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Length of Antibiotic Therapy Among Adults Hospitalized with Uncomplicated Community-Acquired Pneumonia, 2013–2020

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Abstract

Objective: The 2014 United States National Strategy for Combating Antibiotic-Resistant Bacteria aimed to reduce inappropriate inpatient antibiotic use by 20% for monitored conditions, such as community-acquired pneumonia (CAP), by 2020. We evaluated annual trends in length of therapy (LOT) in adults hospitalized with uncomplicated CAP from 2013–2020.

Methods: We conducted a retrospective cohort study among adults with a primary diagnosis of bacterial or unspecified pneumonia using International Classification of Diseases 9th and 10th revision codes in MarketScan[®] and Centers for Medicare & Medicaid Services databases. We included patients with length of stay (LOS) of 2–10 days, discharged home with self-care, and not re-hospitalized in the 3 days following discharge. We estimated inpatient LOT based on LOS from the PINC AI Healthcare Database. Total LOT was calculated by summing estimated inpatient LOT and actual post-discharge LOT. We examined trends from 2013–2020 in patients with total LOT >7 days, which was considered an indicator of likely excessive LOT.

Results: There were 44,976 and 400,928 uncomplicated CAP hospitalizations among patients 18–64 years and ≥65 years, respectively. From 2013 to 2020, the proportion of patients with total LOT >7 days decreased by 25% (68% to 51%) among patients 18–64 years, and by 27% (68% to 50%) among patients ≥65 years.

Conclusions: While likely excessive LOT for uncomplicated CAP patients decreased since 2013, the proportion of patients treated with LOT >7 days still exceeded 50% in 2020. Antibiotic stewardship programs should continue to pursue interventions to reduce likely excessive LOT for common infections.

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Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

No conflicts of interests for all authors.

Keywords

community-acquired pneumonia; hospitalization; length of antibiotic therapy; antibiotic stewardship; pneumonia

Background

Antibiotic stewardship is a key component of the United States (U.S.) National Strategy for Combating Antibiotic-Resistant Bacteria. The 2014 National Strategy aimed to reduce inappropriate hospital antibiotic use for monitored conditions by 20% by 2020 [1]. Since community-acquired pneumonia (CAP) is one of the most common indications for hospital antibiotic use, it is a focus of antibiotic stewardship interventions [2, 3]. One important stewardship goal for CAP is reducing excessive treatment duration, which is often driven by prescribing at the time of hospital discharge. Current clinical practice guidelines recommend “that antibiotic therapy be continued until the patient achieves clinical stability and for no less than a total of 5 days” [4, 5]. While longer durations of therapy may be recommended for specific clinical scenarios, length of therapy (LOT) of more than 7 days or more than 3 days after clinical stability is rarely necessary for patients with CAP [5].

A study by Yi, et al. used national data from MarketScan and the Centers for Medicare & Medicaid Services (CMS) to examine LOT among adults hospitalized with uncomplicated CAP in 2012–2013 [6]. They found the median LOT was 9.5 days, and more than 70% of patients exceeded the recommended duration of antibiotics. In this study, we used data from a large nationwide cohort of acute care hospitals to update the analysis by Yi et al. and determine whether duration of antibiotic therapy for adult patients hospitalized with CAP improved from 2013 through 2020.

Methods

We conducted a retrospective cohort study using administrative data (i.e. MarketScan Commercial Claims and Encounters files and the CMS database) to evaluate LOT annual trends among adults hospitalized with CAP and discharged in 2013 through 2020. We identified the study cohort and calculated LOT using methods described previously by Yi, et al. [6] where CAP hospitalizations were identified by selecting patients with a primary diagnosis of bacterial or unspecified pneumonia using International Classification of Disease 9th and 10th revision (ICD-9-CM and ICD-10-CM) codes (supplementary table S1). We included patients with no hospitalizations in the 30 days prior to index hospitalization. To restrict the cohort to patients with uncomplicated CAP, we limited the population to patients with hospitalization lengths of stay (LOS) of 2–10 days, discharged home with self-care, and not re-hospitalized in the 3 days following index discharge. As we were unable to evaluate clinical stability directly, discharge home with self-care was used as a surrogate for clinical improvement. We also excluded patients with underlying conditions or complications that could potentially require extended LOT including patients with diagnoses of cystic fibrosis, human immunodeficiency virus (HIV), or sickle cell anemia, and patients with a post-discharge antibiotic prescription that exceeded 28 days. If patients had multiple

