirical treatment) (22), and receipt of antibiotics on day 1 or 2 of hospitalization (to exclude hospital-acquired pneumonia [pneumonia developing ≥48 hours after hospitalization]) (20). As in prior studies (23), patients who received insufficient antibiotic therapy (duration ≥2 days shorter than the shortest effective duration recommended by guidelines) were excluded because their treatment was probably stopped due to an alternative diagnosis. Patients were not eligible for inclusion if they received care in an intensive care unit or were on a ventilator at any point during hospitalization, were being treated for an additional infection unrelated to pneumonia (such as cellulitis), were pregnant, were severely immunocompromised (**Appendix**, available at Annals.org), had *Legionella* or a fungal pathogen, had a condition requiring longer antibiotic treatment (for example, bacteremia or empyema), were admitted under comfort care, or left against medical advice. For patients with multiple hospitalizations, only the first was included. Patients were included in the main analyses but were ineligible for a follow-up call if they were confirmed to have died; to be hospitalized; or to be in inpatient hospice, an extended care facility, or prison 30 days after hospital discharge.

Primary Outcome

The primary outcome was the rate of excess antibiotic treatment duration (excess days per 30-day period). Excess days were calculated by subtracting each patient's shortest effective (expected) treatment duration from the actual duration.

Consistent with national guidelines, expected antibiotic treatment duration was determined on the basis of classification of pneumonia (CAP vs. HCAP), organism, and time to clinical stability (defined as being afebrile for ≥48 hours and having ≤1 vital sign abnormality) (15, 19, 21). Patients with CAP were expected to have a treatment duration of at least 5 days, with longer courses expected only if time to clinical stability was longer (4, 21, 24). Patients with HCAP, *Staphylococcus aureus,* or a nonfermenting Gram-negative bacillus (for example, *Pseudomonas aeruginosa*) were expected to have a treatment duration of at least 7 days (details are provided in the **Appendix**) (15).

Treatment duration was defined as the sum of the number of days with inpatient antibiotics administered plus the number of days of antibiotic treatment prescribed at discharge. If patients had a positive culture result, only antibiotics that were effective against the isolated pathogen counted toward the duration. To allow for variation in the timing of antibiotic administration and to be conservative in our estimates, treatment duration was considered to be appropriate if the actual duration was within 1 day of the expected duration.

Predictor Variables

We used the following predictor variables: demographic characteristics; pneumonia severity index; receipt in prior 90 days of any intravenous antibiotic, fluoroquinolone, or linezolid (given their association with development of multidrug-resistant organisms and/or activity against methicillin-resistant *S aureus* or *Pseudomonas* species) (19, 25, 26); signs or symptoms of pneumonia on day 1 or 2 of hospitalization; days to clinical stability; length of stay; CAP versus HCAP; diagnostic testing (for example, culture, procalcitonin, or antigen testing); concurrent exacerbation of chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF); specialty of the attending physician at admission; misdiagnosis of CAP versus HCAP (for example, documentation of CAP despite identifiable risk factor for HCAP); documentation of total antibiotic treatment duration in discharge summary; number of hospital beds; hospital profit type (for example, nonprofit); and self-reported hospital academic status.

Patient Outcomes

Outcomes were collected 30 days after discharge and included death; hospital readmission; emergency department visit; and antibiotic-associated adverse events, which included *C difficile* infection, provider-documented adverse events (for example, QT prolongation), and patient-reported adverse events obtained via a scripted question during the telephone call ("Have you had any side effects from your prescribed antibiotic?"). Patients who answered "yes" were asked about symptoms, additional care, and discontinuation of antibiotic therapy.

Statistical Analysis

To evaluate individual predictors associated with rates of excess antibiotic treatment duration (excess days per 30-day period), we first performed bivariable analyses using negative binomial generalized estimating equation (GEE) models with an exchangeable correlation structure to account for hospital clustering. Coefficients were exponentiated to yield incidence rate ratios comparing rates of excess duration in different patient groups (for example, patients with HCAP vs. CAP).

We next performed multivariable analysis to determine predictors associated with rates of excess treatment duration, using a negative binomial GEE model with stepwise selection based on covariate contributions to model fit (using the Schwarz criterion) (27). Missing data for individual variables (such as race) were imputed through a 10-fold multiple imputation procedure (Markov-chain Monte Carlo) and combined using standard rules (28). Coefficients were exponentiated to yield incidence rate ratios.

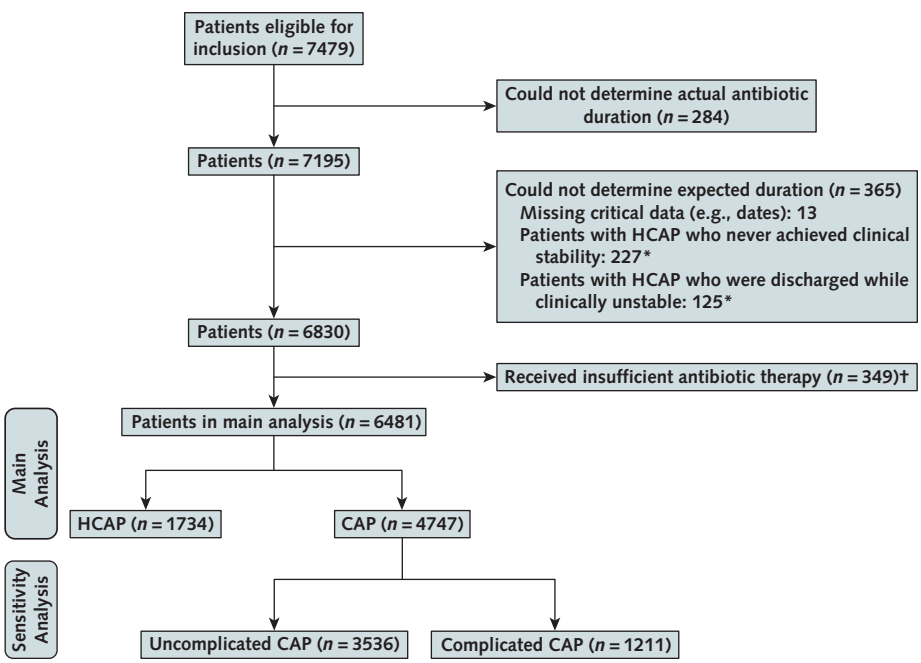
Finally, we report odds ratios (ORs) to evaluate whether days of excess treatment were associated with outcomes. Odds ratios were derived from logit GEE models with inverse probability of treatment weighting (29) by baseline covariates that were known to be associated with outcomes (**Appendix**) or were significant in the multivariable analysis model (23, 30–33). All tests were 2-sided, and a *P* value less than 0.050 was considered statistically significant. SAS, version 9.4 (SAS Institute), was used for analyses (**Appendix Table 1**, available at Annals.org)

Data are limited on whether the shortest effective treatment duration for patients with "complicated CAP" (moderate immunocompromise [**Appendix**], structural lung disease, and moderate to severe COPD) is 5 days or 7 days (6). Thus, we conducted a sensitivity analysis in which patients with complicated CAP had a shortest expected duration of 7 days. Furthermore, because clinical stability may also be defined as being afebrile for 48 hours and having no vital sign abnormalities (vs. ≤1) (34), we conducted a sensitivity analysis based on this definition. Finally, given the large number of patients who received 0 days of excess treatment, we performed sensitivity analyses that used a zero-inflated negative binomial model for the primary outcome and assessed treatment duration as a dichotomous outcome (excess vs. appropriate).

Institutional Review Board Approval

Because the purpose of HMS is to measure and improve the quality of existing care practices, this project received nonregulated status before data collection by the University of Michigan Institutional Review Board.

Figure 1. Flow diagram for patient inclusion.



For the main analysis, patients with uncomplicated and complicated CAP (moderate immune compromise, structural lung disease, or moderate to severe chronic obstructive pulmonary disease) were treated identically. In a sensitivity analysis, patients with complicated CAP had a minimum treatment duration of 7 d. CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.

* Due to lack of evidence or care guidelines, patients with HCAP were excluded if they were not clinically stable by day 7 (defined as being afebrile [temperature <37.9 °C] for ≥48 h and having ≤1 sign of clinical instability [heart rate >100 beats/min, respiratory rate >24 breaths/min, systolic blood pressure <90 mm Hg, arterial saturation <90% on room air or oxygen requirement higher than at baseline, or altered mental status higher than at baseline]) or were discharged while clinically unstable.

† Patients with a treatment duration that was ≥2 d shorter than expected were excluded because they often were found on further review to have an alternative diagnosis (e.g., viral pneumonia or heart failure exacerbation) rather than bacterial pneumonia.

