Treatment Costs Associated With Commonly Used Branded Antibiotics for the Management of Acute Sinusitis, Chronic Bronchitis and Pneumonia

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ABSTRACT

Objective: The purpose of this study was to determine the incidence of treatment failure and associated healthcare costs for outpatient management of community-acquired pneumonia, acute sinusitis, or chronic bronchitis in patients receiving the most commonly prescribed branded antibiotics.

Methods: This was a retrospective analysis of pharmacy and medical claims. Members aged 18 years or older having an outpatient visit with a diagnosis of community-acquired pneumonia, acute sinusitis, or chronic bronchitis, and subsequent antibiotic prescription within 5 days were identified. Treatment failure was defined as a second antibiotic prescription, hospitalization, or emergency room visit for a respiratory infection within 30 days after the episode start. A multivariable regression model was used to compare total healthcare costs for moxifloxacin versus other antibiotics.

Results: There were 45,231 patients who met the study criteria; these patients had 48,251 unique episodes of treated respiratory infections. Failure rates ranged from 15.9% to 24.1% for community-acquired pneumonia, 13.4% to 16.0% for acute sinusitis, and 14.7% to 28.5% for chronic bronchitis. Failure rates did not differ significantly between moxifloxacin and the other antibiotics for any of the diagnoses. The multivariable regression model revealed higher healthcare costs (rate ratio; 95% confidence interval) for community-acquired pneumonia for

amoxicillin/clavulanate (1.41; 1.03-1.93), levofloxacin (1.29; 1.03-1.63) and ciprofloxacin (1.55; 1.01-2.39) compared to moxifloxacin. For chronic bronchitis, cefuroxime (2.15; 1.06-4.36), gatifloxacin (1.60; 1.08-2.39), and clarithromycin (1.57; 1.07-2.29) had higher costs compared to moxifloxacin. No significant differences in healthcare costs existed in the treatment of acute sinusitis.

Conclusions: Although differences in failure rates between moxifloxacin and other antibiotics were not significant, analysis of total healthcare costs revealed that a number of antibiotics had higher adjusted total healthcare costs compared to moxifloxacin to treat a given episode.

INTRODUCTION

Respiratory infections in adults are responsible for a large percentage of physician office visits, emergency room visits, hospitalizations, and days lost from work and are a major cause of morbidity and mortality worldwide. In a global survey of causes of mortality, respiratory tract disease was estimated to be the third leading cause of death, responsible for 4.3 million deaths in 1990.[1] Among adults, nearly one half of all prescriptions dispensed are for common respiratory tract infections (such as bronchitis, sinusitis, and other upper respiratory tract infections).[2]

An estimated 3 to 4 million people in the United States suffer from community acquired pneumonia (CAP) annually.[3] Of these, approximately 1 million are hospitalized with an average mortality rate of approximately 14%, making CAP the sixth leading cause of death in the United States.[4-6] The estimated cost of each CAP episode treated in the hospital is more than 20 times higher than the cost of outpatient treatment ($350 vs. $7,500).[7] Acute sinusitis (AS) is one of the 10 most common diagnoses in ambulatory practice, and is the fifth most common diagnosis for which an antibiotic is prescribed.[8] Acute sinusitis is coupled with significant morbidity, anxiety, reduced quality of life, and lost time from work; the annual direct cost of sinusitis in the United States exceeds $3.3 billion.[9] Chronic bronchitis (CB) is estimated to afflict 5.4% of the US population and has a significant socioeconomic impact.[10,11] CB predisposes patients to more frequent and progressively more severe episodes of acute infection, and is responsible for approximately 10% of hospital admissions.[12]

Choice of antibiotic to use for each of these conditions is an issue due to increasing resistance to many agents and high costs of many branded antibiotics. Narrow-spectrum antibiotics that are available generically are typically preferred as first-line treatment. Previous research has shown that generically available antibiotics are equally effective for the treatment of specific conditions and result in lower healthcare costs compared to branded antibiotics.[13,14] From the perspective of a managed care decision maker, generic antibiotics would most likely be included on all formularies. Despite this, broad-spectrum antibiotics may be required for certain infections, depending upon severity of the infection and resistance to narrow-spectrum antibiotics.