eligible hospitalizations >30 days apart during the study period, then one hospitalization was selected at random for inclusion in the study cohort.

Patients were stratified into 2 demographic cohorts: those aged 18–64 years with private insurance and those aged ≥65 years with Medicare. For the 18–64 years cohort, MarketScan Commercial Claims and Encounters files were used to obtain LOS of the index hospitalization and post-discharge LOT. Patients in this cohort consisted of those enrolled in private insurance with outpatient drug coverage. For the ≥65 years cohort, the 100% Medicare claims and Part D event files from the CMS database were used to obtain index hospitalization LOS and post-discharge LOT. Patients in this ≥65 years cohort included those with traditional fee-for-service Parts A and B plus Part D Medicare coverage.

As MarketScan and CMS claims data do not contain inpatient antibiotic use, we implemented previously validated methods [6], and estimated inpatient days of antibiotic use using linear regression prediction models to derive LOT based on LOS. Inpatient LOT was modeled as a function of LOS for both demographic cohorts using data from the PINC AI Healthcare Database (PHD). The PHD is a comprehensive electronic healthcare database from approximately 1,000 private and academic hospitals, representing approximately 20% of U.S. inpatient discharges—but does not include data by which to derive post-discharge LOT as do MarketScan and CMS databases. The PHD includes all charges accumulated during a hospitalization, including pharmacy products. Patient discharge information such as diagnosis and procedure codes, patient demographics, and facility characteristics were also included. Patients included in the PHD models were limited to the same inclusion criteria as the study cohorts. Using LOS as a categorical predictor, prediction tables of mean inpatient LOT for each cohort and year were developed. LOS in the PHD is reported as whole days, however antibiotic therapy may be given on partial days of admission and/or discharge; therefore, it is plausible for LOT to exceed LOS in some instances. We assessed goodness of fit for each model using the R^2 value.

Using MarketScan and CMS databases, antibiotic prescriptions filled in an outpatient setting 1 day prior to 3 days following discharge were included in post-discharge LOT. If a patient had multiple prescriptions filled during this period, the post-discharge LOT was counted as the number of days with at least one prescription from earliest fill date through the latest supply through date. Total LOT was calculated by summing estimated inpatient LOT (from PHD) and actual post-discharge LOT (from MarketScan and CMS.).

The primary measure of interest was the proportion of uncomplicated CAP patients with likely excessive duration of antibiotic therapy. As clinical practice guidelines suggest >7 days LOT for uncomplicated CAP is rarely necessary [5], we interpreted total LOT >7 days as likely excessive duration. Post-discharge LOT >3 days of therapy was also considered possibly excessive since patient LOS (at least 2 days) plus 3 days of post-discharge therapy should be a patient-specific approximation of recommended LOT of at least 5 days. To estimate temporal trends in the proportion of patients with likely excessive LOT over the study period, we implemented logistic regression models, adjusting for age, sex, discharge year and quarter, region, and intensive care unit (ICU) stay. Lastly, we measured the proportion of total median LOT due to post-discharge LOT. We estimated temporal changes

over the study period using median regression models adjusting for age, sex, discharge year, and quarter. P-values less than 0.05 were considered statistically significant.

This activity was reviewed by CDC and was consistent with applicable federal law and CDC policy (See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq). Data management and analyses were conducted using SAS, version 9.4 (SAS Institute Inc., Cary, North Carolina).

