Outpatient Antimicrobial Stewardship: Targets for Community-acquired Pneumonia

Bethany A. Wattengel, PharmD[1]; John A. Sellick, DO, MS[2,3]; Megan K. Skelly, PharmD[1]; Randal Napierala Jr., PharmD[1]; Jennifer Schroeck, PharmD, BCPS, BCGP[1]; and Kari A. Mergenhagen, PharmD, BCPS, AQ-ID[1]

[1]Department of Pharmacy, Veteran Affairs Western New York Healthcare System, Buffalo, NY, USA; [2]Medical Service, Veteran Affairs Western New York Healthcare System, Buffalo, NY, USA; and [3]Division of Infectious Diseases, Department of Medicine, Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, USA

ABSTRACT

Purpose: Community-acquired pneumonia (CAP) is one of the leading causes of death in the United States. The primary objective of this study was to determine the prevalence of appropriate diagnosis and treatment of outpatients treated for CAP. Knowledge of problems with CAP treatment can be helpful in developing stewardship initiatives to improve care of outpatients with CAP.

Methods: Included in this study were patients 18 years and older who received antibiotic therapy for the treatment of CAP in the outpatient setting. Outpatients were identified by *International Classification of Diseases, Ninth Revision* (ICD-9) and *International Classification of Diseases, Tenth Revision* (ICD-10) codes for CAP in the Veterans Affairs Western New York Healthcare System between January 2008 and January 2018. Appropriate treatment was evaluated using CAP guidelines. Factors associated with an inappropriate regimen were determined via multivariable analyses.

Findings: This study included 518 outpatients, of whom 66% were appropriately diagnosed with CAP. Of the 341 appropriately diagnosed patients, only 31% received an antibiotic regimen consistent with guidelines. Regarding inappropriate regimens, 76.7% contained an incorrect drug based on patient comorbidities, and 39.4% consisted of an inappropriate duration, which was most often attributable to prolonged length of therapy >7 days. The odds of being prescribed an inappropriate regimen if a patient was considered to be at risk for drug-resistant *Streptococcus pneumoniae* (DRSP) was 4.2 (95% CI, 2.4−7.4). The population at risk for DRSP was more likely to present to the health care system again within 30 days compared with low-risk patients (19.4% vs 8.7%, $P = 0.005$).

Implications: Improvement in prescribing is needed for CAP. An outpatient stewardship program that targets patients with risk factors for DRSP would improve adherence to guidelines. (*Clin Ther.* 2019;41:466−476)

Key words: antibiotic, antimicrobial stewardship, community-acquired pneumonia, outpatient, pneumonia.

INTRODUCTION

Community-acquired pneumonia (CAP) is one of the leading causes of death in the United States.[1−6] Approximately 4 million individuals are diagnosed with CAP each year, with the incidence and mortality increasing with age.[7−11] The Centers for Disease Control and Prevention reports that approximately 500,000 emergency department visits are attributable to CAP, as well as >50,000 deaths.[4−6]

Although most data regarding management of CAP come from hospitalized patients, most CAP cases are actually treated on an outpatient basis.[12] CAP is less severe in outpatients, with lower risk of mortality

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(approximately 1%). Severity scoring systems, such as CURB-65 (confusion, uremia, respiratory rate, systolic blood pressure, and age to ≥65 years), are helpful in triaging patients and determining whether a patient's disposition is appropriate for outpatient management.[13]

Diagnosis of CAP can be difficult, especially on an outpatient basis.[12] Clinical signs and symptoms in the presence of radiographic evidence are necessary for diagnosis of CAP.[14,15] Unfortunately, access to imaging is not always available in the outpatient setting, leaving health care professionals to rely solely on signs and symptoms to diagnose CAP. The respiratory symptoms of CAP can be nonspecific and are shared with many viral respiratory conditions as well as chronic obstructive pulmonary disease exacerbations.

Despite Infectious Diseases Society of America (IDSA) guideline recommendations, prescribing antibiotic therapy for CAP is often inappropriate.[16–18] This study sought to evaluate outpatient prescribing practices for CAP in veterans to identify potential stewardship targets.