Table 1. Patient Characteristics and Associations With Excess Antibiotic Treatment Duration: Bivariable Analyses

Variable	Entire Cohort (*n* = 6481)	Appropriate Duration (*n* = 2090)*	Excess Duration (*n* = 4391)†	Median Excess Days per Patient	Rate Ratio (95% CI)‡	*P* Value‡
Demographic characteristics						
White race, *n (%)*§	5146 (79.4)	1630 (78.9)	3516 (81.4)	2	0.95 (0.88–1.03)	0.21
Female, *n (%)*§	3319 (51.2)	1071 (51.2)	2248 (51.2)	2	0.97 (0.91–1.03)	0.30
Median age (IQR), *y*§	70.2 (58.4–80.8)	70.9 (59.3–81.6)	69.9 (57.9–80.3)	NA	0.98 (0.97–1.00) per 10-y increase	0.066
Median Charlson Comorbidity Index score (IQR)	3 (1–4)	3 (1–5)	2 (1–4)	2	0.99 (0.98–1.00)	0.113
Comorbidities, *n (%)*						
Renal disease	1889 (29.2)	669 (32.0)	1220 (27.8)	1	0.94 (0.88–1.01)	0.081
Liver disease	65 (1.0)	21 (1.0)	44 (1.0)	2	1.06 (0.82–1.37)	0.65
CHF	1787 (27.6)	673 (32.2)	1114 (25.4)	1	0.91 (0.85–0.97)	0.007
COPD	3010 (46.4)	984 (47.1)	2026 (46.1)	2	1.04 (0.99–1.10)	0.095
Receiving home oxygen	1047 (16.2)	392 (18.8)	655 (14.9)	1	1.03 (0.94–1.14)	0.51
Structural lung disease‖	496 (7.7)	161 (7.7)	335 (7.6)	2	1.21 (1.02–1.43)	0.030
Current or former smoker	4347 (67.1)	1428 (68.3)	2919 (66.5)	2	0.96 (0.91–1.02)	0.171
Cancer	1402 (21.6)	461 (22.1)	941 (21.4)	2	1.00 (0.94–1.06)	0.89
Immune compromise¶	365 (5.6)	126 (6.0)	239 (5.4)	2	1.08 (0.97–1.20)	0.174
Diabetes mellitus	2017 (31.1)	708 (33.9)	1309 (29.8)	2	0.97 (0.91–1.04)	0.37
Patient risk factors at admission						
Pneumonia severity index, *n (%)*§**						0.066
Class I (<50)	525 (8.1)	139 (6.7)	386 (8.8)	2	1.15 (1.02–1.29)	
Class II (51–70)	901 (13.9)	251 (12.0)	650 (14.8)	2	1.04 (0.95–1.15)	
Class III (71–90)	1332 (20.6)	418 (20.0)	914 (20.8)	2	0.98 (0.91–1.06)	
Class IV (91–130)	2545 (39.3)	863 (41.3)	1682 (38.3)	2	1.02 (0.94–1.10)	
Class V (>130)	1178 (18.2)	419 (20.0)	759 (17.3)	2	Reference	
Any sepsis, *n (%)*††	4840 (74.7)	1576 (75.4)	3264 (74.3)	2	1.02 (0.96–1.08)	0.47
Sepsis	3494 (53.9)	1144 (54.7)	2350 (53.5)	2	1.03 (0.98–1.08)	0.27
Severe sepsis	1346 (20.8)	432 (20.7)	914 (20.8)	2	0.98 (0.93–1.04)	0.54
qSOFA score ≥2 vs. <2, *n (%)*‡‡	591 (9.1)	205 (9.8)	386 (8.8)	2	0.95 (0.88–1.03)	0.188
Received high-risk antibiotic in prior 90 d, *n (%)*§§	1610 (24.8)	536 (25.6)	1074 (24.5)	2	1.04 (0.98–1.11)	0.22
Documented symptoms or signs of pneumonia on day 1 or 2 of hospitalization						
Symptoms						
Cough, *n (%)*	5646 (87.1)	1829 (87.5)	3817 (86.9)	2	1.02 (0.93–1.10)	0.72
Sputum production, *n (%)*	3438 (53.0)	1087 (52.0)	2351 (53.5)	2	1.07 (1.02–1.13)	0.010
Dyspnea, *n (%)*	5852 (90.3)	1920 (91.9)	3932 (89.5)	2	1.00 (0.93–1.09)	0.91
Median symptoms (IQR), *n*	2 (2–3)	2 (2–3)	2 (2–3)	NA	1.03 (1.00–1.07) per symptom	0.050
Signs						
Auscultator findings, *n (%)*	3731 (57.6)	1161 (55.6)	2570 (58.5)	2	1.16 (1.09–1.24)	<0.001
Abnormal leukocyte count, *n (%)*‖‖	4527 (69.9)	1446 (69.2)	3081 (70.2)	2	1.08 (1.03–1.14)	0.003
Hypoxemia, *n (%)*¶¶	2107 (32.5)	708 (33.9)	1399 (31.9)	2	1.04 (0.98–1.10)	0.22
Median signs (IQR), *n*	2 (2–3)	2 (2–3)	2 (2–3)		1.08 (1.05–1.12) per symptom	<0.001
Clinical course						
Median time to clinical stability (IQR), *d****	3 (3–4)	3 (3–4)	3 (3–4)	NA	1.02 (0.99–1.04)	0.20
Median length of stay (IQR), *d*	5 (4–6)	5 (3–6)	5 (4–6)	1 per additional day	1.03 (1.02–1.03) per additional day	0.003
Diagnosis, diagnostic testing, and concurrent disease exacerbations						
Received intravenous antibiotics on day 1 of hospitalization, *n (%)*	6385 (98.5)	2049 (98.0)	4336 (98.7)	2	1.31 (0.93–1.86)	0.122
Azithromycin	3055 (47.1)	953 (45.6)	2102 (47.9)	2	1.03 (0.97–1.09)	0.36
Ceftriaxone	1210 (19.0)	287 (13.7)	923 (21.0)	2	1.22 (1.13–1.33)	<0.001
Levofloxacin	1152 (17.8)	335 (16.0)	817 (18.6)	2	0.95 (0.87–1.04)	0.24
Pneumonia diagnosis, *n (%)*						
Uncomplicated CAP	3536 (54.6)	985 (47.1)	2551 (58.1)	2	Reference	<0.001
Complicated CAP†††	1211 (18.7)	352 (16.8)	859 (19.6)	2	1.10 (1.02–1.19)	
HCAP	1734 (26.8)	753 (36.0)	981 (22.3)	1	0.78 (0.72–0.85)	

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Table 1–Continued

Variable	Entire Cohort (*n* = 6481)	Appropriate Duration (*n* = 2090)*	Excess Duration (*n* = 4391)†	Median Excess Days per Patient	Rate Ratio (95% CI)‡	*P* Value‡
Respiratory culture or nonculture test, *n (%)*‡‡‡						
Not performed	3016 (46.5)	1061 (50.8)	1955 (44.5)	1	Reference	<0.001
Negative result	2975 (45.9)	903 (43.2)	2072 (47.2)	2	1.19 (1.12–1.26)	
Positive result	490 (7.6)	126 (6.0)	364 (8.3)	3	1.50 (1.34–1.68)	
Procalcitonin, *n (%)*						
Not performed	5606 (86.5)	1779 (85.1)	3827 (87.2)	2	Reference	0.33
Negative result	516 (8.0)	203 (9.7)	313 (7.1)	1	0.89 (0.77–1.04)	
Positive result (>0.25 ng/mL)	359 (5.5)	108 (5.2)	251 (5.7)	2	0.97 (0.86–1.09)	
CHF exacerbation, *n (%)*	488 (7.5)	198 (9.5)	290 (6.6)	1	0.84 (0.76–0.92)	<0.001
COPD exacerbation, *n (%)*	1713 (26.4)	571 (27.3)	1142 (26.0)	2	1.02 (0.96–1.09)	0.48
Provider variables						
Specialty of attending physician at admission, *n (%)*						
Hospital medicine	3676 (56.7)	1219 (58.3)	2457 (56.0)	2	Reference	0.002
Family medicine	469 (7.2)	154 (7.4)	315 (7.2)	2	1.03 (0.85–1.25)	
General medicine	2165 (33.4)	662 (31.7)	1503 (34.2)	2	1.14 (1.06–1.24)	
Other	171 (2.6)	55 (2.6)	116 (2.6)	2	1.06 (0.89–1.27)	
CAP misdiagnosed as HCAP, *n (%)*§§§	152 (2.3)	32 (1.5)	120 (2.7)	3	1.40 (1.25–1.56)	<0.001
HCAP misdiagnosed as CAP, *n (%)*§§§	346 (5.3)	161 (7.7)	185 (4.2)	1	0.68 (0.59–0.78)	<0.001
Total antibiotic treatment duration documented in discharge summary, *n (%)*	2080 (32.1)	871 (41.7)	1209 (27.5)	1	0.78 (0.70–0.87)	<0.001
Hospital variables						
Median beds (IQR), *n*	283 (158–443)	304 (186–537)	283 (139–422)	NA	1.00 (1.00–1.00)	0.082
Profit type, *n (%)*						
For-profit	409 (6.3)	121 (5.8)	288 (6.6)	2	Reference	0.65
Governmental	397 (6.1)	136 (6.5)	261 (5.9)	2	0.98 (0.66–1.46)	
Nonprofit	5675 (87.6)	1833 (87.7)	3842 (87.5)	2	1.10 (0.81–1.51)	
Self-reported academic hospital, *n (%)*	5443 (83.9)	1831 (87.6)	3612 (82.3)	2	0.83 (0.70–0.99)	0.037