Many broad spectrum antibiotics, particularly the fluoroquinolones, are increasingly accepted as choices for acute exacerbations of CB (AECB)[15], and are empirically used in CAP.[16] One study found substantially higher costs with levofloxacin versus others in the second-line antibiotic class, including moxifloxacin, gatifloxacin, as well as non-fluoroquinolone broad-spectrum drugs in the treatment of acute sinusitis, chronic bronchitis, and pneumonia.[17] Another study compared moxifloxicin and levofloxacin in the treatment of AECB in relation to workplace-related costs and found moxifloxacin costs were significantly less than levofloxacin.[18] However, as studies examining the effectiveness and costs between the second-line antibiotic agents are sparse, it is difficult to determine the most cost-effective, broad-spectrum antibiotic to use.

The purpose of this study was to evaluate treatment failure rates and the cost of healthcare resources utilized for patients who received moxifloxacin compared to those who received other commonly prescribed branded antibiotics for the treatment of CAP, AS, or CB in a naturalistic setting through use of a managed care administrative claims database.

METHODS

Study Population

This study was conducted within a western US health plan. This health plan is one of the largest health plans in the United States, with approximately 7.5 million enrolled members during the fourth quarter of 2002.

Medical claims were examined, in order to identify patients with an outpatient office visit generating a diagnosis of CAP, AS, or CB between January 1, 2000 and December 31, 2001 (intake period). Each episode was identified and analyzed as a separate event; patients could contribute more than 1 treatment episode during the intake period. For each episode, the date of the CAP, AS, or CB diagnosis was identified as the *Episode Index Date*. Pharmacy claims were then reviewed to identify subjects who had a prescription for a "branded" oral antibiotic (moxifloxacin, amoxicillin/clavulanate, azithromycin, cefuroxime, ciprofloxacin, clarithromycin, clarithromycin XL, gatifloxacin, and levofloxacin) with an FDA-approved indication for the associated respiratory infection during the 5-day period following the *Episode Index Date*. Only oral antibiotics with FDA approved indications for each condition were analyzed (azithromycin was excluded from analyses for AS, cefuroxime was excluded from analyses for CAP).

Upon identification of patients who were treated for one of the above-mentioned respiratory infections, plan eligibility was examined to ensure continuous member enrollment during the 6-month period prior to, and 30-day period following each *Episode Index Date*. Patients without continuous enrollment during this period were excluded. Patients were also excluded from the analysis if they were less than 18 years of age or if they were hospitalized or had received an antibiotic prescription during the 30 day period before the *Episode Index Date*. The remaining patients represented the study cohort. Complete medical and pharmacy claims data were retrieved for these patients.

Data Analysis

Data were analyzed to determine the incidence of treatment failure of CAP, AS, and CB. Treatment failure was defined as the occurrence of any of the following within the 30-day period following the *Episode Index Date*: (a) receipt of a prescription for a second antibiotic (repeat or different antibiotic for the same condition), (b) hospitalization with a diagnosis of the same respiratory infection for which the patient was first treated following the outpatient office visit, or (c) an emergency room visit with a diagnosis of the same respiratory infection for which the patient was first treated following the outpatient office visit.

In the absence of a clinical indicator for severity of illness, the Deyo-Charlson Co-morbidity Index and baseline pharmacy and medical costs in the 6 months prior to the *Episode Index Date* were used as proxies for severity. The Deyo-Charlson Co-morbidity Index is a validated instrument used to quantify co-morbidity by adding assigned weights specific to various diagnoses.[19,20] Higher baseline medical and pharmacy costs have been demonstrated to be indicative of sicker patients.[21]

The total cost of healthcare resources, including initial antibiotic therapy, additional antibiotic therapies, physician office visits, hospital ER visits, and laboratory tests was evaluated through the use of cost rates and rate ratios (RR). Cost rates were defined as dollar amounts spent (payments made by the health plan plus patient co-payments) within the 30-day interval following the *Episode Index Date*. Rate ratios were obtained by dividing the cost rate for particular antibiotic group by the respective cost rate for the moxifloxacin group.

Statistical Analyses

The primary grouping variable was the type of antibiotic, with all groups compared to moxifloxacin. Descriptive analysis included mean, standard deviation (SD) and relative frequencies for continuous and categorical data, respectively. All pair-wise comparisons were conducted in a bivariate manner. Chi-squared tests were utilized for comparing both continuous and nominal outcomes, with nonparametric tests chosen for outcomes with highly skewed distributions (ie, cost data).