PATIENTS AND METHODS

Study Design

This study was a retrospective medical record review of patients with a diagnosis of CAP identified by *International Classification of Diseases, Ninth Revision* (ICD-9) and *International Classification of Diseases, Tenth Revision* (ICD-10) codes. ICD-9 codes 480 to 486 and ICD-10 codes J12 to J18 were used. A randomized, consecutive, qualified sampling process was used to select patients. The Veterans Affairs Computerized Patient Record System was used to collect information, and the Vista FileMan program was used to extract data using the ICD-9 and ICD-10 codes. Patients were seen in the Veterans Affairs Western New York Healthcare System emergency department, primary care clinics, home-based primary care, or community-based outpatient clinics between the dates of January 1, 2008, and January 1, 2018.

Patient Population

Patients were included in the study if they were 18 years or older and were treated in the outpatient setting for CAP. Patients were excluded if they were younger than 18 years or had HIV. They were also excluded if they were admitted to the hospital, were treated for a concomitant infection, or were hospitalized within the previous 90 days and received intravenous antibiotic therapy. Patients were excluded if the encounter was erroneously coded and they were not diagnosed with or being treated for CAP, if the coded encounter was a follow-up appointment for previously treated CAP, if the coded encounter was a duplicate and the patient was already included for such episode, or if there was significant missing or incomplete data in the medical record. Lastly, if the patient died before being able to initiate outpatient therapy for CAP, were given hospice or comfort care and did not receive antibiotic therapy, were transferred to another facility, or were evaluated and diagnosed at an outside facility, they also were excluded from the study.

Outcome Measures

Determination of stewardship targets for outpatient treatment of CAP was the primary objective of this study. The entire cohort was examined to determine whether the ICD-9 or ICD-10 diagnosis of CAP was consistent with guidelines. Of those who had an appropriate diagnosis of CAP, a combined analysis of drug, dose, and duration was used to determine risk factors for inappropriate treatment regimen. To better identify individual targets, antibiotic selection, dose, and duration were analyzed separately to determine degree of improper prescribing and risk factors associated with each factor. Patients at risk for drug-resistant *Streptococcus pneumoniae* (DRSP) were analyzed to determine whether these patients had outcomes or presentations which differed from that of the general population.

Treatment failure, 30-day readmission rates, and 30- and 90-day mortality were secondary objectives. The secondary objectives were studied in terms of overall treatment regimen and in terms of errors in drug selection, dosing of the antibiotic, and duration of treatment. Baseline demographic characteristics included age, sex, race, body mass index, and creatinine clearance. Medical history included the following comorbidities: diabetes, chronic obstructive pulmonary disease, asthma, heart failure, coronary artery disease, chronic kidney disease, liver disease, malignant tumor, and asplenia. Charlson comorbidity scores were calculated for each patient.[19] Social history, including tobacco and alcohol use, was

included. The immunization history of each patient was also included, particularly for the influenza vaccine, the pneumococcal conjugate vaccine Prevnar 13, and the pneumococcal polysaccharide vaccine Pneumovax 23. Symptoms included patient-reported cough, sputum production, dyspnea, fever or chills, and pleuritic chest pain. Diagnostic and therapeutic information collected included white blood cell count, body temperature, sputum and blood cultures, imaging, antibiotic prescribed, dose of antibiotic, and duration of antibiotic therapy. CURB-65 scores were calculated for each patient using the appropriate information collected from their medical records.[20] Treatment failure included admission to the hospital after treatment or subsequent presentation to 1 of the outpatient locations. Mortality data were also included, specifically 30- and 90-day all-cause mortality.

Definitions

Appropriate Diagnosis of CAP

An appropriate diagnosis of CAP was an acute illness with radiographic evidence of pneumonia in addition to at least 1 of the following symptoms: altered breath sounds, dyspnea, fever or chills, pleuritic chest pain, or new cough with or without sputum production.[14] Radiographic evidence of CAP included a chest radiograph or computed tomogram that showed a new infiltrate, consolidation, or opacity, as well as findings deemed suggestive of pneumonia by the reading radiologist.