Results

There were 45,089 and 400,928 uncomplicated CAP patients aged 18–64 and ≥ 65 years, respectively, included in the study cohorts (Supplementary Figure S1). Demographic and hospitalization characteristics are described in Table 1. Median (Q1–Q3) LOS was 3 (2–5) days for both cohorts. Patients in both cohorts were similar in their receipt of outpatient care in the 30 days prior to CAP hospitalization and number of post-discharge prescriptions.

There were 227,969 discharges included from PHD to estimate inpatient LOT. Patient and hospitalization characteristics of discharges included in the PHD models were similar to the MarketScan and CMS cohorts (Supplementary Figure S2, Table S2). Predicted inpatient LOTs were generated for each value of LOS stratified by cohort and year (Supplementary Figure S3, Table S3). The R^2 value of these predictions ranged from 0.69–0.80 for all age groups and years. Based on these models, the estimated median (Q1–Q3) inpatient LOT for ages 18–64 years was 3.5 (2.6–5.4) days in 2013 and 3.7 (2.7–4.6) days in 2020. Among patients aged ≥ 65 years the estimated median (Q1–Q3) inpatient LOT was 3.4 (3.4–5.3) days in 2013 and 3.6 (2.7–4.6) days in 2020 (Supplementary Table S4).

In patients 18–64 years, the median (Q1–Q3) post-discharge LOT was 6.0 (3.0–7.0) days in 2013 and 4.6 (2.0–7.0) days in 2020. Among patients ≥ 65 years the median (Q1–Q3) post-discharge LOT for was 5.0 (3.0–7.0) days in 2013 and 5.0 (2.0–7.0) days in 2020. From 2013 to 2020, the median total LOT decreased in both cohorts; from 9.6 (7.5–12.4) to 8.6 (6.7–10.7) among patients 18–64 years, and from 9.5 (7.4–11.4) to 7.7 (6.6–10.5) days among patients ≥ 65 years (Supplementary Table S4).

The mean total LOT decreased from 9.8 to 8.8 among patients 18–64 years, and from 9.6 to 8.6 among patients ≥ 65 years, which was driven primarily by post-discharge LOT decreases (Figure 1). After adjusting for patient and hospital characteristics, the proportion of total LOT comprised by post-discharge LOT decreased by 10% from 2016 to 2020 among patients 18–64 years ($p<.0001$); similarly, the proportion of post-discharge LOT in patients ≥ 65 years decreased by 8% from 2016 to 2020 ($p<.0001$) (Supplementary Table S5).

Overall, the presence of any post-discharge antibiotic prescription increased as the LOS decreased; there were also higher proportions of patients with no post-discharge prescriptions among those with longer LOS. Beginning in 2017, the proportion of patients with one post-discharge prescription declined, as the proportion of patients with 2 or more prescriptions increased (Supplementary Table S6 and S7).

After adjusting for patient and hospitalization characteristics, the proportion of patients with likely excessive antibiotic therapy decreased significantly in both cohorts ($p<.0001$). Among patients 18–64 years, there was a relative decrease of 14% over the study period in post-discharge LOT > 3 days, from 73% in 2013 to 63% in 2020. The proportion of patients 65 years with post-discharge LOT > 3 days had a relative decrease of 16%, from 73% in 2013 to 62% in 2020. The proportion of patients 18–64 years with total LOT > 7 days had a relative decrease of 25%, from 68% in 2013 to 51% in 2020; among patients 65 years, there was a relative decrease of 27% from 68% in 2013 to 50% in 2020 (Figure 2).