Cost rates and RR were determined through use of a multivariable regression model (Generalized Linear Model [GLM] family of models). The gamma distribution was found to be a good choice for cost data and the logarithmic link function was used, allowing for interpretation of the exponentiated regression coefficients as rate ratios. Deyo-Charlson Co-morbidity Index, baseline pharmacy and medical expenditures (both used as a proxy for severity of illness), age, and treatment failure indicators were all found to be significant predictors in the model. *Index* antibiotic and treatment failure were included in the model by generating dummy variables. During construction, model adequacy was checked and independent variables were examined for multicollinearity.

For all analyses, an a priori 2-sided level of significance was set at the 0.05 level. A P value of < 0.05 was considered significant, and all P values were derived in comparison to moxifloxacin. All data manipulations and generation of cohort identifiers was performed using SAS system (Version 8, SAS Institute Inc, Cary, NC). Stata software (Version 7, Stata Corporation, College Station, Tex) was used for GLM regression analyses.

RESULTS

A total of 48,251 episodes of respiratory infections treated with branded antibiotics were identified in 45,231 patients. AS accounted for the majority of identified episodes (N = 40,375 [83.7%]), with far fewer CAP episodes (N = 5,669 [11.7%]) and CB episodes (2,207 [4.6%]). Table 1 presents the index antibiotic prescribed for each of the conditions. Azithromycin was the most frequently prescribed antibiotic for the treatment of both CAP (30.6% of episodes) and CB (34.9%), while amoxicillin/ clavulanate was the most frequently prescribed antibiotic for the treatment of AS (33.7%). The mean age for CB, CAP, and AS patients were 47.5, 46.1, and 42.7 years; statistically significant differences in age existed between moxifloxacin and some of the other agents for each of these conditions. (Table 1)

The Deyo-Charlson analysis revealed that the majority of patients

Table 1. Number of Treatment Episodes and Mean Patient Age, Stratified by Diagnosis

Drug	CAP		AS		CB	
	N	Mean Age ± SD	N	Mean Age ± SD	N	Mean Age ± SD
Amoxicillin/Clavulanate	348	45.5 ± 14.9	13,592	42.2 ± 11.7*	172	44.1 ± 15.7
Azithromycin†	1,734	45.5 ± 16.7*	-----	-----	771	47.7 ± 16.7
Cefuroxime‡	-----	-----	5,885	42.9 ± 15.3	93	49.8 ± 16.4
Ciprofloxacin	221	48.0 ± 16.4	2,200	43.9 ± 14.1	137	51.1 ± 16.4
Clarithromycin	1,021	45.4 ± 16.0	5,665	42.5 ± 15.1*	260	46.1 ± 16.1
Clarithromycin XL	372	44.2 ± 13.5*	3,642	42.4 ± 12.1*	131	41.4 ± 13.7*
Gatifloxacin	395	48.2 ± 15.9	2,944	43.0 ± 10.9	141	50.7 ± 16.6
Levofloxacin	1,379	47.0 ± 14.9	4,954	43.2 ± 14.1	406	48.5 ± 16.1
Moxifloxacin	199	47.6 ± 14.1	1,493	43.4 ± 11.6	96	47.9 ± 17.6
Total	**5,669**	**46.1**	**40,375**	**42.7**	**2,207**	**47.5**

* $P < 0.05$ vs. moxifloxacin. †Azithromycin does not have an FDA approved indication for acute sinusitis. ‡Oral Cefuroxime does not have an FDA approved indication for community acquired pneumonia.