Appropriate Treatment

Appropriate drug, dose, and duration were evaluated for patients who had an appropriate diagnosis of CAP. Regimens could have contained multiple inappropriate components. In terms of appropriate antibiotic choice, current guidelines recommend use of a macrolide (azithromycin or clarithromycin) or doxycycline for previously healthy patients without risk factors for DRSP.[14] Patients at risk for DRSP should be prescribed a respiratory fluoroquinolone (levofloxacin or moxifloxacin) or a β-lactam (amoxicillin, amoxicillin/clavulanate, or a third-generation cephalosporin) with a macrolide or doxycycline. Dose was considered appropriate if in accordance with guidelines and renal function. A minimal duration of 5 days is recommended in the guidelines, with longer durations acceptable if initial therapy was not active against an identified pathogen or if clinical course is complicated by extrapulmonary infections. A 7-day treatment course is generally considered appropriate for most patients.[15]

Patients at Risk for DRSP

Patients at risk for DRSP were defined in accordance with guidelines and the most common cause is macrolide resistance.[14,21] Patients at risk for DRSP were defined as patients with chronic diseases, such as chronic heart, lung, liver, or renal disease. Other comorbidities included were diabetes mellitus, alcoholism, and malignant tumor. Patients were also considered at risk if they were asplenic, had an immunosuppressing condition or were using immunosuppressing agents, or had a history of antibiotic use within the previous 3 months.

Treatment, Early, and Late Failure

Treatment failure was considered lack of response or worsening of clinical or radiologic status that required renewal of or changes in antibiotic therapy. This was determined via review of the medical record. Early failure was considered treatment failure as previously defined occurring within 72 h from prescribing of antibiotic therapy. Late failure was considered treatment failure as previously defined occurring $\geq$72 h from prescribing of antibiotic therapy.

Subsequent Presentation for CAP

Some patients presented to the emergency department, primary care clinics, home-based primary care clinics, or community-based outreach clinics after initial presentation during which antibiotic therapy was prescribed. Subsequent presentation did not necessarily result in treatment failure because antibiotic therapy was not always affected.

Statistical Analysis

Bivariate analysis was used to compare patients who were appropriately diagnosed with CAP versus those who were not, those who were treated appropriately versus those who were inappropriately treated, and patients who subsequently presented to the health care facility within 30 days and those who did not. The independent sample *t* test was used for

continuous variables, and the χ^2 or Fisher exact test was used for categorical variables to evaluate significant baseline differences.

Factors that contribute to inappropriate regimen were analyzed by using aggregate significant baseline characteristics and symptoms ($P < .05$) from the bivariate analysis and building them into a multivariable logistic regression analysis. Factors were eliminated in a backwards elimination fashion until a stable model was created. Results are presented as odds ratios with 95% CIs.

Admission rates and subsequent treatment rates with and without appropriate treatment and antibiotic use are presented with descriptive statistics. All statistics were determined using JMP, version 13 (SAS Institute, Cary, North Carolina).

RESULTS

This study included 518 veterans with a diagnosis of CAP. Of the 2857 patient visits reviewed, 2339 were excluded (Figure 1). Antibiotic use was varied; however, all patients in this cohort received antibiotics regardless of whether they met the clinical definition of CAP. Azithromycin was most commonly used (45%) followed by respiratory fluoroquinolones (38.2%), doxycycline (10.0%), and β-lactam plus atypical agent (azithromycin or doxycycline) (2.3%). CURB-65 scores were calculated for each included patient. A CURB-65 score of 0 was obtained in 217 patients, a score of 1 in 201 patients, a score of 2 in 80 patients, and a score of 3 in 20 patients.

Appropriate Diagnosis

Sixty-six percent of veterans were appropriately diagnosed with CAP based on symptoms and imaging. Most patients (96.3%) had imaging performed to assess for radiographic evidence of CAP. Of those who were inappropriately diagnosed with CAP, 158 (approximately 89%) underwent imaging; however, only 7% had radiographic evidence of CAP. This 7% had no signs or symptoms of CAP, and radiographic findings were incidental (Table I).