Discussion

In this study, the total LOT for adult patients hospitalized with uncomplicated CAP decreased from 2013 to 2020. Among patients 18–64 years and 65 years, likely excessive total LOT had a relative decrease of 25% and 27% respectively, exceeding the National Strategy target reduction of 20%. There were also relative reductions in the proportion of patients with likely excessive post-discharge LOT: 14% among patients 18–64 years, and 16% among patients 65 years. However, despite these declines, half of patients with uncomplicated CAP were treated with LOT > 7 days in 2020, and almost two-thirds (62%–63%) of patients were treated with likely excessive post-discharge antibiotic therapy in 2020.

An assessment of appropriateness of antimicrobial use in U.S. hospitals highlighted that treatment was unsupported in 80% of patients with CAP, commonly due to excessive duration of therapy[7]. Excessive duration of antibiotic therapy has been associated with adverse events in patients hospitalized with pneumonia[8]. A recent meta-analysis highlighted that each additional day of antibiotic therapy is associated with 4% increased odds of experiencing an adverse event[9]. Thus, optimizing treatment duration is an important focus for hospital antibiotic stewardship programs[3, 10, 11]. Studies have found that stewardship interventions improved adherence to clinical guidelines for patients hospitalized with CAP [12–14]. Syndrome-focused antibiotic stewardship interventions for CAP have been shown to have a sustained impact on prescribing practices[11].

Previous studies have indicated that prolonged antibiotic therapy among CAP hospitalizations is often the result of excessive post-discharge therapy [8, 15–17]. In this analysis, the proportion of total LOT represented by post-discharge prescribing was stable from 2013–2016, and then decreased from 2016–2020. This suggests that reductions in total LOT may have been driven by the reductions in post-discharge prescribing in more recent years. Declines in inpatient LOT were most apparent in the 3rd quartile of the inpatient LOT distribution. As inpatient LOT is largely driven by LOS, any decreases in inpatient LOT may be due to factors influencing LOS.

A 2022 study evaluating antibiotic stewardship strategies for optimizing therapy at hospital discharge found discharge-specific strategies may have the greatest impact on lowering antibiotic overuse at discharge [18]. A single-center study implementing a pharmacist-driven antibiotic timeout at discharge found the intervention was feasible and decreased inappropriate antibiotic use[19]. Another pharmacist-driven transition of

care model implemented in multiple facility types was also associated with improved antibiotic prescribing at discharge[20]. Resources developed for this pharmacist-driven intervention can be modified to optimize practice models and workflow at discharge in different community and academic hospital settings[21]. Most stewardship programs rely on manual assessments of appropriateness to define and target specific conditions for improvement. Leveraging the hospital electronic health record data for automated assessments of appropriateness can enable monitoring of prescribing practices, providing feedback to prescribers, and ensuring sustainability of stewardship interventions.

There were several limitations with the use of claims data for this analysis. We used ICD-9 and ICD-10 codes to identify patients with CAP, so there was potential misclassification without confirming diagnosis with clinical data. While the ICD-9 codes for CAP diagnoses have been found to have good sensitivity (84%) and positive predictive value (92%)[22], sensitivity and positive predictive values using ICD-10 codes to identify pneumonia in older adults were lower, 74% and 79% respectively[23]. Additionally, the transition from ICD-9 to ICD-10 codes could have further impacted the misclassification of patients with CAP; however, there were no substantial fluctuations in the data between 2015 and 2016 when the ICD codes transition occurred. We used discharge to home as a surrogate for clinical stability, which may have mischaracterized a patient's health status. We used insurance claims data to identify outpatient antibiotic utilization so could not capture discharge antibiotic prescriptions obtained without using the outpatient prescription drug benefit. Despite our intended focus on CAP, we may not have excluded all patients with pneumonia associated with prior hospitalization using these data sources, though previous work [6] has shown that using our definitions, its likely only a small portion of patients would be misclassified as CAP. Furthermore, the proportion of patients with hemodialysis or long-term care facility residence in our cohorts was low, 4% and 1% respectively. While we excluded patients with cystic fibrosis, HIV, and sickle cell anemia, we did not have access to microbiology data, and did not exclude all risk factors for complicated CAP that might warrant prolonged treatment, such as presence of another infection. Previous work has shown that these conditions are rare and should not account for overall long LOT in our large cohort. Patients without health insurance, or with insurance but without drug coverage were not included in this cohort, thus these data may not be fully representative of the U.S. population. Additionally, the definition of uncomplicated CAP and data source requirements resulted in a high exclusion rate, so it is possible the study population is not representative of all patients with CAP. Lastly, we included 2020 data in the analysis to observe how LOT may have changed among inpatients with uncomplicated CAP during the first year of the COVID-19 pandemic. However, it is important to note that the pandemic had a marked effect on the US healthcare system and may have affected diagnosis or treatment practices for uncomplicated CAP, as well potential identification of CAP patients in the 2020 cohort.