Table 2. Deyo-Charlson Analysis, Stratified by Diagnosis

Antibiotic	CAP			AS			CB		
	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*
Amoxicillin/Clavulanate	348	0.595 ± 1.08	0.4747	13,592	0.222 ± 0.70	< 0.0001	172	1.326 ± 0.79	0.6454
Azithromycin	1,734	0.520 ± 1.12	0.6517	-----	-----	-----	771	1.348 ± 0.92	0.5804
Cefuroxime	-----	-----	-----	5,885	0.221 ± 0.61	< 0.0001	93	1.376 ± 0.76	0.3707
Ciprofloxacin	221	0.982 ± 1.55	0.0002	2,200	0.361 ± 0.94	0.2372	137	1.664 ± 1.35	0.0092
Clarithromycin	1,021	0.516 ± 1.15	0.5924	5,665	0.253 ± 0.68	0.0009	260	1.342 ± 0.92	0.6651
Clarithromycin XL	372	0.427 ± 1.08	0.0946	3,642	0.226 ± 0.60	< 0.0001	131	1.290 ± 0.95	0.8207
Gatifloxacin	395	0.666 ± 1.21	0.1572	2,944	0.271 ± 0.65	0.0725	141	1.447 ± 1.18	0.2133
Levofloxacin	1,379	0.806 ± 1.49	0.0088	4,954	0.338 ± 0.84	0.4554	406	1.672 ± 1.33	0.0034
Moxifloxacin	199	0.523 ± 0.92	----	1,493	0.329 ± 0.89	----	96	1.281 ± 0.71	----

Table 3. Baseline Pharmacy Costs, Stratified by Diagnosis

Antibiotic	CAP			AS			CB		
	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*
Amoxicillin/Clavulanate	348	$706.71 ± 1,001.70	0.1586	13,592	$626.17 ± 1,143.37	< 0.0001	172	$1,298.36 ± 2,736.51	0.339
Azithromycin	1,734	$574.06 ± 1,312.72	< 0.0001	----	----- -----	-----	771	$936.71 ± 1,192.54	0.002
Cefuroxime	-----	------ -----	-----	5,885	$678.67 ± 885.60	< 0.0001	93	$1,214.38 ± 1,151.09	0.421
Ciprofloxacin	221	$904.91 ± 1,673.55	0.7974	2,200	$865.38 ± 1,118.99	0.1934	137	$1,411.26 ± 1,671.68	0.816
Clarithromycin	1,021	$595.10 ± 1,022.21	0.0001	5,665	$603.07 ± 1,324.17	< 0.0001	260	$1,034.40 ± 1,422.96	0.054
Clarithromycin XL	372	$547.52 ± 850.77	0.0002	3,642	$609.16 ± 801.42	< 0.0001	131	$882.57 ± 1,448.98	0.003
Gatifloxacin	395	$1,020.66 ± 1,820.50	0.3447	2,944	$736.34 ± 1,001.09	0.0023	141	$1,241.86 ± 1,144.06	0.653
Levofloxacin	1,379	$844.62 ± 1,185.56	0.9422	4,954	$836.72 ± 1,349.56	0.9414	406	$1,720.95 ± 1,715.67	0.026
Moxifloxacin	199	$869.98 ± 1,300.91	----	1,493	$827.56 ± 1,154.69	----	96	$1,314.55 ± 1,209.26	----

Table 4. Baseline Medical Costs, Stratified by Diagnosis

Antibiotic	CAP			AS			CB		
	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*	Cases	Mean ± SD	*P*
Amoxicillin/Clavulanate	348	$1,159.88 ± 2,760.44	0.3702	13,592	$1,010.67 ± 3,034.96	< 0.0001	172	$2,465.10 ± 9,195.81	0.4273
Azithromycin	1,734	$1,405.17 ± 5,422.80	0.1321	-----	----- -----	-----	771	$1,582.08 ± 3,333.95	0.6368
Cefuroxime	-----	----- -----	-----	5,885	$1,086.66 ± 2,755.03	0.0046	93	$2,320.79 ± 4,537.68	0.2511
Ciprofloxacin	221	$2,410.34 ± 5,925.73	0.0291	2,200	$1,326.88 ± 3,255.04	0.2068	137	$3,408.52 ± 7,762.75	0.0100
Clarithromycin	1,021	$1,630.05 ± 12,447.37	0.0793	5,665	$1,047.00 ± 3,244.51	< 0.0001	260	$1,905.70 ± 4,137.23	0.3844
Clarithromycin XL	372	$864.23 ± 1,769.86	0.0095	3,642	$1,014.01 ± 2,650.48	< 0.0001	131	$946.93 ± 2,032.66	0.0541
Gatifloxacin	395	$1,484.40 ± 3,882.92	0.9012	2,944	$1,156.05 ± 3,098.75	0.2551	141	$1,998.57 ± 3,231.43	0.1995
Levofloxacin	1,379	$2,086.33 ± 6,836.65	0.2235	4,954	$1,325.82 ± 3,613.61	0.3882	406	$3,194.22 ± 6,775.12	0.0030
Moxifloxacin	199	$1,364.30 ± 2,807.04	----	1,493	$1,276.31 ± 4,334.06	----	96	$2,246.25 ± 6,895.10	----