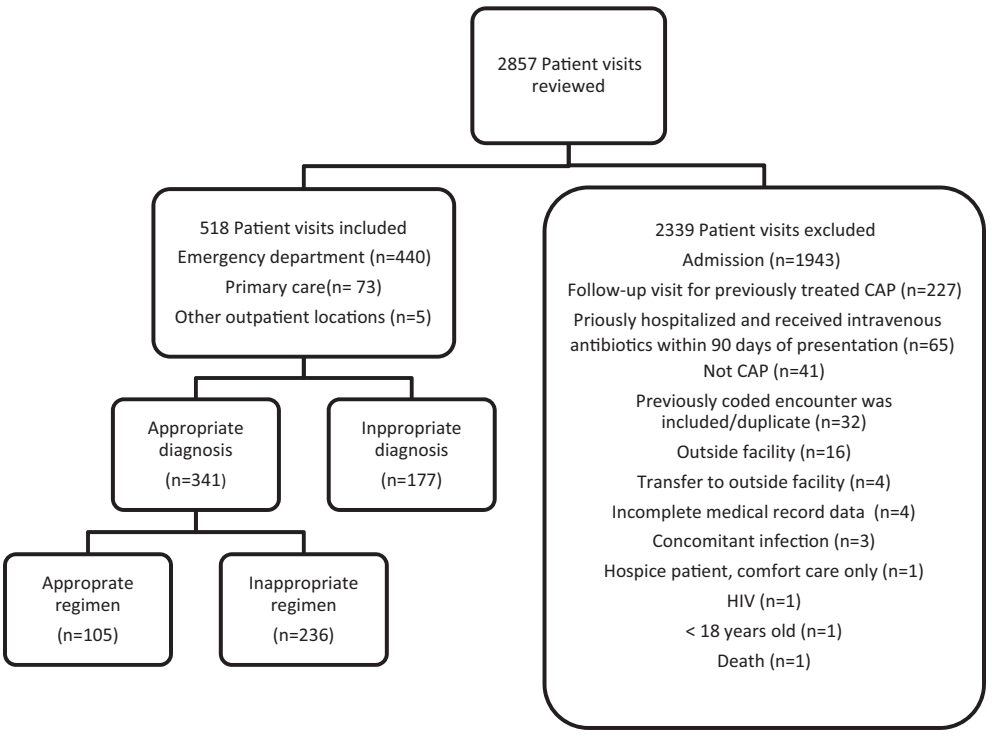

Figure 1. Study inclusion and exclusion criteria. CAP = community-acquired pneumonia.

Table I. Inappropriate versus appropriate diagnosis of community-acquired pneumonia.*

Variable	Inappropriate Diagnosis (n = 177 [34.2%])	Appropriate Diagnosis (n = 341 [65.8%])	*P*
Demographic and patient characteristics			
Location			0.14
Emergency department	144 (81.4)	296 (86.8)	
Other	1 (0.6)	4 (1.2)	
Primary care	32 (18.1)	41 (12.0)	
Long-term care resident	10 (5.7)	10 (2.9)	0.13
Male	163 (92.1)	312 (91.5)	0.82
Age, mean (SD), y	60.8 (15.6)	63.8 (15.7)	0.042
Race			0.93
African American	31 (17.5)	62 (18.2)	
Other	5 (2.8)	8 (2.4)	
White	141 (80.0)	271 (79.5)	
Body mass index, mean (SD), kg/m^2	30.3 (8.1)	30.3 (7.2)	0.95
Creatinine clearance, mean (SD), mL/min	103.7 (42.1)	95.9 (42.3)	0.088
Tobacco use			0.73
No	98 (55.4)	179 (52.5)	
Past	29 (16.4)	65 (19.1)	
Yes	50 (28.3)	97 (28.5)	
Influenza vaccination	80 (45.2)	154 (45.2)	0.99
Prevnar 13	27 (15.2)	118 (34.6)	<0.0001
Pneumovax 23	104 (58.8)	244 (71.6)	0.0033
At risk population for DRSP	116 (65.5)	275 (80.7)	0.0002
Diabetes	47 (26.6)	107 (31.4)	0.25
Chronic obstructive pulmonary disease	29 (16.4)	94 (27.6)	0.0046
Asthma	7 (4.0)	35 (10.3)	0.013
Heart failure	8 (4.5)	35 (10.3)	0.025
Coronary artery disease	32 (18.1)	96 (29.2)	0.012
Chronic kidney disease	8 (4.5)	36 (10.6)	0.019
CURB-65 score			0.017
0—1	153 (86.4)	265 (77.7)	
2—3	24 (13.6)	76 (22.3)	
Charlson Comorbidity Index			0.023
0—4	168 (94.9)	303 (88.9)	
5—9	9 (5.1)	38 (11.1)	
Antibiotics within 30 days	19 (10.7)	39 (11.4)	0.80
Prior hospitalization in 90 days	8 (4.6)	18 (5.3)	0.72
Diagnostics and treatment regimens			
Cough	147 (84)	297 (87.4)	0.30
Sputum	102 (60.4)	204 (60.5)	0.97
Dyspnea	78 (44.8)	146 (43.3)	0.75
Reported fever or chills	71 (40.3)	125 (36.9)	0.44
Pleuritic chest pain	40 (22.9)	90 (26.6)	0.36

