Infection Control & Hospital Epidemiology (2024), **45**, 726–732
doi:10.1017/ice.2024.14

SHEA

Original Article

Length of antibiotic therapy among adults hospitalized with uncomplicated community-acquired pneumonia, 2013–2020

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Abstract

Objective: The 2014 US National Strategy for Combating Antibiotic-Resistant Bacteria (CARB) 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 through 2020.

Methods: We conducted a retrospective cohort study among adults with a primary diagnosis of bacterial or unspecified pneumonia using *International Classification of Diseases Ninth and Tenth Revision* codes in MarketScan and the 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 rehospitalized in the 3 days following discharge. We estimated inpatient LOT based on LOS from the PINC AI Healthcare Database. The total LOT was calculated by summing estimated inpatient LOT and actual postdischarge LOT. We examined trends from 2013 to 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 aged 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 aged 18–64 years and by 27% (68%–50%) among patients aged ≥65 years.

Conclusions: Although 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.

(Received 15 November 2023; accepted 5 January 2024; electronically published 14 February 2024)

Antibiotic stewardship is a key component of the US National Strategy for Combating Antibiotic-Resistant Bacteria (CARB). The 2014 CARB strategy aimed to reduce inappropriate hospital antibiotic use for monitored conditions by 20% by 2020.[1] Because 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] Although longer durations of therapy may be recommended for specific clinical scenarios, length of therapy (LOT) of >7 days or >3 days after clinical stability is rarely necessary for patients with CAP.[5]

Yi et al[6] 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. In their study, the median LOT was 9.5 days, and >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[6] and to determine whether the 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 (ie, 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

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PREVIOUS PRESENTATION. A portion of the findings in this manuscript were presented as abstracts from SHEA 2023 and IDWeek 2022.

Cite this article: McCarthy N. L., Baggs J., Wolford H., *et al.* Length of antibiotic therapy among adults hospitalized with uncomplicated community-acquired pneumonia, 2013–2020. *Infect Control Hosp Epidemiol* 2024. 45: 726–732, doi: 10.1017/ice.2024.14

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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 Ninth and Tenth Revision* (ICD-9-CM and ICD-10-CM) codes (Supplementary Table S1 online). 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 rehospitalized in the 3 days following index discharge. Because 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 who could potentially require extended LOT, including patients with diagnoses of cystic fibrosis, human immunodeficiency virus (HIV), or sickle cell anemia and patients with a postdischarge antibiotic prescription that exceeded 28 days. If a patient had multiple eligible hospitalizations >30 days apart during the study period, then 1 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 those aged 18–64 years, MarketScan Commercial Claims and Encounters files were used to obtain the LOS of the index hospitalization and postdischarge LOT. Patients in this cohort consisted of those enrolled in private insurance with outpatient drug coverage. For those aged ≥65 years, the 100% Medicare claims and Part D event files from the CMS database were used to obtain the index hospitalization LOS and postdischarge LOT. Patients in this ≥65 years cohort included those with traditional fee-for-service Parts A and B plus Part D Medicare coverage.

Because MarketScan and CMS claims data do not contain inpatient antibiotic use, we implemented previously validated methods,[6] and we 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 ~1,000 private and academic hospitals, representing ~20% of US inpatient discharges. However, it does not include data from which to derive postdischarge LOT, as do the 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 the MarketScan and CMS databases, antibiotic prescriptions filled in an outpatient setting 1 day prior to 3 days following discharge were included in postdischarge LOT. If a patient had multiple prescriptions filled during this period, the postdischarge LOT was counted as the number of days with at least 1 prescription from earliest fill date through the latest supply through date. Total LOT was calculated by summing estimated inpatient LOT (from PHD) and actual postdischarge LOT (from MarketScan and CMS.).

The primary measure of interest was the proportion of uncomplicated CAP patients with likely excessive duration of antibiotic therapy. Because clinical practice guidelines suggest >7 days LOT for uncomplicated CAP is rarely necessary,[5] we interpreted total LOT >7 days as likely excessive duration. Postdischarge LOT >3 days of therapy was also considered possibly excessive because patient LOS (at least 2 days) plus 3 days of postdischarge 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 postdischarge LOT. We estimated temporal changes over the study period using median regression models adjusting for age, sex, discharge year, and quarter. $P < .05$ was considered statistically significant.

This activity was reviewed by CDC and was consistent with applicable federal law and CDC policy (see eg, 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 software (SAS Institute, Cary, NC).