CAP = community-acquired pneumonia; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HCAP = health care–associated pneumonia; IQR = interquartile range; NA = not applicable (independent variable was continuous and not associated with rate of excess treatment duration); qSOFA = quick Sequential Organ Failure Assessment.
* Actual duration was within 1 d of expected duration.
† Actual duration was >1 d longer than expected.
‡ *P* values are shown for rate ratios in bivariable models comparing rates of excess treatment duration (excess days over a 30-d period), with hospital-level clustering accounted for. Covariates were not adjusted.
§ Proportions vary because of missing data on sex (*n* = 3), age (*n* = 1), race (*n* = 95), and pneumonia severity index (*n* = 31).
‖ Bronchiectasis, pulmonary fibrosis, or interstitial lung disease.
¶ Includes patients with HIV and CD4 count >0.200 × 10^9 cells/L, chemotherapy in prior 30 d, ≥10 mg of prednisone per day (or equivalent) for ≥30 d, congenital or acquired immunodeficiency, or systemic immune suppression (e.g., treatment with biologic, cyclosporine, or azathioprine).
** Includes age, sex, comorbidities, vital sign and laboratory abnormalities, and pleural effusion on imaging. Higher scores indicate more severe disease.
†† Sepsis was defined as ≥2 of the following: temperature >38 °C or <36 °C, heart rate >90 beats/min, respiratory rate >20 breaths/min, and leukocyte count >12 × 10^9 cells/L or <4 × 10^9 cells/L or >10% immature bands. Severe sepsis was defined as sepsis plus evidence of organ dysfunction, defined as any of the following: systolic blood pressure <90 mm Hg, lactate level >2 mmol/L, international normalized ratio >1.5 (in patients not receiving anticoagulation), platelet count <100 × 10^9 cells/L, bilirubin level >2 mg/dL, or creatinine level >2 mg/dL (without documentation of moderate or severe chronic kidney disease).
‡‡ One point for each of 3 criteria: systolic blood pressure <100 mm Hg, respiratory rate >22 breaths/min, and Glasgow Coma Scale score <15.
§§ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid, given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.
‖‖ >10 × 10^9 cells/L or <4 × 10^9 cells/L or presence of >15% immature granulocytes.
¶¶ Arterial saturation <90%, Po_2 <60 mm Hg on room air, or oxygen requirement higher than at baseline.
*** Includes only patients who achieved clinical stability, defined as being afebrile (temperature <37.9 °C) for ≥48 h and having ≤1 sign of clinical instability (heart rate >100 beats/min, respiratory rate >24 breaths/min, systolic blood pressure <90 mm Hg, arterial saturation <90% on room air or oxygen requirement higher than at baseline, or mental status altered from baseline).
††† Defined as presence of moderate immune compromise, structural lung disease, or moderate to severe COPD.
‡‡‡ Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
§§§ Patients were considered misdiagnosed if the provider documented CAP but there was ≥1 identifiable risk factor for HCAP (nursing home residence, hospitalization within 90 d, intravenous chemotherapy, home wound care or infusion therapy, or long-term hemodialysis) or if the provider documented HCAP in the absence of identifiable risk factors.

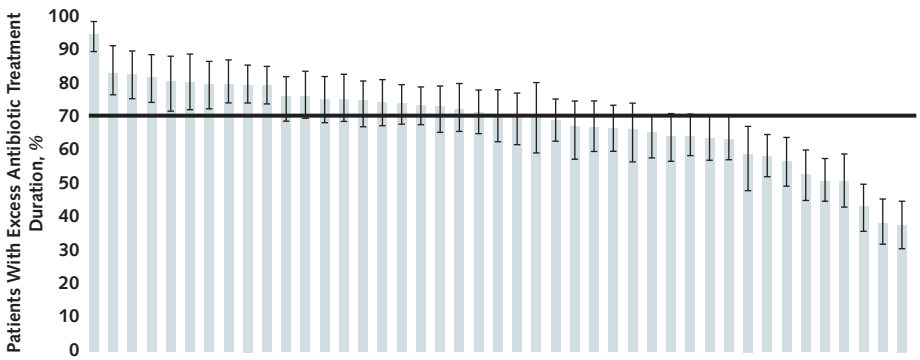
Role of the Funding Source

The funder had no role in the design or conduct of the study; collection, management, analysis, or interpretation of data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

RESULTS

A total of 6481 (86.7%) of 7479 eligible patients were included (**Figure 1**), among whom 4747 (73.2%) had CAP and 1734 (26.8%) had HCAP. More than half (51.2% [3319 of 6481]) were women, and the median age was 70.2 years (interquartile range [IQR], 58.4 to

Figure 2. Proportion of patients with excess antibiotic treatment duration, by hospital (n = 43).



Each bar represents 1 hospital. Error bars represent 95% CIs. The horizontal line represents the mean proportion of patients (70.8%) with an excess treatment duration.

80.8 years). Most (57.4% [3723 of 6481]) had severe pneumonia (pneumonia severity index class IV or V); 26.4% (1713 of 6481) had a concurrent COPD exacerbation, and 7.5% (488 of 6481) had a concurrent CHF exacerbation. Most patients (77.8% [5039 of 6481]) had at least 1 blood culture done, 32.3% (2095 of 6481) had at least 1 respiratory culture done, and 15.9% (1028 of 6481) had at least 1 nonculture diagnostic test done. Only 7.6% (490 of 6481) had a bacterial pathogen identified, most commonly *Streptococcus pneumoniae* (1.2% [78 of 6481]). Most patients improved quickly, with 86.7% (5616 of 6481) clinically stable or discharged by day 5 (**Table 1**).

Excess Treatment Duration

Two thirds (67.8% [4391 of 6481]) of patients received antibiotics for longer than the shortest effective duration consistent with guidelines (71.8% [3410 of 4747] for CAP and 56.6% [981 of 1734] for HCAP). The median duration was 8 days (IQR, 7 to 11 days) overall, 8 days (IQR, 7 to 10 days) for CAP, and 9 days (IQR, 7 to 11 days) for HCAP. The median excess duration was 2 days (IQR, 0 to 4 days) overall, 2 days (IQR, 0 to 4 days) for CAP, and 1 day (IQR, 0 to 3 days) for HCAP. This led to 2526 excess days of treatment per 1000 patients hospitalized with pneumonia. The percentage of patients (±SE) who received excess treatment varied from 38.1% ± 3.7% to 95.0% ± 2.3% among hospitals (**Figure 2**).

Prescribing at Discharge

Antibiotics prescribed at discharge accounted for 49.5% (28 947 of 58 473) of total days with antibiotic therapy and 93.2% (15 262 of 16 373) of excess days. Although patients with CAP and those with HCAP had different expected treatment durations at discharge, prescribed durations were similar (**Figure 3**). Nearly all patients (99.6% [6452 of 6481]) had an expected duration of 5 or fewer days at discharge, yet the most common duration prescribed at discharge was 5 days.

The most common antibiotics prescribed at discharge were fluoroquinolones (typically levofloxacin), which accounted for 31.3% (2032 of 6491) of discharge prescriptions and 39.3% (6441 of 16 373) of excess days, followed by azithromycin and amoxicillin–clavulanate. Only a third of patients (32.1% [2080 of 6481]) had a total treatment duration documented in their discharge summary.

Factors Associated With Excess Treatment

Patient characteristics associated with rates of excess treatment duration in bivariable models are shown in **Table 1**. The rate of excess duration was 7% higher in patients who had sputum production than in those who did not (rate ratio, 1.07 [95% CI, 1.02 to 1.13]). Although number of hospital beds and hospital profit status were not associated with excess treatment duration, the rate of excess treatment at hospitals with self-reported academic status was lower than among those not identifying as academic (rate ratio, 0.83 [CI, 0.70 to 0.99]).

In the multivariable analysis, having a respiratory culture (positive or negative result) or a nonculture diagnostic test, a longer hospital stay, high-risk antibiotic use in the prior 90 days, and CAP and not having total treatment duration documented in the discharge summary were associated with higher rates of excess treatment (**Table 2**; **Appendix Table 2**, available at Annals.org).

Patient Outcomes

After adjustment, excess treatment duration was not associated with 30-day mortality, readmission, or emergency department visit (**Table 3**; **Appendix Table 3**, available at Annals.org). Although excess duration was not associated with *C difficile* infection or provider-documented adverse events, odds of a patient-reported adverse event (among patients contacted by telephone) were 5% (CI, 2% to 8%) greater for each excess day of treatment.

Most patients (91.7% [5943 of 6481]) were eligible to receive a telephone call at 30 days. Of these, 60.4% (3592 of 5943) were reached. **Appendix Table 4** (available at Annals.org) compares patients who were reached with those who were not. Diarrhea, gastrointestinal distress, and mucosal candidiasis were the most common antibiotic-associated adverse events reported by patients (**Appendix Table 5**, available at Annals.org). Patients who reported an antibiotic-

associated adverse event were more likely to answer "yes" to the question "Did you go to the doctor for the side effect?" if they had received excess (38% [43 of 114]) versus appropriate (31% [8 of 26]) antibiotic treatment ($P = 0.003$) (**Appendix Table 6**, available at Annals.org).