Table I. (*Continued*)

Variable	Inappropriate Diagnosis (n = 177 [34.2%])	Appropriate Diagnosis (n = 341 [65.8%])	*P*
White blood cell count, mean (SD),/μL	9.6 (4.3)	9.5 (3.6)	0.84
T_{max}, mean (SD), °C	36.9 (0.8)	36.9 (0.9)	0.34
Antibiotic			0.032
Azithromycin	79 (44.6)	154 (45.2)	
beta-lactam plus atypical	4 (2.3)	8 (2.4)	
Doxycycline	10 (5.7)	42 (12.3)	
Miscellaneous respiratory[†]	13 (7.3)	10 (2.9)	
Fluoroquinolone	71 (40.1)	127 (37.2)	
Total duration, mean (SD), d	7.2 (2.4)	6.8 (2.6)	0.14
Imaging	158 (89.3)	341 (100)	<0.0001
Chest radiography	153 (86.4)	330 (96.8)	<0.0001
CT	10 (5.7)	66 (19.4)	<0.0001
Pleural effusion	7 (4.5)	36 (10.6)	0.023

DRSP = drug-resistant *Streptococcus pneumoniae*.
* Data are presented as number (percentage) of patients unless otherwise indicated.
† Amoxicillin, amoxicillin/clavulanate, cefuroxime, ciprofloxacin, and sulfamethoxazole/trimethoprim.

Patients who were appropriately diagnosed with CAP were more likely to be older (mean age, 64 vs 61 years; $P = 0.04$). Specific comorbidities that were associated with an appropriate diagnosis of CAP were asthma (10.3% vs 4%, $P = 0.013$), chronic obstructive pulmonary disease (27.6% vs 16.4%, $P = 0.0046$), heart failure (10.3% vs 4.5%, $P = 0.025$), coronary artery disease (29.2% vs 18.1%, $P = 0.012$), and chronic kidney disease (10.6% vs 4.5%, $P = 0.019$). Diabetes, liver disease, malignant tumor, and asplenia did not have a statistically significant effect on patients being more likely to have an appropriate diagnosis (Table I).

Stewardship Targets (Combined Analysis of Drug, Dose, and Duration)

Of the 341 patients who were considered to have an appropriate CAP diagnosis, only 105 patients (30.8%) were prescribed an antibiotic regimen consistent with the IDSA guidelines. Patients were more likely to receive an inappropriate regimen (antibiotic selection, dose, duration) if they presented with symptoms of cough (90.2%, $P = 0.018$) or sputum production (64.5%, $P = 0.024$) (Table II). Reasons for inappropriate antibiotic regimens were inappropriate choice of antibiotic (181 [76.7%]), inappropriate duration (93 [39.4%]), and inappropriate dose (12 [5.1%]). The population with comorbidities placing them at risk for DRSP was more likely to be prescribed an inappropriate regimen (88.1% inappropriate vs 63.8% appropriate, $P < 0.0001$). Significant baseline characteristics were entered into a multivariate logistic regression. On the basis of the regression, the odds ratio of being prescribed an inappropriate regimen if a patient was considered at risk for DRSP was 4.2 (95% CI, 2.4–7.4). Overall, once appropriate diagnosis is determined, stewardship targets include antibiotic selection, dose, and duration.