Table 5. Mean Days of Therapy Received (All Indicated Diagnoses)

Antibiotic	Cases	Mean	SE	*P*
Azithromycin*	2,505	6.52	0.03	**< 0.0001**
Moxifloxacin	1,788	10.16	0.12	--
Clarithromycin XL	4,145	10.47	0.07	**< 0.0001**
Gatifloxacin	3,480	10.82	0.09	**< 0.0001**
Clarithromycin	6,946	11.26	0.06	**< 0.0001**
Cefuroxime†	5,978	11.42	0.06	**< 0.0001**
Ciprofloxacin	2,558	11.42	0.11	**< 0.0001**
Amoxicillin/Clavulanate	14,112	11.75	0.04	**< 0.0001**
Levofloxacin	6,739	11.76	0.07	**< 0.0001**

*Azithromycin does not have an FDA approved indication for acute sinusitis.
†Oral Cefuroxime does not have an FDA approved indication for community acquired pneumonia.

(78.9%) had none of the select co-morbidities in their claims data; chronic pulmonary disease, diabetes, and malignancy/metastatic tumors were the most commonly identified co-morbid conditions. Table 2 summarizes the Deyo-Charlson results for CAP, AS, and CB, respectively. CB patients had the highest Deyo-Charlson mean weight (1.290–1.672), whereas AS had the lowest (0.221–0.338). There were statistically significant differences in the co-morbidity weight between moxifloxacin and the other agents for each of these conditions. Analysis of baseline pharmacy costs (Table 3) and baseline medical costs (Table 4) demonstrated that, on average, patients receiving non-fluoroquinolone therapy had lower baseline pharmacy and medical costs compared to patients receiving moxifloxacin, while patients receiving non-moxifloxacin fluoroquinolone therapy had similar baseline pharmacy and medical costs compared to that patients receiving moxifloxacin. These results demonstrate patients treated with fluoroquinolone therapy were of poorer health than those treated with non-fluoroquinolones.

Table 5 presents the mean days of therapy patients received for their Index prescription for all three indications. Patients utilizing azithromycin had a lower mean days of therapy received compared to moxifloxacin (10.16 days vs. 6.52 days; $P < 0.001$). All other agents had significantly higher mean days of therapy received compared to moxifloxacin (range: 10.47–11.76; all $P < 0.001$). Similar results were seen for each of the three indications individually except for clarithromycin XL, which did not have a significantly different mean days of therapy received compared to moxifloxacin for the indications of CB or AS.

Table 6 summarizes the unadjusted treatment failure rates of each antibiotic according to diagnosis. There were no statistically significant differences between moxifloxacin and all other antibiotics for all 3 diagnoses. The failure rate ranged from 15.9% to 24.1% for CAP (moxifloxacin: 19.1%), 13.4% to 16.0% for AS (moxifloxacin: 15.1%), and 14.7% to 28.5% for CB (moxifloxacin: 17.7%).

The regression model results summarize the adjusted total costs calculated for the 30-day interval following the *Episode Index Date*, and are presented in Tables 7, 8, and 9. Table 7 presents the