Sensitivity Analyses

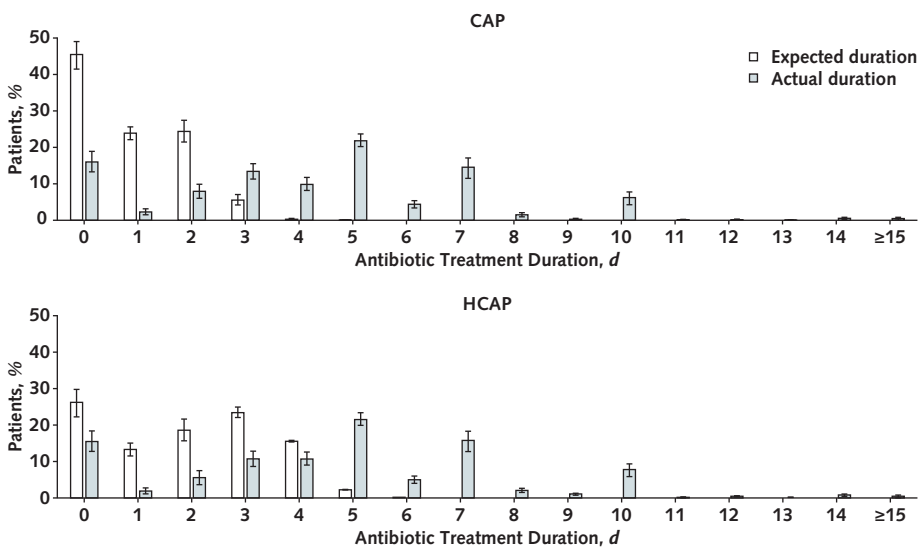
In the sensitivity analysis in which patients with complicated CAP (18.7% [1211 of 6481]) had at least 7 days of antibiotic treatment, slightly fewer patients (64.9% [4042 of 6224]) received excess treatment. Predictors of rates of excess treatment duration were similar to those in the main analysis (**Appendix Table 7**, available at Annals.org), and days of excess treatment remained associated with patient-reported adverse events (OR, 1.06 [CI, 1.03 to 1.09]). In a sensitivity analysis in which clinical stability was defined as being afebrile for 48 hours and having no vital sign abnormalities, an additional 972 patients were excluded (946 who received insufficient treatment and 26 who never achieved clinical stability or were discharged while unstable). Of those remaining, slightly fewer (65.6% [3615 of 5509]) received excess treatment. Predictors of excess treatment duration were similar to those in the primary analysis (**Appendix Table 8**, available at Annals.org). Days of excess treatment remained associated with patient-reported adverse events (OR, 1.05 [CI, 1.01 to 1.10]). Findings were similar in sensitivity analyses that used zero-inflated models (**Appendix Table 9**, available at Annals.org) and assessed treatment duration as a dichotomous outcome (**Appendix Table 10**, available at Annals.org).

Discussion

In this study of more than 6000 patients with pneumonia at 43 hospitals, two thirds received an excess antibiotic treatment duration, largely due to excessive prescribing at discharge. Specifically, a diagnosis of CAP predicted excess treatment despite randomized trials demonstrating that most patients with CAP can be treated with 5 days of antibiotics. Our findings add to growing evidence that shorter-course antibiotic therapy is safe—excess treatment was not associated with lower rates of any adverse clinical outcomes but was associated with higher rates of patient-reported adverse events after discharge. Together, these findings provide evidence that reducing excessive antibiotic treatment durations, especially in patients with CAP via discharge stewardship, is safe and may improve patient care.

Consistent with prior studies, we found that the vast majority of patients with CAP receive an excess antibiotic therapy duration (4, 6, 23, 35). In our study, this was not explained by differences in clinical stability or disease severity. Indeed, most patients with CAP (86.7%) stabilized quickly and thus were candidates for 5 days of therapy, yet fewer than 24.7% received 5 (±1) days of therapy. We did not find that misdiagnosis of CAP as HCAP explained excess treatment duration in patients with CAP; rather, providers seemed to treat both diseases with similar durations. Providers may not differentiate between CAP and HCAP because of the national movement away from the latter term or the difficulty with risk stratification at the point of care. One contribution to the low rate of 5-day treatment

Figure 3. Expected vs. actual antibiotic treatment duration after discharge for hospitalized patients with CAP (*top*) and HCAP (*bottom*) ($n = 6481$).



Although CAP and HCAP have different distributions of expected treatment durations after discharge, patients with CAP and those with HCAP were treated similarly at discharge, which may explain why those with CAP were more likely to have an excess duration. Expected durations after discharge were calculated on the basis of classification of pneumonia (CAP vs. HCAP), time to clinical stability (defined as being afebrile [temperature <37.9 °C] for ≥48 h and having ≤1 vital sign abnormality), and treatment duration during hospitalization. Actual treatment duration after discharge was the duration prescribed at discharge. Error bars represent 95% CIs. CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.

Table 2. Variables Associated With Excess Antibiotic Treatment Duration: Multivariable Analysis (n = 6481)*

Variable	Predicted Excess Days per Patient	Adjusted Rate Ratio (95% CI)†	*P* Value†
Respiratory culture or nonculture test‡			
Not performed (n = 3016 [46.5%])	2.1	Reference	<0.001
Negative result (n = 2975 [45.9%])	2.5	1.15 (1.09–1.23)	
Positive result (n = 490 [7.6%])	3.2	1.49 (1.33–1.68)	
Length of hospital stay (per 1-d increase)	0.2	1.02 (1.02–1.02)	<0.001
Documentation of total antibiotic treatment duration in discharge summary			
No (n = 4401 [67.9%])	2.9	Reference	<0.001
Yes (n = 2080 [32.1%])	2.3	0.78 (0.70–0.87)	
Received high-risk antibiotic in 90 d before hospitalization§			
No (n = 4871 [75.2%])	2.5	Reference	<0.001
Yes (n = 1610 [24.8%])	2.9	1.17 (1.10–1.25)	
Pneumonia diagnosis			
HCAP (n = 1734 [26.8%])	2.2	Reference	<0.001
CAP (n = 4747 [73.2%])	3.2	1.43 (1.32–1.55)	

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.
* Variables associated with rates of excess antibiotic treatment duration (number of excess days over a 30-d period) and their rate ratios are shown for the multivariable model determined using stepwise selection, accounting for clustering by hospital, and simultaneously adjusted for all variables in the first column. The predicted numbers of excess days per patient represent the population marginal means when all covariates were held constant at their respective means.
† *P* values are shown for rate ratios from covariates in the multivariable model comparing rates of excess treatment duration (number of excess days over a 30-d period), with hospital-level clustering accounted for and simultaneous adjustment for all variables in the first column.
‡ Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
§ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid, given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

may be the lack of explicit recommendations in the 2007 CAP guidelines to use the shortest effective duration (21). Because some studies have evaluated antibiotic treatment durations as short as 1 to 3 days (9), we may be conservative in our estimates of excess duration.

We found certain patient characteristics to be predictive of excess treatment duration. For example, a longer hospital stay predicted excess therapy, potentially indicating more severe disease or hesitation among providers to stop antibiotic therapy while patients are hospitalized. Similar to prior studies (6, 23), we found that nearly half of patients did not have respiratory testing despite being hospitalized, potentially due to difficulty in producing a quality sputum sample or because prior guidelines did not universally recommend testing (21, 36). Patients who did have testing, especially with positive results, were more likely to receive excess treatment (6, 23). Diagnostic testing may reflect greater concern about severe disease or (for respiratory cultures) more sputum production, both of which may drive longer antibiotic treatment. In addition, providers may await final culture results before stopping therapy. We also found that providers were more likely to treat patients excessively if they had received a high-risk antibiotic before hospitalization, perhaps reflecting concern about outpatient failure or higher risk for resistant organisms. Of note, documentation of antibiotic treatment duration in the discharge summary was associated with lower rates of excess duration. It is unclear whether hospitals with better documentation are more likely to appropriately treat patients (for example, due to stewardship initiatives) or whether documentation itself triggers a mindful moment that leads to improved treatment duration (37). Regardless, documentation is a core stewardship strategy (1), and hospitals should strive to improve it, particularly at discharge. That academic hospitals had lower rates of excess treatment merits additional exploration. Academic hospitals have more institutional support for stewardship and follow more of the Centers for Disease Control and Prevention's recommendations (38), which may explain this difference. Furthermore, differences in antibiotic stewardship interventions related to treatment duration could contribute to hospital variation (7).

In our study, nearly all excess therapy (93.2%) resulted from antibiotics prescribed at discharge. This highlights an urgent and unmet need for "discharge stewardship," or coordinated interventions to improve antibiotic prescribing at discharge. It is notable that only 18% of patients received 0 or 1 day of antibiotics after discharge despite it being expected for 61.6%. Instead, the clock seemed to restart, given that 44.7% received full antibiotic courses (5, 7, or 10 days) after discharge. Increasing use of short-course therapy at discharge may require multimodal interventions to change prescriber behavior and culture (39).