Results

We included 45,089 and 400,928 uncomplicated CAP patients aged 18–64 and ≥65 years, respectively, in the study cohorts (Supplementary Fig. S1 online). Demographic and hospitalization characteristics are described in Table 1. The median LOS was 3 days (Q1–Q3, 2–5) 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 postdischarge prescriptions.

In total, 227,969 discharges were 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 Fig. S2 and Supplementary Table S2 online). Predicted inpatient LOTs were generated for each value of LOS stratified by cohort and year (Supplementary Fig. S3 and Supplementary Table S3 online). The R^2 values of these predictions ranged from 0.69 to 0.80 for all age groups and years. Based on these models, the estimated median inpatient LOTs for those aged 18–64 years were 3.5 days (Q1–Q3, 2.6–5.4) in 2013 and 3.7 days (Q1–Q3, 2.7–4.6) in 2020. Among patients aged ≥65 years the estimated median inpatient LOTs were 3.4 days (Q1–Q3, 3.4–5.3) in 2013 and 3.6 days (Q1–Q3, 2.7–4.6) in 2020 (Supplementary Table S4 online).

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

The mean total LOT decreased from 9.8 to 8.8 days among patients aged 18–64 years and from 9.6 to 8.6 days among patients aged ≥65 years, which was driven primarily by postdischarge LOT decreases (Fig. 1). After adjusting for patient and hospital

https://doi.org/10.1017/ice.2024.14 Published online by Cambridge University Press

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

Variable	Aged 18–64 Years, Private Insurance (n=45,089)		Aged ≥65 Years, Medicare Insurance (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
Age group	No.	(%)	No.	(%)
18–44 y	11,334	25.1	. . .	
45–64 y	33,755	74.9	. . .	
65–84 y	. . .		320,165	79.9
85+ y	. . .		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 1 outpatient claim	18,372	40.7	193,320	48.2
Index hospitalization (2–10 d 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
Length of stay (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
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

(*Continued*)

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Table 1. (*Continued*)

Variable	Aged 18–64 Years, Private Insurance (n=45,089)		Aged ≥65 Years, Medicare Insurance (n=400,928)	
	Mean, Median	Q1–Q3	Mean, Median	Q1–Q3
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
Postdischarge 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

Note. Q1–Q3, quartiles 1 and 3; MCC, major complications/comorbidities; CC, complications/comorbidities.

characteristics, the proportion of total LOT comprised by postdischarge LOT decreased by 10% from 2016 to 2020 among patients aged 18–64 years ($P < .0001$); similarly, the proportion of postdischarge LOT in patients aged ≥65 years decreased by 8% from 2016 to 2020 ($P < .0001$) (Supplementary Table S5 online).

Overall, the presence of any postdischarge antibiotic prescription increased as the LOS decreased; there were also higher proportions of patients with no postdischarge prescriptions among those with longer LOS. Beginning in 2017, the proportion of patients with 1 postdischarge prescription declined as the proportion of patients with 2 or more prescriptions increased (Supplementary Tables S6 and S7 online).

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 aged 18–64 years, there was a relative decrease of 14% over the study period in postdischarge LOT >3 days, from 73% in 2013 to 63% in 2020. The proportion of patients aged ≥65 years with postdischarge LOT >3 days had a relative decrease of 16%, from 73% in 2013 to 62% in 2020. The proportion of patients aged 18–64 years with total LOT >7 days had a relative decrease of 25%, from 68% in 2013 to 51% in 2020. Among patients aged ≥65 years, there was a relative decrease of 27% from 68% in 2013 to 50% in 2020 (Fig. 2).

Discussion

In this study, the total LOT for adult patients hospitalized with uncomplicated CAP decreased from 2013 to 2020. Among patients aged 18–64 years and those aged ≥65 years, likely excessive total LOT had a relative decrease of 25% and 27%, respectively, exceeding the CARB target reduction of 20%. There were also relative reductions in the proportion of patients with likely excessive postdischarge LOT: 14% among patients aged 18–64 years and 16% among patients aged ≥65 years. Despite these declines, however, half of patients with uncomplicated CAP were treated with LOT >7 days in 2020, and 62%–63% of patients were treated with likely excessive postdischarge antibiotic therapy in 2020.