Table 6. Failure Rates for All Antibiotics According to Diagnosis

	CAP		AS		CB	
Antibiotic	**Failures (%)**	**Odds Ratio (CI)**	**Failures (%)**	**Odds Ratio (CI)**	**Failures (%)**	**Odds Ratio (CI)**
Amoxicillin/Clavulanate	69 (19.8%)	1.04 (0.66-1.68)	1,814 (13.4%)	0.86 (0.74-1.00)	32 (18.6%)	1.06 (0.53-2.18)
Azithromycin*	276 (15.9%)	0.80 (0.55-1.20)	-----	----	113 (14.7%)	0.80 (0.45-1.49)
Cefuroxime†	-----	-----	878 (14.9%)	0.98 (0.84-1.16)	23 (24.7%)	1.53 (0.71-3.31)
Ciprofloxacin	51 (23.1%)	1.27 (0.77-2.10)	351 (16.0%)	1.06 (0.88-1.28)	39 (28.5%)	1.85 (0.94-3.75)
Clarithromycin	167 (16.4%)	0.83 (0.55-1.26)	825 (14.6%)	0.96 (0.81-1.12)	47 (18.1%)	1.03 (0.54-2.02)
Clarithromycin XL	65 (17.5%)	0.90 (0.56-1.44)	515 (14.1%)	0.92 (0.78-1.10)	23 (17.6%)	0.99 (0.47-2.12)
Gatifloxacin	65 (16.5%)	0.83 (0.53-1.34)	431 (14.6%)	0.96 (0.80-1.15)	22 (15.6%)	0.86 (0.41-1.84)
Levofloxacin	274 (19.9%)	1.05 (0.71-1.58)	682 (13.8%)	0.89 (0.76-1.06)	86 (21.2%)	1.25 (0.69-2.37)
Moxifloxacin	38 (19.1%)	-----	226 (15.1%)	-----	17 (17.7%)	-----
Total	**1,005 (17.7%)**		**5,722 (14.2%)**		**402 (18.2%)**	

*Azithromycin does not have an FDA approved indication for acute sinusitis.
†Oral Cefuroxime does not have an FDA approved indication for community acquired pneumonia.

Table 7. Adjusted Cost Rates and Rate Ratios, CAP Diagnosis

Drug	$ Cost Rate (CI) "success"	$ Cost Rate (CI) "failure"	Cost Rate Ratio* (CI) All Costs
Ciprofloxacin	$379.34 (256.1-562.0)	$2,099.78 (1,385.5-3,182.2)	1.55 (1.01-2.39)†
Amoxicillin/Clavulanate	$344.62 (268.9-441.7)	$1,907.61 (1,405.9-2,588.3)	1.41 (1.03-1.93)†
Levofloxacin	$315.82 (278.7-371.7)	$1,748.19 (1,361.3-2,245.0)	1.29 (1.03-1.63)†
Gatifloxacin	$294.43 (233.2-371.7)	$1,629.81 (1,220.6-2,176.2)	1.21 (0.89-1.62)
Clarithromycin	$284.07 (241.5-334.1)	$1,572.42 (1,202.7-2,055.8)	1.16 (0.90-1.50)
Azithromycin	$251.61 (201.3-314.5)	$1,392.76 (1,061.4-1,827.6)	1.03 (0.78-1.37)
Moxifloxacin	$244.34 (200.9-297.2)	$1,352.52 (1,045.0-1,750.6)	1.00
Clarithromycin XL	$242.26 (189.4-309.9)	$1,341.00 (965.7-1,862.1)	0.99 (0.72-1.36)

*Rate ratios were obtained by dividing the cost rate for the particular antibiotic group by the cost rate for the moxifloxacin group.
†Significant compared to moxifloxacin.

Table 8. Adjusted Cost Rates, AS Diagnosis

Drug	$ Cost Rate (CI) "success"	$ Cost Rate (CI) "failure"	Cost Rate Ratio* (CI) All Costs
Ciprofloxacin	$293.74 (243.1-355.0)	$644.26 (513.1-808.9)	1.23 (0.90-1.67)
Levofloxacin	$279.11 (241.0-323.2)	$612.17 (527.5-710.4)	1.17 (0.88-1.56)
Cefuroxime	$275.67 (247.2-307.4)	$604.61 (532.2-686.9)	1.16 (0.89-1.51)
Amoxicillin/Clavulanate	$253.95 (241.1-267.5)	$556.99 (508.8-609.7)	1.07 (0.83-1.37)
Moxifloxacin	$237.87 (185.2-305.5)	$521.71 (411.3-661.8)	1.00
Clarithromycin XL	$219.97 (200.5-241.3)	$482.46 (423.4-549.8)	0.92 (0.71-1.21)
Gatifloxacin	$218.85 (195.9-244.5)	$480.00 (422.3-545.6)	0.92 (0.70-1.21)
Clarithromycin	$210.94 (194.8-228.4)	$462.66 (416.7-513.7)	0.89 (0.69-1.15)

* Rate ratios were obtained by dividing the cost rate for the particular antibiotic group by the cost rate for the moxifloxacin group.