Antibiotic Selection

The incorrect antibiotic was chosen in 181 patients (53%) with an appropriate diagnosis of CAP. Patients at risk for DRSP were more likely to be treated inappropriately. Eighty-nine percent of the population at risk for DRSP received an inappropriate outpatient antibiotic for CAP.

Table II. Inappropriate versus appropriate antibiotic regimens in patients correctly diagnosed with community-acquired pneumonia.*

Variable	Inappropriate Regimen (n = 236 [69.2%])	Appropriate Regimen (n = 105 [30.8%])	*P*
Demographic and patient characteristics			
Age, mean (SD), y	64.7 (15.6)	61.6 (15.8)	0.09
Creatinine clearance, mean (SD), mL/min	95.9 (44.0)	95.7 (37.8)	0.97
Influenza vaccination	109 (46.2)	45 (42.9)	0.57
Prevnar 13	91 (38.6)	27 (25.7)	0.021
Pneumovax 23	177 (75.0)	67 (63.8)	0.035
At risk population for DRSP	208 (88.1)	67 (63.8)	<0.0001
Charlson comorbidity Index			0.91
0—4	210 (89.0)	93 (88.6)	
5—9	26 (11.0)	12 (11.4)	
Malignant tumor	54 (22.9)	11 (10.5)	0.0071
Diagnostics and treatment regimens			
Dyspnea	100 (42.9)	46 (44.2)	0.82
Cough	212 (90.2)	85 (81.0)	0.018
Sputum	151 (64.5)	53 (51.5)	0.024
Reported fever or chills	89 (37.9)	36 (34.6)	0.57
Pleuritic chest pain	61 (26.0)	29 (27.9)	0.71
White blood cell count, mean (SD),/μL	9.6 (3.7)	9.3 (3.4)	0.52
T_{max}, mean (SD), °C	36.9 (0.9)	36.9 (0.8)	0.83
Antibiotic			<0.0001
Azithromycin	119 (50.4)	35 (33.3)	
â-lactam plus atypical	7 (3.0)	1 (1.0)	
Doxycycline	39 (16.5)	3 (2.9)	
Miscellaneous†	10 (4.2)	0 (0.0)	
Respiratory	61 (25.9)	66 (62.9)	
Fluoroquinolone			
Total duration, mean (SD), d	7.2 (3.0)	6.0 (1.0)	<0.0001
Chest radiography	229 (97.0)	101 (96.2)	0.68
CT	41 (17.4)	25 (23.8)	0.16
Pleural effusion	21 (8.9)	15 (14.3)	0.14

DRSP = drug-resistant *Streptococcus pneumoniae*.
* Data are presented as number (percentage) of patients unless otherwise indicated.
† Amoxicillin, amoxicillin/clavulanate, cefuroxime, ciprofloxacin, and sulfamethoxazole/trimethoprim.

Azithromycin was prescribed in 45% of patients appropriately diagnosed with CAP and accounted for 64% of inappropriate antibiotic selection. Of the inappropriate antibiotic use, doxycycline accounted for 18% and fluoroquinolones for 11%.

Antibiotic Dose

Dosing was inappropriate in only 12 patients (3.5%) with a correct diagnosis of CAP. Patients with chronic kidney disease were more likely to receive an incorrect dose (33% vs 9.7%; $P = 0.009$).

Antibiotic Duration

An inappropriate duration was found in 27% of the population who was considered to have an appropriate diagnosis. Inappropriate duration was most often attributable to prolonged length of therapy >7 days ($n = 86$ [92.5%], $P < 0.0001$). Prolonged duration of therapy was more common in older patients; 66 years was the mean age of patients who were treated for >7 days compared with a mean age of 62 years for patients treated with ≤7 days of therapy ($P = 0.009$). Patients were more likely to be treated with >7 days of therapy if they received antibiotic therapy within the preceding 30 days (15.5% vs 9.5%; $P = 0.047$). Patients who received an inappropriate duration were also more likely to receive an incorrect dose (7.5% vs 2%, $P = 0.01$). The population at risk for DRSP was not more likely to receive an inappropriate duration ($P = 0.54$).