While likely excessive LOT for uncomplicated CAP patients has decreased since 2013, the proportion of patients treated with LOT > 7 days still exceeded 50% in 2020. The high proportion of patients with likely excessive post-discharge LOT demonstrates the need for antibiotic stewardship to optimize prescribing at hospital discharge. Antibiotic stewardship programs should continue to pursue interventions to reduce excessive LOT for common infections.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

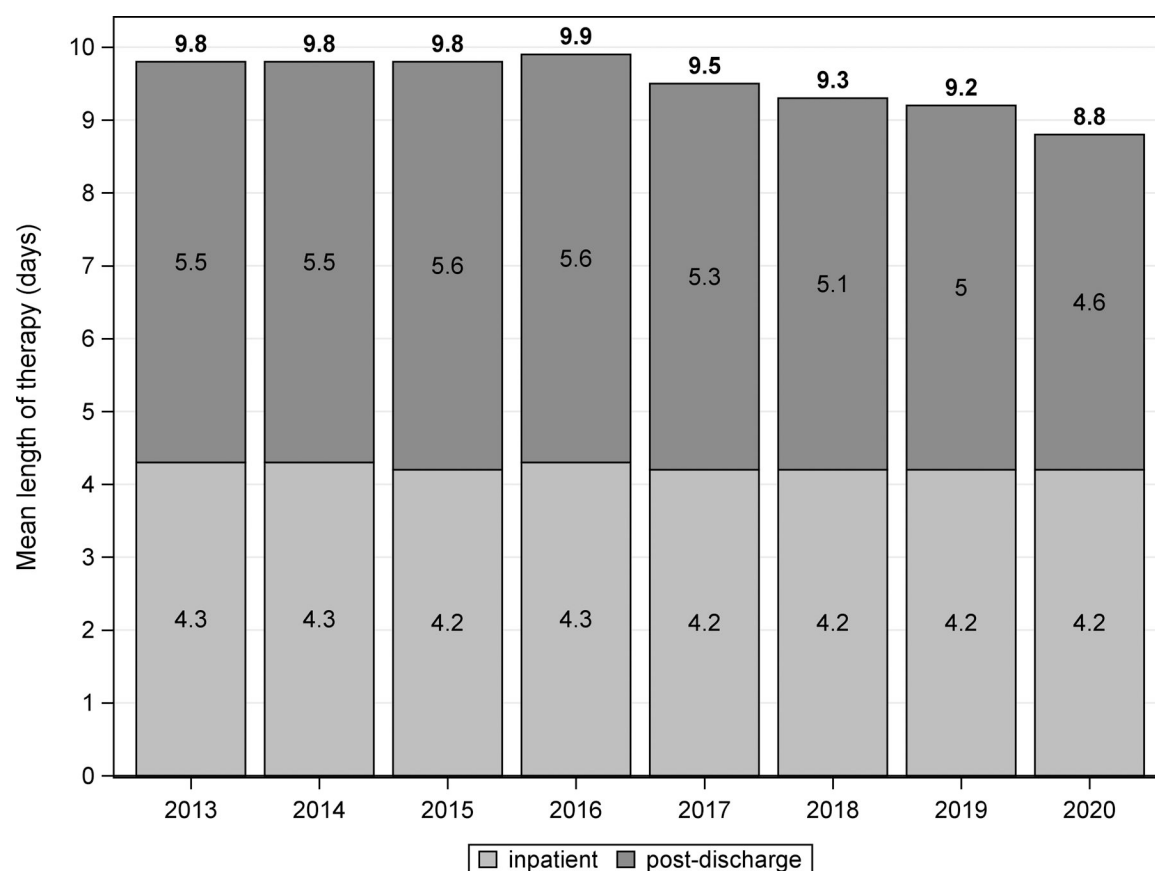
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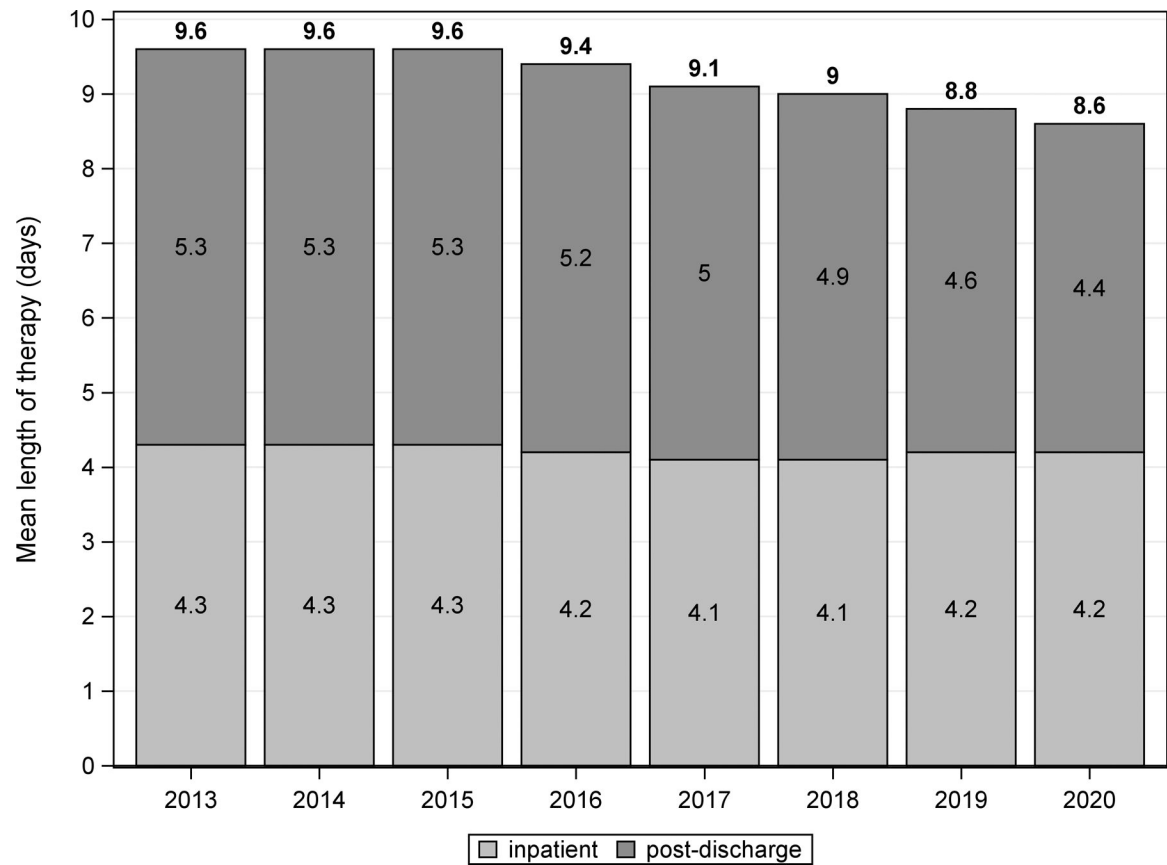


Figure 1.