adjusted total costs for the successful treatment of CAP, adjusted total costs for treatment failures of CAP, and the associated cost rate ratio for the treatment of all patients (successes and failures). For the successful treatment of CAP, cost rates ranged from $242.26 for clarithromycin XL to $379.34 for ciprofloxacin (moxifloxacin $244.34), while cost rates for treatment failures ranged from $1,341.00 for clarithromycin XL to $2,099.78 for ciprofloxacin (moxifloxacin $1,352.52). Evaluation of the cost rate ratios revealed that the cost to treat all patients with CAP was significantly higher for ciprofloxacin (RR = 1.55; 95% CI 1.01–2.39), amoxicillin/clavulanate (RR = 1.41; 95% CI 1.03–1.93), and levofloxacin (RR = 1.29; 95% CI 1.03–1.63) compared to moxifloxacin.

Table 8 presents the adjusted total costs for the successful treatment of AS, adjusted total costs for treatment failures of AS, and the associated cost rate ratio for the treatment of all patients (successes and failures). For the successful treatment of AS, cost rates ranged from $210.94 for clarithromycin to $293.74 for ciprofloxacin (moxifloxacin $237.87), while cost rates for treatment failures ranged from $462.66 for clarithromycin to $644.26 for ciprofloxacin (moxifloxacin $521.71). Evaluation of the cost rate ratios revealed that there were no significant differences in the

Table 9. Adjusted Cost Rates, CB Diagnosis

Drug	$ Cost Rate (CI) "success"	$ Cost Rate (CI) "failure"	Cost Rate Ratio* (CI) All Costs
Cefuroxime	$471.70 (243.5-913.8)	$2,116.30 (1070.9-4,182.3)	2.15 (1.06-4.36)†
Gatifloxacin	$352.26 (263.2-471.5)	$1,580.44 (1095.1-2,280.9)	1.60 (1.08-2.39)†
Clarithromycin	$344.41 (264.0-449.3)	$1,545.21 (1105.9-2,159.0)	1.57 (1.07-2.29)†
Ciprofloxacin	$339.77 (225.9-510.9)	$1,524.40 (917.1-2,533.9)	1.54 (0.94-2.53)
Amoxicillin/Clavulanate	$297.69 (222.4-398.4)	$1,335.59 (928.4-1,921.5)	1.35 (0.91-2.02)
Levofloxacin	$279.52 (243.2-321.3)	$1,254.08 (948.1-1,658.8)	1.27 (0.93-1.73)
Azithromycin	$277.18 (229.7-334.5)	$1,243.57 (919.2-1,682.5)	1.26 (0.90-1.76)
Moxifloxacin	$219.80 (166.4-290.4)	$986.16 (685.7-1,418.4)	1.00
Clarithromycin XL	$177.34 (138.4-227.2)	$795.64 (564.9-1,120.6)	0.81 (0.56-1.17)

* Rate ratios were obtained by dividing the cost rate for the particular antibiotic group by the cost rate for the moxifloxacin group.
† Significant compared to moxifloxacin.

costs to treat all AS patients between moxifloxacin and the other study drugs.

Table 9 presents the adjusted total costs for the successful treatment of CB, adjusted total costs for treatment failures of CB, and the associated cost rate ratio for the treatment of all patients (successes and failures). For the successful treatment of CB, cost rates ranged from $177.34 for clarithromycin XL to $471.70 for cefuroxime (moxifloxacin $219.80), while cost rates for treatment failures ranged from $795.64 for clarithromycin XL to $2,116.30 for cefuroxime (moxifloxacin $986.19). Evaluation of the cost rate ratios revealed that the cost to treat all patients with CB was significantly higher for cefuroxime (RR = 2.15; 95% CI 1.06-4.36), gatifloxacin (RR = 1.60; 95% CI 1.08-2.39), and clarithromycin (RR = 1.57; 95% CI 1.07-2.29) compared to moxifloxacin.