An assessment of appropriateness of antimicrobial use in US 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] In several studies, stewardship

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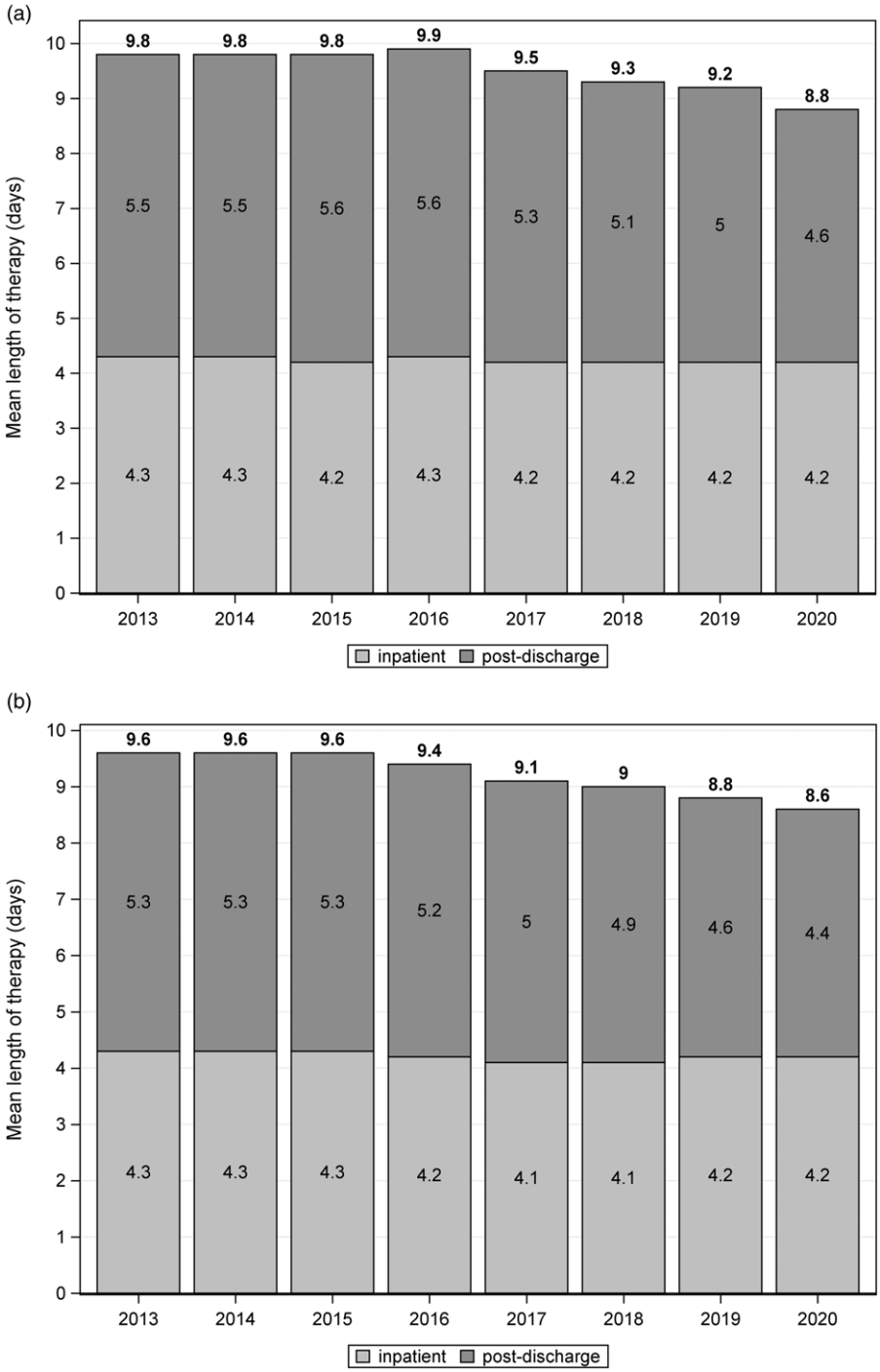

Fig. 1. Mean length of antibiotic therapy among adults hospitalized for uncomplicated community-acquired pneumonia, 2013–2020. (a) Age 18–64 years, MarketScan Commercial Claims and Encounters database. (b) Age ≥65 years, Centers for Medicare & Medicaid Services databases

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]