Our study found that excess antibiotic treatment duration was not associated with mortality, readmission, or emergency department visits as it was previously believed to be. However, it was associated with higher odds of patient-reported adverse events. This adds to growing literature that short-course therapy in

pneumonia is safe and that longer durations are not just unnecessary but potentially harmful. Therefore, reducing excess treatment durations should be a top priority for antibiotic stewardship nationally. Furthermore, patients may have been more likely to seek additional medical care for adverse events if they received excess treatment. Though it is unclear whether such visits were truly preventable, this may have resulted in additional costs. The difference in antibiotic-associated adverse events reported by patients and those documented by physicians suggests that full capture of adverse events requires both mechanisms.

Our study has limitations. First, it was an observational study and therefore could not prove causation. Second, because we did not know exact times of antibiotic administration, we considered durations within 1 day of expected to be appropriate and thus may have underestimated excess durations. Third, although we used terminology and duration guidelines as currently defined (19), guidelines may be moving away from the concept of HCAP as a distinct entity. The 2016 hospital-acquired and ventilator-associated pneumonia guidelines purposefully did not address HCAP, deferring recommendations to the upcoming CAP guidelines (15). Furthermore, because data addressing the effectiveness of 5-day treatment for HCAP are scarce, some of our patients with HCAP who were excluded because of shorter-than-expected durations may have received appropriate therapy. Fourth, we depended on provider documentation, which may underestimate adverse events. Studies using physician review found antibiotic-associated adverse events in up to 20% of hospitalized patients (10). Fifth, patient-reported adverse events are subject to recall bias and incorrect reporting. Whether reported physician visits represented increased use is unclear because we were unable to verify outpatient visits. Sixth, although we had data on receipt of intravenous antibiotics, fluoroquinolones, and linezolid before admission, we did not have full data on antibiotics received before admission, which could affect inpatient prescribing patterns. Finally, although antibiotic treatment duration has been linked to antibiotic resistance (40, 41), we were unable to evaluate the association between them.

Strengths of our study include its large size and its comprehensive assessment of excess antibiotic treatment duration. We included academic and nonacademic hospitals of varying size, increasing external validity and adding to prior studies that were limited to single health care systems or used administrative data to estimate excess duration (23, 35). Second, we had detailed patient data abstracted by trained abstractors, which allowed us to more confidently assess appropriateness and confounders. Third, we assessed discharge prescribing, which is often difficult to link to inpatient prescribing. Finally, we contacted nearly 60% of patients after discharge, allowing us to identify outcomes not typically captured in observational studies (10).

Our findings have implications for policy and research efforts. First, we found that excess antibiotic treatment duration was not associated with improved

Table 3. Association of Excess Antibiotic Treatment Duration With 30-Day Adverse Outcomes (n = 6481)*

Outcomes at 30 Days	Appropriate Duration (n = 2090), n (%)†	Excess Duration (n = 4391), n (%)‡	Unadjusted OR per Excess Day (95% CI)§	Unadjusted P Value§	Adjusted OR per Excess Day (95% CI)§	Adjusted P Value§
Mortality‖	40 (1.9)	88 (2.0)	0.99 (0.94–1.03)	0.52	1.01 (0.97–1.05)	0.60
Readmission‖	294 (14.1)	497 (11.3)	0.99 (0.96–1.02)	0.48	1.00 (0.98–1.03)	0.92
Emergency department visit‖	238 (11.4)	480 (10.9)	0.97 (0.94–1.00)	0.021	0.98 (0.95–1.01)	0.166
Antibiotic-associated adverse event¶	72 (3.4)	210 (4.8)	1.04 (1.01–1.07)	0.012	1.03 (1.00–1.06)	0.038
Clostridioides difficile infection**	11 (0.5)	22 (0.5)	0.92 (0.81–1.05)	0.21	0.93 (0.81–1.07)	0.30
Provider-documented††‡‡	43 (2.1)	87 (2.0)	1.00 (0.94–1.05)	0.86	0.99 (0.94–1.05)	0.85
Patient-reported††§§	26/1132 (2.3)	114/2460 (4.6)	1.05 (1.02–1.08)	<0.001	1.05 (1.02–1.08)	0.001
Composite adverse outcome‖	499 (23.9)	897 (20.4)	0.98 (0.96–1.00)	0.078	0.99 (0.97–1.01)	0.40

OR = odds ratio.
* Outcomes were collected via the medical record and a follow-up telephone call at 30 d, and their associations with number of excess days of antibiotic treatment are shown. Outcomes were adjusted for hospital clustering, were inverse probability of treatment weighted, and were adjusted for known predictors of the outcome of interest (see footnotes below).
† Actual duration was within 1 d of expected duration.
‡ Actual duration was >1 d longer than expected.
§ OR and P values relate to patient outcomes at 30 d (dependent variable) per day of excess treatment duration (continuous independent variable).
‖ Also adjusted for health care–associated pneumonia diagnosis, age, nursing home residence before hospitalization, pneumonia severity index score, Charlson Comorbidity Index score, chronic obstructive pulmonary disease exacerbation, congestive heart failure exacerbation, and length of stay.
¶ Also adjusted for age, history of antibiotic use and number of antibiotics, obesity, inflammatory bowel disease, receipt of chemotherapy, gastric tube, proton-pump inhibitor use, length of stay, Charlson Comorbidity Index score, and sex.
** Also adjusted for age, history of antibiotic use and number of antibiotics, obesity, inflammatory bowel disease, receipt of chemotherapy, gastric tube, proton-pump inhibitor use, and length of stay. Patients were considered to have developed *C difficile* infection if they had a positive test result for *C difficile* on day 3 or later of hospitalization; if they had a readmission, emergency department visit, or outpatient visit related to *C difficile* infection in the 30 d after the index hospitalization; or if they reported during their telephone call that they had been diagnosed with *C difficile* infection.
†† Also adjusted for age, Charlson Comorbidity Index score, and sex.
‡‡ Includes any adverse event documented in the medical record as being caused by an antibiotic (e.g., allergic reaction).
§§ Proportions shown are among patients who were able to be reached by telephone. Of those who were eligible for a telephone call, 60.4% of patients were reached (3592 of 5943 [58.8% {1132 of 1924} with appropriate duration and 61.2% {2460 of 4019} with excess duration]; P = 0.21). Patients were considered to have had an antibiotic-associated adverse event if they answered "yes" to the question, "Have you had any side effects from your prescribed antibiotic?" during their 30-d postdischarge call.

patient outcomes, which should increase comfort with prescribing shorter-course treatment. Specifically, the next iteration of CAP and HCAP guidelines should explicitly recommend (rather than imply) that providers prescribe the shortest effective duration, similar to recommendations made in the hospital-acquired and ventilator-associated pneumonia guidelines (15). Furthermore, excess antibiotic treatment duration may be associated with adverse events and care seeking, which warrants further evaluation. We also found that excess antibiotic prescribing continues despite national efforts to contain it. Future improvement may be more effective by focusing on discharge stewardship, including antibiotic documentation at discharge, and on patients with high rates of overuse, such as those with CAP. Given that discharge prescriptions account for a large proportion of overuse, national use metrics should incorporate antibiotics prescribed at discharge.

In conclusion, most patients hospitalized with pneumonia are treated with antibiotics for longer than necessary. Excess antibiotic treatment duration was associated with patient-reported adverse events after discharge. Further study is warranted to assess whether excess treatment duration in patients hospitalized with pneumonia may be reduced by improving antibiotic use and documentation at discharge.

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Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect those of the Centers for Disease Control and Prevention or the position or policy of the Department of Veterans Affairs.

Financial Support: Support for the Michigan Hospital Medicine Safety Consortium is provided by Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network as part of the BCBSM Value Partnerships program.

Disclosures: Dr. Flanders reports personal fees for expert testimony, grants from Blue Cross Blue Shield of Michigan and the Agency for Healthcare Research and Quality, and personal fees from Wiley Publishing outside the submitted work. Dr. Chopra reports grants from Blue Cross Blue Shield of Michigan during the conduct of the study and royalties from Wolters Kluwer Publishing and Oxford University Press, personal fees from universities and medical centers for visiting professorships, and personal fees for serving as an expert witness outside the submitted work. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M18-3640.

Reproducible Research Statement: *Study protocol:* Available from Dr. Vaughn (e-mail, valmv@med.umich.edu). *Statistical code:* Available from Ms. Snyder (e-mail, amsn@med.umich.edu). *Data set:* Not available.

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Appendix: Additional Information

Expected Antibiotic Treatment Duration

For all patients:

- If respiratory culture result was positive, only antibiotics effective against the isolated pathogen counted toward actual duration.
- If a respiratory culture grew *S aureus* or a nonfermenting, Gram-negative bacillus (such as *Pseudomonas*), the minimum expected duration was 7 days.

CAP: Minimum expected duration was 5 days (4, 21, 25).