DISCUSSION

Practitioners have many options when it comes to selecting an initial antibiotic therapy for the treatment of CAP, AS, and CB. Practitioners often consider factors such as efficacy, spectrum of activity, duration of therapy required, dosage forms available, side effect profile, and cost of therapy when selecting the antibiotic regimen they will prescribe.[22,23] Numerous clinical trials have evaluated the efficacy of these agents with similar results,[24-27] while few studies have evaluated impact on healthcare costs. In a previous study of these same diagnoses, levofloxacin resulted in higher treatment costs compared to a number of other antibiotics.[17]

Overall, 17.7%, 14.2%, and 18.2% of treatment episodes for CAP, AS, and CB met the criteria for a treatment failure, respectively. The failure rates for AS and CB in our trial appear to be higher than the failure rates seen in a similar trials of branded antibiotics for the treatment of AS (9.2%)[13] and CB (12.1%);[12] these disparities may be a result of differences in the definition of a treatment failure[13] or the length of the follow-up period.[12] Compared to moxifloxacin, we found that there were no significant differences between the treatment failure rates for any of the antibiotics for any of the 3 studied indications. This finding matches the results of numerous clinical trials that have found similar efficacies between moxifloxacin and other branded antibiotics for these indications.[26-31]

We found that patients utilizing azithromycin had a lower mean days of therapy received compared to moxifloxacin. That result was to be expected, as azithromycin's indications for CAP and CB call for a shorter duration of therapy (5 days, and 3 or 5 days of therapy, respectively) compared to a range of 5 to 14 days of therapy for moxifloxacin. All other agents had significantly higher mean days of therapy received compared to moxifloxacin; slight differences in the indicated duration of therapy for those agents compared to moxifloxacin may have contributed to the differences we observed.

When examining total costs of therapy, moxifloxacin was found to have lower costs (in terms of total costs of therapy) than a number of other antibiotics for CAP and CB. Compared to moxifloxacin, CAP costs were 55% higher for ciprofloxacin, 41% higher for amoxicillin/clavulanate, and 29% higher for levofloxacin; CB costs were 115% higher for cefuroxime, 60% higher for gatifloxacin, and 57% higher for clarithromycin. None of the products examined in this analysis were found to be less costly than moxifloxacin for any of the studied indications. It is interesting to note that of the 9 antibiotic preparations examined in this analysis, moxifloxacin was the least utilized agent (used in only 3.7% of the treatment episodes). Increasing the utilization of moxifloxacin for the treatment of respiratory disorders (especially in substitution of certain agents for the treatment of CAP and CB) may result in a decrease in overall healthcare expenditures.

Diagnosing bacterial sinusitis is unreliable without sampling sinus contents by surgery or needle aspiration.[32] According to epidemiologic estimates, only 0.2% to 2% of viral upper respiratory infections are complicated by bacterial rhinosinusitis; AS often resolves in most patients without antibiotic treatment.[33,34] However, patients with evidence of an abnormal radiograph, severe unilateral maxillary pain, or symptoms persisting longer than 7 days are likely suffering from bacterial sinusitis. It is these patients for whom antibiotic therapy is most appropriate.[34]

This analysis had several limitations that merit mention. As this was a retrospective database analysis, the prescribing physician's rationale for selecting one antibiotic regimen over another is unknown; the severity of the condition or other patient characteristics may have influenced the physician's selection. Further, the nature of the data did not allow for the determination of patient adherence with therapy; poor adherence may have led to treatment failures requiring re-treatment with a second antibiotic prescription or hospitalization. Also, this study examined total healthcare costs and not disease-specific costs. Although our analysis adjusted for preexisting illnesses using the Deyo-Charlson Co-morbidity Index and baseline pharmacy and medical expenditures, payments for illnesses unrelated to the diagnosis of interest that occurred during the 30-day period following the Episode Index Date may have influenced the results. Lastly, generic antibiotics were excluded from this study; all analyses focused on branded antibiotics only. This study was performed from the perspective of a managed care decision maker. Generic products with similar safety and efficacy profiles as branded products are often included in managed care formularies due to their lower acquisition costs. However, for branded products, a plan with a closed or tiered formulary will likely need additional information to aid it in determining which products it may want to include as preferred products. Thus, this analysis of the branded products could supply them with information that is lacking and provides more than just looking at the medication costs alone.

CONCLUSION

The results of this retrospective, observational analysis demonstrated that there are considerable costs associated with treatment of CAP, AS, and CB with "branded" antibiotics. Although there was no significant difference in the treatment failure rates between moxifloxacin and the other "branded" antibiotics, this analysis established that the treatment of patients with moxifloxacin, when utilized in appropriate situations, has the potential to decrease overall medical costs of care for patients with CAP, AS, and CB.

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