Patients at Risk for DRSP

Of the patients at risk for DRSP, 80.7% had an appropriate diagnosis; however, only 63.8% received an appropriate regimen. A few patients had complications from their outpatient treatment of CAP. The population at risk for DRSP was more likely to subsequently present within 30 days compared with patients at low risk to an outpatient location for any cause (19.4% vs 8.7%, $P = 0.005$) or to the hospital for admission for CAP ($n = 9$ vs 0, $P = 0.08$).

Outcomes of Patients With CAP

Patients who had an appropriate diagnosis of CAP were more likely to subsequently present within 30 days for CAP compared with those who had an inappropriate diagnosis of CAP (5.6% vs 1.1%, $P = 0.02$). They were also more likely to experience late failure (5.9% vs 1.1%, $P = 0.01$). Patients who received the influenza vaccine were less likely to subsequently present within 30 days for CAP (19.1% vs 81%, $P = 0.014$). Subsequent presentation for CAP within 30 days was associated with higher rates of 30-day mortality (4.8% vs 0.6%, $P = 0.033$) and 90-day mortality (10% vs 0.8%, $P = 0.0002$). Inappropriate drug choice was associated with higher rates of late treatment failure (8.3% vs 3.1%, $P = 0.04$). Appropriate regimen did not affect factors or mortality (Table III).

DISCUSSION

CAP was appropriately diagnosed in 66% of patients. Of those who received an appropriate diagnosis, 69.2% received an inappropriate regimen. The most common reasons for inappropriate prescribing were incorrect initial drug choice based on presence of chronic diseases and excessive days of therapy. Patients at risk for DRSP were more likely to have symptoms and imaging consistent with pneumonia but were also more likely to receive an inappropriate regimen with respect to the IDSA guidelines. This

Table III. Secondary outcomes.

Outcome	Inappropriate Drug		Inappropriate Dose		Inappropriate Duration		Inappropriate Regimen	
	No. (%) of Patients	*P*	No. (%) of Patients	*P*	No. (%) of Patients	*P*	No. (%) of Patients	*P*
Subsequent presentation within 30 days (all cause)	34 (18.8)	0.76	1 (8.3)	0.37	16 (17.2)	0.77	43 (18.2)	0.98
Subsequent presentation within 30 days for CAP	12 (6.6)	0.37	0	0.39	5 (5.4)	0.92	14 (5.9)	0.66
30-Day mortality	0	0.13	0	0.79	1 (1.1)	0.47	1 (0.4)	0.56
90-Day mortality	3 (1.7)	0.38	0	0.70	0	0.22	3 (1.3)	0.81
Early treatment failure	2 (1.1)	0.64	0	0.74	1 (1.1)	0.81	2 (0.9)	0.92
Late treatment failure	15 (8.3)	0.04	1 (8.3)	0.71	5 (5.4)	0.81	17 (7.2)	0.11

CAP = community-acquired pneumonia.

finding is consistent with the literature because discordance with guidelines has been described for patients hospitalized with CAP.[16–18] In a study[17] conducted across 5 US hospitals, only half of the patients received CAP treatment consistent with guidelines.

Macrolides, such as azithromycin, are the most commonly prescribed antibiotics in adults in the outpatient setting.[22] This trend is consistent with findings from our study because azithromycin was the most commonly prescribed antibiotic in our cohort (45%). Respiratory fluoroquinolones were the second most frequently prescribed antibiotic in our cohort (38%). This finding is consistent with an epidemiologic study involving the National Ambulatory Medical Care Survey by Wortham et al[23] in which 35% of the population received respiratory fluoroquinolones between 2008 and 2009. Monotherapy with a β-lactam occurred infrequently in our cohort. *S pneumoniae* resistance is infrequent for penicillin: only 2.2% of isolates were resistant in 2016.[21] Considering overall prescribing patterns from our study, the high frequency of azithromycin use in this study suggests an area for intervention from an outpatient antimicrobial stewardship program or for further education to health care professionals.