- If, by day 5 of hospitalization, the patient had been afebrile for 48 hours and had no more than 1 sign of clinical instability, expected duration was 5 days (4, 21, 25).
- If the patient became afebrile for 48 hours with no more than 1 sign of clinical instability after day 5 (for example, hospital day 6), expected duration was that day (6 days) (4, 21, 25).
- For patients discharged without having been afebrile for 48 hours or having no more than 1 sign of clinical instability, we assumed clinical stability at discharge. Thus:
  - If, on the day of discharge, the patient either had been febrile or had more than 1 sign of clinical instability, expected duration was 5 days or length of stay plus 2 days (whichever was greater).
  - If, on the day of discharge, the patient had been febrile on the prior day but was afebrile on the day of discharge, expected duration was 5 days or length of stay plus 1 day (whichever was greater).

HCAP: Minimum expected duration was 7 days (24).

- If, by day 6 of hospitalization, the patient had been afebrile for 48 hours and had no more than 1 sign of clinical instability, expected duration was 7 days (19).
- On the basis of guideline suggestions that longer durations may be indicated in patients who have a slower rate of improvement (19), patients discharged on day 6 without having been afebrile for 48 hours or having no more than 1 sign of clinical instability had an expected duration of 10 days.
- Patients who had not been afebrile for 48 hours or continued to have more than 1 sign of clinical instability by day 6 of hospitalization (when vital sign collection stopped) were excluded due to insufficient data on how to manage them. Similarly, patients discharged before day 6 who had more than 1 sign of clinical instability on the day of discharge or had not been afebrile for 48 hours were excluded.

Variables Used to Control for Patient Outcomes

For mortality, readmission, emergency department visit, and the composite adverse outcome, we controlled for HCAP diagnosis, age, nursing home use before hospitalization, pneumonia severity index, Charl-

son Comorbidity Index score, COPD exacerbation, CHF exacerbation, and length of stay (23). For *C difficile* infection, we controlled for age, history of antibiotic use and number of antibiotics, obesity, inflammatory bowel disease, receipt of chemotherapy, presence of gastric tube, proton-pump inhibitor use, and length of stay (31, 33, 34). For antibiotic-associated adverse drug events (patient- or physician-reported), we controlled for age, Charlson Comorbidity Index score, and sex (32). For overall antibiotic-associated adverse events, we adjusted for age, history of antibiotic use and number of antibiotics, obesity, inflammatory bowel disease, receipt of chemotherapy, gastric tube, proton-pump inhibitor use, length of stay, Charlson Comorbidity Index score, and sex (31–34).

Definitions

Moderate immune compromise: HIV with CD4 count above 0.200×10^9 cells/L, chemotherapy within 30 days, treatment for leukemia or lymphoma within 6 months, long-term steroid use (≥10 mg of prednisone per day or equivalent), use of a biologic agent (such as a tumor necrosis factor inhibitor), or presence of a congenital or acquired immunodeficiency (for example, asplenia, nephrotic syndrome, or renal transplant >1 year prior).

Severe immune compromise: AIDS (CD4 count $<0.200 \times 10^9$ cells/L), neutropenia (absolute neutrophil count $\leq 0.500 \times 10^9$ cells/L), history of solid organ or bone marrow transplant, or receipt of 2 or more immunosuppressive agents.

Appendix Table 1. Statistical Appendix

Method	10-Fold Multiple Imputation (Markov-Chain Monte Carlo)	Inverse Probability Weighting	Negative Binomial GEE Model With Stepwise Selection	Calculation of Predicted Excess Days	Zero-Inflated Negative Binomial GEE Model	Logistic GEE Model
Program	SAS 9.4	SAS 9.4	SAS 9.4	SAS 9.4	SAS 9.4	SAS 9.4
Command	Proc mi	Proc genmod with `weight' statement	Proc hpgenselect with selection method= stepwise (choose=sbc)	Proc genmod with lsmeans, estimate statement	Proc genmod	Proc genmod
Description	The Proc mi command in SAS was used with the Markov-chain Monte Carlo method to impute missing values. All variables considered as bivariate predictors were included in the imputation model. Ten multiply imputed data sets were created, with results from each combined in all subsequent analyses.	Proc logistic was used to construct a propensity score for the probability of excess treatment using potential confounding variables for each outcome. Each patient was then weighted by the reciprocal of their predicted probability of excess treatment, derived from the propensity score and normalized to the sample mean. This weight was then used in the `weight' statement of the Proc genmod command for each outcome.	Proc hpgenselect was used for stepwise variable selection in the negative binomial GEE model. This model considered all candidate predictors and used the Schwarz Bayesian criteria to choose the covariates for the final multivariable model. An exchangeable correlation structure was used for SE estimation.	Using the model identified in the stepwise selection for the negative binomial GEE model, the lsmeans statement was added to Proc genmod to calculate the population marginal means when all covariates were held constant at their respective means.	Using variables identified in the stepwise selection for the negative binomial GEE model, Proc genmod was used, with a logistic and negative binomial mixture GEE model with exchangeable correlation structure for the probability of excess treatment and number of excess days, respectively.	Using variables identified in the stepwise selection for the negative binomial GEE model, Proc genmod was used, using a logistic GEE model with exchangeable correlation structure for the probability of excess treatment.

GEE = generalized estimating equation.

Appendix Table 2. Variables Associated With Excess Antibiotic Treatment Duration: Unexponentiated Coefficients Corresponding to Multivariable Analysis in Table 2 (n = 6481)*

Variable	Estimate (95% CI)
Respiratory culture or nonculture test†	
Not performed	Reference
Negative result	0.143 (0.082 to 0.205)
Positive result	0.401 (0.285 to 0.518)
Length of hospital stay (per 1-d increase)	0.022 (0.019 to 0.024)
Documentation of antibiotic treatment duration in discharge summary	
No	Reference
Yes	−0.250 (−0.358 to −0.142)
Received high-risk antibiotic in 90 d before hospitalization‡	
No	Reference
Yes	0.160 (0.099 to 0.221)
Pneumonia diagnosis	
HCAP	Reference
CAP	0.359 (0.276 to 0.441)

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.

* Variables associated with rates of excess antibiotic treatment duration (excess days over a 30-d period) and their unexponentiated parameter estimates are shown for the multivariable model determined using stepwise selection and accounting for clustering by hospital.

† Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.

‡ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

Appendix Table 3. Covariate Balance After Propensity Score Weighting

Covariate	Appropriate Duration		Excess Duration		*P* Value	Standardized Mean Difference
	Mean (±SE)	Percentage	Mean (±SE)	Percentage		
Pneumonia diagnosis						
Uncomplicated CAP	–	55.0	–	55.2	0.90	−0.006
Complicated CAP*	–	18.7	–	18.8	0.93	−0.004
HCAP	–	26.5	–	26.1	0.87	0.008
Age	68.6 ± 0.6	–	68.0 ± 0.6	–	0.56	−0.743
Admitted from nursing home	–	1.5	–	1.6	0.93	−0.006
Pneumonia severity index†	97.5 ± 1.2	–	97.1 ± 1.4	–	0.84	−0.392
Charlson Comorbidity Index score	3.6 ± 0.1	–	3.6 ± 0.1	–	0.90	−0.048
CHF exacerbation	–	7.8	–	7.3	0.68	0.021
COPD exacerbation	–	25.7	–	24.7	0.69	0.024
Length of stay	5.7 ± 0.6	–	5.4 ± 0.1	–	0.50	−0.493
Sputum production	–	51.9	–	52.9	0.72	−0.021
Auscultator findings	–	57.2	–	58.8	0.75	−0.033
Abnormal leukocyte count‡	–	69.4	–	69.7	0.85	−0.008
Respiratory culture or nonculture test§						
Not performed	–	44.3	–	42.5	0.69	0.035
Negative result	–	46.4	–	47.7	0.73	−0.027
Positive result	–	8.1	–	7.9	0.87	0.007

CAP = community-acquired pneumonia; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HCAP = health care–associated pneumonia.
* Defined as presence of moderate immune compromise, structural lung disease, and moderate to severe COPD.
† Includes age, sex, comorbidities, vital sign and laboratory abnormalities, and pleural effusion on imaging. Higher scores indicate more severe disease.
‡ $>10 \times 10^9$ cells/L or $<4 \times 10^9$ cells/L or presence of >15% immature granulocytes.
§ Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.