Mean length of antibiotic therapy among adults hospitalized for uncomplicated community-acquired pneumonia, 2013–2020

- a. 18–64 years, MarketScan Commercial Claims and Encounters database
- b. 65 years, Centers for Medicare & Medicaid Services databases

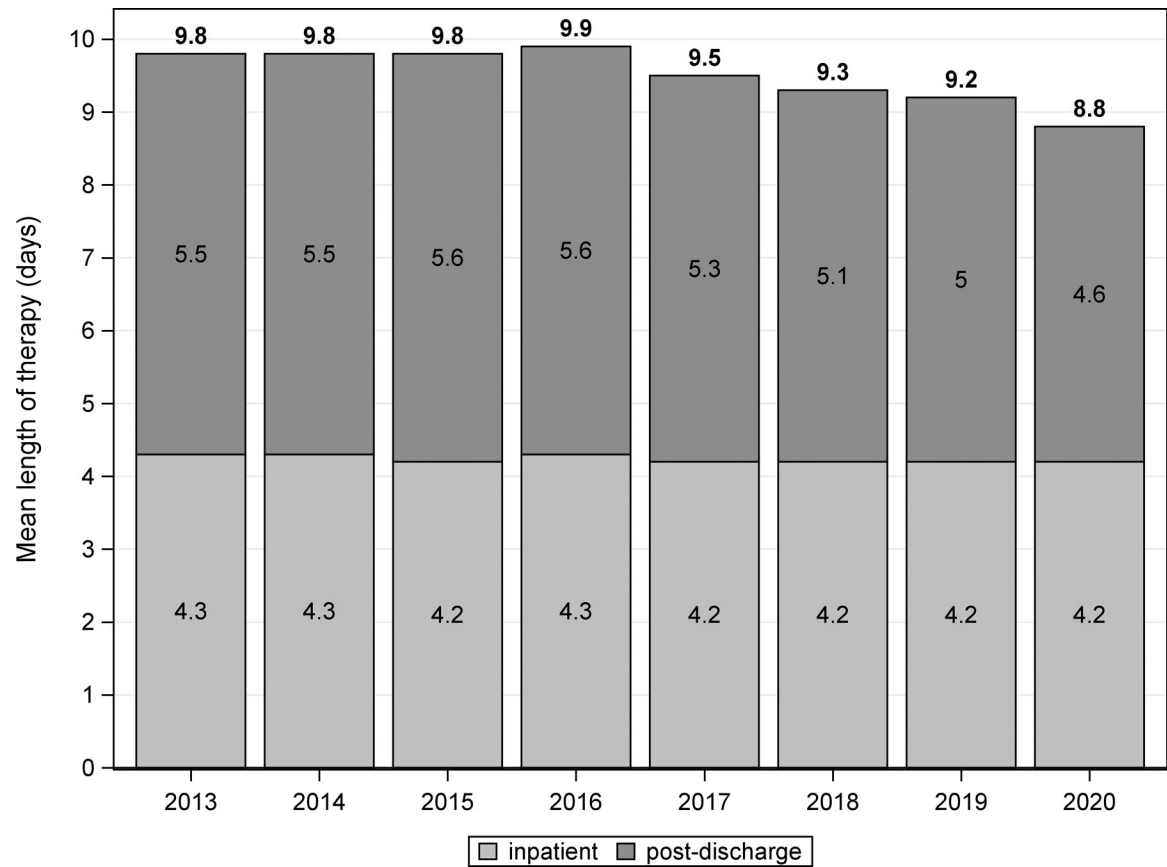


Figure 2.

Proportion of patients hospitalized with uncomplicated community-acquired pneumonia, with likely excessive length of antibiotic therapy (LOT), MarketScan Commercial Claims and Encounters and Centers for Medicare & Medicaid Services databases, 2013–2020

Table 1.