A recent review found that incorrect prescribing was associated with factors such as complacency, indifference, ignorance, and fear.[24] It is possible that patients at risk for DRSP were more likely to be treated with an inappropriate regimen, which was often attributable to an excessive duration of therapy caused by fear of poor outcomes. Prescribers may have also been unaware of IDSA guidelines that state patients with select comorbidities are at risk for DRSP and therefore require therapy with a respiratory fluoroquinolone or combination of a β-lactam with a macrolide, such as azithromycin. Azithromycin was the most frequently prescribed antibiotic in this study overall and in the population at risk for DRSP, which may support the idea that health care professionals were unaware of IDSA guideline recommendations that require use of a β-lactam with azithromycin in patients at risk for DRSP.

Macrolide resistance has been steadily trending up since 1999 in the United States.[25] In 2012, macrolide resistance of *S pneumoniae* reached a high of 34%. Current survey data from around the world also support this trend. Data collected for macrolide resistance of *S pneumoniae and Haemophilus influenzae* indicated high rates of resistance, leading to recommendations against macrolide monotherapy for the treatment of CAP in other areas around the world.[26] Currently in the United States, macrolide monotherapy is only recommended for patients at low risk for DRSP.[14] Given the increase of macrolide-resistant *S pneumoniae*, this vulnerable population is at risk for worse outcomes. Several inpatient studies have looked at the effect of guideline concordant therapy on outcomes of hospitalized patients with CAP and found that patients treated with guideline concordant therapy had better mortality rates and shorter times to clinical stability compared with patients treated with guideline-discordant therapy.[16,18] Patients in our study at risk for DRSP had higher all-cause subsequent presentation rates compared with patients at low risk. This finding therefore presents an important outpatient antimicrobial stewardship target (patients at risk for DRSP) to ensure these patients are appropriately treated with guideline concordant therapy.

Several articles have suggested that vaccination against influenza may have a protective effect in regard to pneumonia and may even lead to improved outcomes.[27,28] Our results support this finding that patients in our study who received the seasonal influenza vaccine were less likely to subsequently present within 30 days for CAP after receiving antibiotic therapy. Only 45% of patients received the influenza vaccination, indicating that this is an area for potential stewardship intervention: ensuring all patients, especially those at risk for DRSP, receive seasonal influenza vaccination.

This study had limitations. One limitation was the retrospective design; data collection was dependent on information documented in the electronic medical record. Another limitation was that it was an outpatient study and therefore diagnostic information was not always available. Cases were identified via ICD-9 and ICD-10 codes, and thus cases of CAP may have been omitted because of coding inaccuracies. Approximately 4% of patients did not undergo imaging and were therefore deemed to have an inappropriate diagnosis of CAP because of lack of radiographic evidence; however, it is possible that they may have met the criteria for diagnosis if imaging would have been performed. The outpatient nature of this study also limited the availability of

follow-up information, and patient adherence could not be assessed. In addition, this study was conducted in a single region of New York State with a largely male population, which could potentially limit its external validity.

CONCLUSION

Improvement is needed in the diagnosis and treatment of CAP, which indicates a need for antimicrobial stewardship. Although antibiotics are always warranted for CAP, the choice of antibiotic is dependent on comorbidities and is a potential stewardship target. In addition, the diagnosis of CAP can be challenging in the outpatient setting, and antibiotics are often unnecessarily prescribed for viral infections and bronchitis, providing another potential stewardship target. Inappropriate diagnosis and use of antibiotics not only contribute to antimicrobial resistance but can also harm patients by exposing them to unnecessary agents and adverse effects. It is therefore important to use stewardship in the management of CAP on the outpatient basis to ensure proper diagnosis and appropriate treatment of patients. Overall, potential stewardship interventions include education for duration of therapy and appropriate empirical choices based on the presence of comorbidities. Special attention should be given to patients at risk for DRSP because they are often mistreated and have worse outcomes.

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CONFLICTS OF INTEREST

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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Address correspondence to: Kari A. Mergenhagen, Department of Pharmacy, Veteran Affairs Western New York Healthcare System, 3495 Bailey Ave, Buffalo, NY 14215, USA. E-mail: kari.mergenhagen@va.gov