Appendix Table 4. Characteristics of Patients Eligible for Follow-up Telephone Call at 30 Days Who Were Contacted Versus Those Who Were Unable to Be Contacted: Bivariable Analyses (n = 5943)

Variable	Unable to Be Contacted (n = 2351)	Contacted (n = 3592)	*P* Value*
Excess antibiotic treatment duration, *n (%)*†	1557 (66.2)	2460 (68.5)	0.069
White race, *n (%)*‡	1791 (77.6)	2913 (82.1)	<0.001
Female, *n (%)*‡	1181 (50.2)	1897 (52.9)	0.048
Median age (IQR), *y*‡	68.7 (56.4–80.0)	69.9 (58.5–79.9)	0.067
Median Charlson Comorbidity Index score (IQR)	3 (1–4)	2 (1–4)	0.45
Comorbidities, *n (%)*			
Renal disease	667 (28.4)	1011 (28.2)	0.86
Liver disease	32 (1.4)	27 (0.8)	0.023
CHF	594 (25.3)	973 (27.1)	0.125
COPD	1062 (45.2)	1700 (47.3)	0.105
Receiving home oxygen	336 (14.3)	593 (16.5)	0.021
Structural lung disease§	156 (6.6)	303 (8.4)	0.011
Current or former smoker	1551 (66.0)	2465 (68.6)	0.034
Cancer	473 (20.1)	793 (22.1)	0.075
Immune compromise‖	120 (5.1)	215 (6.0)	0.167
Diabetes mellitus	701 (29.8)	1129 (31.4)	0.196
Pneumonia severity index, *n (%)*‡¶			0.040
Class I (<50)	207 (8.8)	309 (8.6)	
Class II (51–70)	357 (15.2)	520 (14.5)	
Class III (71–90)	465 (19.8)	804 (22.4)	
Class IV (91–130)	900 (38.3)	1399 (38.9)	
Class V (>130)	422 (17.9)	560 (15.6)	
Any sepsis, *n (%)***	1758 (74.8)	2693 (75.0)	0.88
Sepsis	1254 (53.3)	2002 (55.7)	0.070
Severe sepsis	504 (21.4)	691 (19.2)	0.040
qSOFA score ≥2 vs. <2, *n (%)*††	239 (10.2)	277 (7.7)	0.001
Received high-risk antibiotic in prior 90 d, *n (%)*‡‡	533 (22.7)	915 (25.5)	0.014
Documented symptoms on day 1 or 2 of hospitalization			
Cough, *n (%)*	2056 (87.5)	3192 (88.9)	0.098
Sputum production, *n (%)*	1212 (51.6)	2027 (56.4)	<0.001
Dyspnea, *n (%)*	2122 (90.3)	3258 (90.7)	0.57
Median symptoms (IQR), *n*	2 (2–3)	3 (2–3)	<0.001
Documented signs on day 1 or 2 of hospitalization			
Auscultator findings, *n (%)*	1409 (59.9)	2027 (56.4)	0.008
Abnormal leukocyte count, *n (%)*§§	1628 (69.2)	2530 (70.4)	0.33
Hypoxemia, *n (%)*‖‖	737 (31.3)	1195 (33.3)	0.120
Median signs (IQR), *n*	2 (2–3)	2 (2–3)	0.84
Median time to clinical stability (IQR), *d*¶¶	3 (3–4)	3 (3–4)	0.48
Median length of stay (IQR), *d*	5 (4–6)	4 (3–6)	0.150
Received intravenous antibiotics on day 1 of hospitalization, *n (%)*	2317 (98.6)	3539 (98.5)	0.927
Azithromycin	1047 (44.5)	1818 (50.6)	<0.001
Ceftriaxone	414 (17.6)	713 (19.9)	0.031
Levofloxacin	428 (18.2)	625 (17.4)	0.427
Pneumonia diagnosis, *n (%)*			<0.001
Uncomplicated CAP	1324 (56.3)	2026 (56.4)	
Complicated CAP***	396 (16.8)	744 (20.7)	
HCAP	631 (26.8)	822 (22.9)	
Respiratory culture or nonculture test, *n (%)*†††			0.001
Not performed	1139 (48.4)	1580 (44.0)	
Negative result	1043 (44.4)	1732 (48.2)	
Positive result	169 (7.2)	280 (7.8)	
Procalcitonin, *n (%)*			0.067
Not performed	2184 (92.9)	3279 (91.3)	
Negative result	96 (4.1)	190 (5.3)	
Positive result (>0.25 ng/mL)	71 (3.0)	123 (3.4)	
CHF exacerbation, *n (%)*	160 (6.8)	272 (7.6)	0.27
COPD exacerbation, *n (%)*	580 (24.7)	1025 (28.5)	0.001
Specialty of attending physician at admission, *n (%)*			0.037
Hospital medicine	1283 (54.6)	2081 (57.9)	
Family medicine	175 (7.4)	252 (7.0)	
General medicine/other	893 (38.0)	1259 (35.1)	

Continued on following page

Appendix Table 4–Continued

Variable	Unable to Be Contacted (n = 2351)	Contacted (n = 3592)	*P* Value*
CAP misdiagnosed as HCAP, *n (%)*‡‡‡	55 (2.3)	73 (2.0)	0.43
HCAP misdiagnosed as CAP, *n (%)*‡‡‡	133 (5.7)	181 (5.0)	0.30
Total antibiotic treatment duration documented in discharge summary, *n (%)*	743 (31.6)	1163 (32.4)	0.53
Median beds (IQR), *n*	283 (139–443)	304 (186–443)	<0.001
Profit type, *n (%)*			<0.001
For-profit	212 (9.0)	160 (4.5)	
Governmental	150 (6.4)	194 (5.4)	
Nonprofit	1989 (84.6)	3238 (90.1)	
Self-reported academic hospital, *n (%)*	1985 (84.4)	3034 (84.5)	0.97

CAP = community-acquired pneumonia; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; HCAP = health care–associated pneumonia; IQR = interquartile range; qSOFA = quick Sequential Organ Failure Assessment.
* *P* values are shown for bivariable testing (χ^2 test for categorical variables, *t* test for normally distributed continuous variables, and Wilcoxon rank-sum test for nonnormally distributed continuous variables).
† Actual duration >1 d more than expected.
‡ Proportions vary because of missing data on sex (n = 3), age (n = 1), race (n = 95), and pneumonia severity index (n = 31).
§ Bronchiectasis, pulmonary fibrosis, or interstitial lung disease.
‖ Includes patients with HIV and CD4 count >0.200 × 10^9 cells/L, chemotherapy in prior 30 d, ≥10 mg of prednisone per day (or equivalent) for ≥30 d, congenital or acquired immunodeficiency, or systemic immune suppression (e.g., treatment with biologic, cyclosporine, or azathioprine).
¶ Includes age, sex, comorbidities, vital sign and laboratory abnormalities, and pleural effusion on imaging. Higher scores indicate more severe disease.
** Sepsis was defined as ≥2 of the following: temperature >38 °C or <36 °C, heart rate >90 beats/min, respiratory rate >20 breaths/min, and leukocyte count >12 × 10^9 cells/L or <4 × 10^9 cells/L or >10% immature bands. Severe sepsis was defined as sepsis plus evidence of organ dysfunction, defined as any of the following: systolic blood pressure <90 mm Hg, lactate level >2 mmol/L, international normalized ratio >1.5 (in patients not receiving anticoagulation), platelet count <100 × 10^9 cells/L, bilirubin level >2 mg/dL, or creatinine level >2 mg/dL (without documentation of moderate or severe chronic kidney disease).
†† One point for each of 3 criteria: systolic blood pressure <100 mm Hg, respiratory rate >22 breaths/min, and Glasgow Coma Scale score <15.
‡‡ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid, given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.
§§ >10 × 10^9 cells/L or <4 × 10^9 cells/L or presence of >15% immature granulocytes.
‖‖ Arterial saturation <90%, Po_2 <60 mm Hg on room air, or oxygen requirement higher than at baseline.
¶¶ Includes only patients who achieved clinical stability, defined as being afebrile (temperature <37.9 °C) for ≥48 h and having ≤1 sign of clinical instability (heart rate >100 beats/min, respiratory rate >24 breaths/min, systolic blood pressure <90 mm Hg, arterial saturation <90% on room air or oxygen requirement higher than at baseline, or mental status altered from baseline).
*** Defined as presence of moderate immune compromise, structural lung disease, or moderate to severe COPD.
††† Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
‡‡‡ Patients were considered misdiagnosed if the provider documented CAP but there was ≥1 identifiable risk factor for HCAP (nursing home residence, hospitalization within 90 d, intravenous chemotherapy, home wound care or infusion therapy, or long-term hemodialysis) or if the provider documented HCAP but there were no identifiable risk factors for it.