Characteristics of adults hospitalized for uncomplicated community-acquired pneumonia, MarketScan Commercial Claims and Encounters and Centers for Medicare & Medicaid Services databases, 2013–2020

Category	Value	Aged 18–64 Years, Private Insurance		Aged 65 Years, Medicare Insurance	
		n= 45,089		n= 400,928	
		Mean, Median	Q1–Q3	Mean, Median	Q1–Q3
Length of stay		3.7, 3.0	2.0–5.0	3.8, 3.0	2.0–5.0
Age, y		50.8, 54.0	44–60	77.1, 76.0	70–83
		No.	(%)	No.	(%)
Age, y	18–44	11,334	25.1	—	—
	45–64	33,755	74.9	—	—
	65–84	—	—	320,165	79.9
	85+	—	—	80,763	20.1
Sex	Male	19,936	44.2	181,237	45.2
	Female	25,153	55.8	219,691	54.8
Race	White	—	—	339,976	84.8
	Black	—	—	30,904	7.7
	Other	—	—	30,048	7.5
Healthcare use 30 d prior to hospitalization					
	At least one outpatient claim	18,372	40.7	193,320	48.2
Index hospitalization (2–10 day LOS) admission source					
	Nonhealthcare facility point of origin	—	—	386,518	96.4
	Transfer from healthcare facility	—	—	14,410	3.6
Pneumonia, present on admission					
	Present	—	—	400,186	99.8
	Not present	—	—	141	0.0
	Other (undetermined, insufficient info, exempt)	—	—	601	0.1
Intensive care unit status					
	Any stay	2,576	5.7	82,729	20.6
	No stay	42,513	94.3	318,199	79.4
LOS, d					
	2	14,041	31.1	114,499	28.6
	3	12,018	26.7	108,083	27.0
	4	7,520	16.7	71,756	17.9
	5	4,433	9.8	43,375	10.8
	6	2,899	6.4	26,538	6.6
	7	1,880	4.2	16,809	4.2

Category	Value	Aged 18–64 Years, Private Insurance		Aged 65 Years, Medicare Insurance	
		n= 45,089		n= 400,928	
		Mean, Median	Q1–Q3	Mean, Median	Q1–Q3
	8	1,102	2.4	9,933	2.5
	9	739	1.6	6,085	1.5
	10	457	1.0	3,850	1.0
Diagnosis-related group					
	193: Simple pneumonia and pleurisy with MCC	15,670	34.8	124,309	31.0
	194: Simple pneumonia and pleurisy with CC	18,793	41.7	166,455	41.5
	195: Simple pneumonia and pleurisy without CC/MCC	8,208	18.2	68,437	17.1
	Other	2,421	5.4	41,442	10.3
Hospitals					
Hospital census region					
	Northeast	7,148	15.9	67,095	16.7
	South	22,116	49.0	176,604	44.1
	Midwest	10,412	23.1	94,957	23.7
	West	4,409	9.8	62,266	15.5
	Unknown	1,104	2.4	6	0.0
Hospital size, number of beds					
	1–199	—		136,627	34.1
	200–299	—		74,123	18.5
	300–499	—		106,487	26.6
	500	—		83,685	20.9
	Unknown			6.0	0.0
Discharge quarter					
	January–March	13,283	29.5	126,946	31.7
	April–June	11,439	25.4	101,896	25.4
	July–September	9,218	20.4	76,466	19.1
	October–December	11,149	24.7	95,620	23.9
Number of post-discharge prescriptions filled					
	0	8,601	19.1	71,881	17.9
	1	28,172	62.5	229,262	57.2
	2	8,006	17.8	86,194	21.5
	3	310	0.7	13,591	3.4

Abbreviations: Q1–Q3, Quartiles 1 and 3; d, days; y, years; LOS, Length of Stay; MCC, Major Complications/Comorbidities; CC, Complications/Comorbidities.