In some studies, prolonged antibiotic therapy among CAP hospitalizations was the result of excessive postdischarge therapy.[8,15–17] In our analysis, the proportion of total LOT represented by postdischarge prescribing was stable from 2013 to 2016 and then decreased from 2016 to 2020. The reductions in total LOT may have been driven by the reductions in postdischarge prescribing in more recent years. Decreases in inpatient LOT were most apparent in the third quartile of the inpatient LOT distribution. Because 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] In a single-center study implementing a pharmacist-driven antibiotic timeout at discharge, the intervention was feasible and decreased inappropriate antibiotic use.[17] Another pharmacist-driven transition of care model implemented in multiple facility types was also associated with improved antibiotic prescribing at discharge.[19] Resources developed for this

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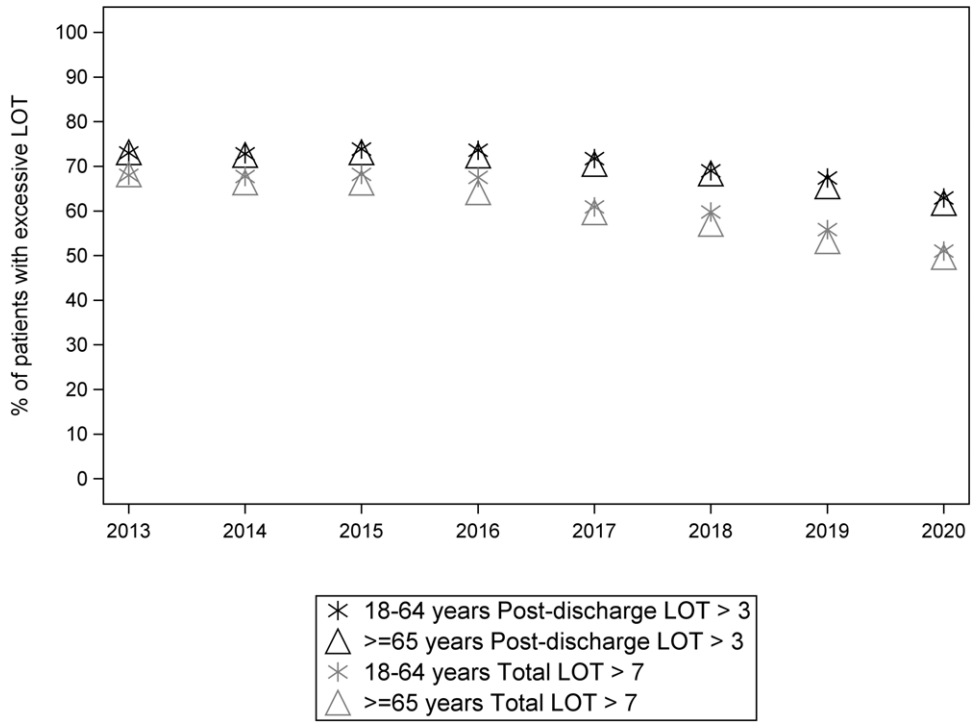

Fig. 2. Proportion of patients hospitalized with uncomplicated community-acquired pneumonia, with likely excessive length of antibiotic therapy (LOT), MarketScan Commercial Claims and Encounters and Centers for Medicare & Medicaid Services databases, 2013–2020.

pharmacist-driven intervention can be modified to optimize practice models and workflow at discharge in different community and academic hospital settings.[20] 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.

This study had several limitations. We used ICD-9 and ICD-10 codes to identify patients with CAP, so there was potential misclassification without confirming diagnosis with clinical data. Although the ICD-9 codes for CAP diagnoses have good sensitivity (84%) and positive predictive value (92%),[21] sensitivity and positive predictive values using ICD-10 codes to identify pneumonia in older adults were lower, 74% and 79%, respectively.[22] Additionally, the transition from ICD-9 to ICD-10 codes could have further affected 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 we 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 research[6] has shown that using our definitions, it is likely that only a small portion of patients would be misclassified as CAP. Furthermore, the proportion of patients with hemodialysis or residence in a long-term care facility in our cohorts were low, 4% and 1% respectively. Although we excluded patients with cystic fibrosis, HIV, and sickle-cell anemia, we did not have access to microbiology data, and we 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 US population. Additionally, the definition of uncomplicated CAP and data source requirements resulted in a high exclusion rate, and the study population may not represent 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, 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.

Likely excessive LOT for uncomplicated CAP patients has decreased since 2013, but the proportion of patients treated with LOT >7 days still exceeded 50% in 2020. The high proportion of patients with likely excessive postdischarge 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. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2024.14

Acknowledgments. 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.

Financial support. No financial support was provided relevant to this article.

Competing interests. All authors report no conflicts of interest relevant to this article.

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