Appendix Table 5. Provider-Documented and Patient-Reported Antibiotic-Associated Adverse Events, by Antibiotic Treatment Duration (n = 270)*

Outcome	Provider-Documented (n = 130)		Patient-Reported (n = 140)	
	Appropriate Duration (n = 43)	Excess Duration (n = 87)	Appropriate Duration (n = 26)	Excess Duration (n = 114)
Diarrhea	6 (14)	18 (21)	11 (42)	57 (50)
Gastrointestinal distress	4 (9)	8 (9)	4 (15)	19 (17)
Mucosal (vaginal or oral) candidiasis	2 (5)	4 (5)	8 (31)	14 (12)
Rash (not otherwise specified)	19 (44)	28 (32)	1 (4)	15 (13)
Neurologic (e.g., mental status changes, headache)	2 (5)	4 (5)	2 (8)	11 (10)
Angioedema or facial swelling	0 (0)	3 (3)	0 (0)	2 (2)
Itching	9 (21)	11 (13)	0 (0)	2 (2)
Hives	3 (7)	10 (11)	1 (4)	0 (0)
Tendinitis	0 (0)	1 (1)	0 (0)	1 (1)
Trouble breathing	1 (2)	2 (2)	0 (0)	1 (1)
QT prolongation or cardiac arrhythmia	4 (9)	4 (5)	0 (0)	0 (0)
Drug rash with eosinophilia and systemic symptoms	1 (2)	2 (2)	0 (0)	0 (0)
Anaphylaxis	0 (0)	2 (2)	0 (0)	0 (0)
Fever	1 (2)	1 (1)	0 (0)	0 (0)
Intravenous catheter site reaction	1 (2)	3 (3)	0 (0)	0 (0)
Redman syndrome	2 (5)	2 (2)	0 (0)	0 (0)
Renal failure	0 (0)	2 (2)	0 (0)	0 (0)
Leukopenia	0 (0)	1 (1)	0 (0)	0 (0)
Liver abnormalities	0 (0)	1 (1)	0 (0)	0 (0)
Other	0 (0)	2 (2)	0 (0)	1 (1)

* Data are numbers (percentages). Patients could have >1 adverse event. Patients were considered to have an appropriate antibiotic treatment duration if the actual duration was within 1 d of the expected duration.

Appendix Table 6. Follow-up Questions for Patients Reporting an Adverse Event (n = 140)

Question	Patients Answering "Yes," *n (%)*		Odds Ratio per Excess Day of Antibiotic Treatment (95% CI)	*P* Value
	Appropriate Duration (n = 26)*	Excess Duration (n = 114)		
"Did you go to the doctor for the side effect?"	8 (31)	43 (38)	1.16 (1.05–1.28)	0.003
If yes, "Did the doctor change or stop your antibiotics because of this side effect?"	8 (100)	43 (100)	–	
"Did you take your entire antibiotic course as directed?"	22 (85)	99 (87)	0.91 (0.82–1.01)	0.088

* Patients were considered to have an appropriate antibiotic treatment duration if the actual duration was within 1 d of the expected duration.

Appendix Table 7. Sensitivity Analysis of Variables Associated With Excess Antibiotic Treatment Duration When Patients With Complicated CAP Had a Minimum Expected Duration of 7 Days: Multivariable Analysis (n = 6224)*

Variable	Adjusted Rate Ratio (95% CI)	*P* Value
Respiratory culture or nonculture test†		
Not performed (n = 2902 [46.6%])	Reference	<0.001
Negative result (n = 2846 [45.7%])	1.15 (1.08–1.22)	
Positive result (n = 476 [7.6%])	1.63 (1.43–1.85)	
Length of hospital stay (per 1-d increase)	1.03 (1.03–1.03)	<0.001
Documentation of antibiotic treatment duration in discharge summary		
No (n = 4233 [68.0%])	Reference	<0.001
Yes (n = 1991 [32.0%])	0.77 (0.69–0.87)	
Received high-risk antibiotic in 90 d before hospitalization‡		
No (n = 4645 [74.6%])	Reference	<0.001
Yes (n = 1579 [25.4%])	1.19 (1.12–1.27)	
Pneumonia diagnosis		
HCAP (n = 1734 [27.9%])	Reference	<0.001
Complicated CAP (n = 954 [15.3%])	1.00 (0.86–1.16)	
Uncomplicated CAP (n = 3536 [56.8%])	1.43 (1.32–1.55)	

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.
* Variables associated with rates of excess antibiotic treatment duration (excess days over a 30-d period) and their rate ratios are shown for the adjusted multivariable model in which patients who had complicated CAP (moderate immune compromise, structural lung disease, and moderate to severe chronic obstructive pulmonary disease) had an expected minimum treatment duration of 7 d. An additional 257 patients were excluded because of insufficient treatment duration (≥2 d shorter than expected), leaving 6224 patients. Overall, results are similar to the primary analysis. Rate ratios were simultaneously adjusted for all variables in the first column.
† Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
‡ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid, given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

Appendix Table 8. Sensitivity Analysis of Variables Associated With Excess Antibiotic Treatment Duration When Clinical Stability Was Defined as Being Afebrile for 48 Hours and Having No Vital Sign Abnormalities: Multivariable Analysis (n = 5509)*

Variable	Adjusted Rate Ratio (95% CI)	*P* Value
Respiratory culture or nonculture test†		
Not performed (n = 2554 [46.4%])	Reference	<0.001
Negative result (n = 2579 [46.8%])	1.11 (1.03–1.20)	
Positive result (n = 376 [6.8%])	1.40 (1.20–1.63)	
Length of hospital stay (per 1-d increase)	1.00 (1.00–1.01)	<0.001
Documentation of antibiotic treatment duration in discharge summary		
No (n = 3741 [67.9%])	Reference	<0.001
Yes (n = 1768 [32.1%])	0.77 (0.69–0.87)	
Received high-risk antibiotic in 90 d before hospitalization‡		
No (n = 4318 [78.4%])	Reference	<0.001
Yes (n = 1191 [21.6%])	1.19 (1.11–1.29)	
Pneumonia diagnosis		
HCAP (n = 1036 [18.8%])	Reference	<0.001
CAP (n = 4473 [81.2%])	1.31 (1.18–1.46)	

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.
* Variables associated with rates of excess antibiotic treatment duration (excess days over a 30-d period) and their rate ratios are shown for the multivariable model determined using stepwise selection and accounting for clustering by hospital. Compared with the primary analysis, 972 patients were excluded (946 had insufficient treatment duration [≥2 d shorter than expected] and 26 never achieved clinical stability or were discharged while clinically unstable). Rate ratios were simultaneously adjusted for all variables in the first column.
† Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
‡ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid given that these are associated with increased risk for development of multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

Appendix Table 9. Sensitivity Analysis of Variables Associated With Excess Antibiotic Treatment Duration: Zero-Inflated Multivariable Analysis (n = 6481)*

Variable	Adjusted Rate Ratio (95% CI)†	*P* Value†
Respiratory culture or nonculture test‡		
Not performed (n = 3016 [46.5%])	Reference	<0.001
Negative result (n = 2975 [45.9%])	1.10 (1.04–1.17)	
Positive result (n = 490 [7.6%])	1.39 (1.25–1.54)	
Length of hospital stay (per 1-d increase)	1.02 (1.01–1.03)	<0.001
Documentation of antibiotic treatment duration in discharge summary		
No (n = 4401 [67.9%])	Reference	<0.001
Yes (n = 2080 [32.1%])	0.83 (0.78–0.88)	
Received high-risk antibiotic in 90 d before hospitalization§		
No (n = 4871 [75.2%])	Reference	<0.001
Yes (n = 1610 [24.8%])	1.16 (1.08–1.24)	
Pneumonia diagnosis		
HCAP (n = 1734 [26.8%])	Reference	0.001
CAP (n = 4747 [73.2%])	1.13 (1.05–1.22)	

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.
* Variables associated with presence of excess antibiotic treatment duration (excess days over a 30-d period) and their rate ratios are shown for the zero-inflated multivariable model determined using stepwise selection and accounting for clustering by hospital. Rate ratios were simultaneously adjusted for all variables in the first column.
† *P* values are shown for rate ratios from covariates in the multivariable model comparing rates of excess treatment duration (excess days over a 30-d period), with hospital-level clustering accounted for.
‡ Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
§ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid given that these are associated with increased risk for development of multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

Appendix Table 10. Sensitivity Analysis of Variables Associated With Dichotomized Antibiotic Treatment Duration: Multivariable Analysis (n = 6481)*

Variable	Adjusted Odds Ratio (95% CI)†	*P* Value†
Respiratory culture or nonculture test‡		
Not performed (n = 3016 [46.5%])	Reference	<0.001
Negative result (n = 2975 [45.9%])	1.26 (1.11–1.42)	
Positive result (n = 490 [7.6%])	1.60 (1.28–2.01)	
Length of hospital stay (per 1-d increase)	1.00 (1.00–1.01)	0.138
Documentation of antibiotic treatment duration in discharge summary		
No (n = 4401 [67.9%])	Reference	<0.001
Yes (n = 2080 [32.1%])	0.60 (0.50–0.71)	
Received high-risk antibiotic in 90 d before hospitalization§		
No (n = 4871 [75.2%])	Reference	0.002
Yes (n = 1610 [24.8%])	1.26 (1.09–1.46)	
Pneumonia diagnosis		
HCAP (n = 1734 [26.8%])	Reference	<0.001
CAP (n = 4747 [73.2%])	2.20 (1.89–2.55)	

CAP = community-acquired pneumonia; HCAP = health care–associated pneumonia.
* Variables associated with antibiotic treatment duration (dichotomized as excess vs. appropriate) and their odds ratios are shown for the multivariable model determined using stepwise selection and accounting for clustering by hospital. Rate ratios were simultaneously adjusted for all variables in the first column.
† *P* values are shown for odds ratios from covariates in the multivariable model comparing rates of excess treatment duration (excess days over a 30-d period), with hospital-level clustering accounted for.
‡ Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.
§ Includes any intravenous antibiotic, any fluoroquinolone, or linezolid given that these are associated with increased risk for development of multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.