An Economic Evaluation of Levofloxacin Versus Cefuroxime Axetil in the Outpatient Treatment of Adults with Community-Acquired Pneumonia

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Abstract

Objective: **To examine treatment costs of community-acquired pneumonia (CAP) in adult outpatients given oral (po) levofloxacin or cefuroxime axetil as initial therapy.**

Study Design: **Patients with a primary diagnosis of CAP were enrolled in a multicenter, prospective, randomized, open-label, active-controlled Phase III clinical trial. Both inpatients and outpatients were assigned to 1 of 2 treatment groups: (1) intravenous (IV) or po levofloxacin; or (2) IV ceftriaxone and/or po cefuroxime axetil.**

Methods: **To make legitimate and meaningful cost comparisons between similar types of patients receiving drugs via the same route of administration (ie, orally), this outpatient economic study examined the resource utilization of the 211 patients enrolled as outpatients who received oral formulations as initial treatment (levofloxacin, 103 patients; cefuroxime axetil, 108 patients). Resource utilization data and clinical trial data were collected concurrently. To generate cost estimates, Medicare cost estimates for resources were multiplied by the resource units used by patients in each treatment arm.**

Results: **Cost estimates indicated a total cost difference that favored the levofloxacin group (base case: $169; sensitivity analysis: $223 [*P* = .008]). The results for the base case were not significant (*P* = .094). In addition, within the cost categories, there was a statistically significant study drug cost differential favoring levofloxacin ($86; *P* = .0001 for both the base case and sensitivity analysis).**

Conclusion: **Oral levofloxacin is less costly than oral cefuroxime axetil in the outpatient treatment of adults with CAP.**

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Community-acquired pneumonia (CAP) has an estimated annual incidence in the US population of 4 million ambulatory patients, or 12 cases per 1000 persons.[1] The frequency of CAP in the United States mandates the constant development of antimicrobial agents that are effective in the empiric management of this disease. In addition, both the continuing evolution of antimicrobial resistance in typical respiratory tract pathogens, such as that of *Streptococcus pneumoniae* to penicillin, β-lactams, macrolides, and other agents, and that of *Haemophilus influenzae* and *Moraxella catarrhalis* to β-lactams, and the increasing frequency of CAP caused by atypical respiratory pathogens (eg, *Legionella*, *Chlamydia*, and *Mycoplasma* species) necessitate an ongoing search for new antimicrobial agents. In the current healthcare environment, how-

ever, which is characterized by cost-consciousness, medical need alone may be insufficient justification for adopting new products. Cost considerations have become a significant factor in drug selection. This study reports results from an economic evaluation intended to inform decision makers who must choose products for the treatment of adult outpatient CAP. The product under review is levofloxacin, a new fluoroquinolone antimicrobial agent.

Levofloxacin is a new broad-spectrum fluoroquinolone with activity against gram-negative and gram-positive aerobic respiratory tract pathogens. It demonstrates excellent in vitro activity against *S pneumoniae,* regardless of the organism's degree of susceptibility to penicillin,[2,3] and has produced successful results in clinical trials against this as well as other respiratory pathogens, such as *H influenzae, Staphylococcus aureus,* and *M catarrhalis.*[4-7] In addition, levofloxacin exhibits excellent activity against atypical respiratory tract pathogens, including *Mycoplasma, Chlamydia,* and *Legionella* species.[8-11] In vitro and clinical studies indicate that levofloxacin can be used successfully as monotherapy for community-acquired respiratory infections.[12] Furthermore, compared with other antimicrobial agents traditionally used in the management of CAP, once-daily dosing of this highly bioavailable agent[13] may increase compliance in the outpatient setting.

Most economic evaluations require a relevant, active control treatment for comparison, as the goal of economic analysis, unlike that of registration trials, is to be prescriptive. Registration trials assess safety and efficacy so that physicians can know candidate treatments are safe and effective. This determination is a precondition of economic evaluation, but economic analysis attempts to go further by suggesting *optimal* courses of action that can help physicians choose among appropriate treatments with specific formulations geared to a particular setting (eg, oral formulations for outpatients). This task is necessarily a comparative one and must use a comparator that has relevance to the practical situation in the market (ie, the comparator cannot be a placebo). Our research examines the economic performance of oral (po) levofloxacin (Levaquin®, Ortho-McNeil Pharmaceutical, Raritan, NJ) and po cefuroxime axetil (Ceftin®, Allen & Hanburys, Research Triangle Park, NC) in the treatment of CAP.

This economic analysis is based on data collected as part of a Phase III clinical efficacy study[4] that compared levofloxacin with 2 cephalosporins: ceftriaxone and cefuroxime axetil. Cephalosporins are among the most commonly used antibiotics for the treatment of inpatient and outpatient CAP. Although both ceftriaxone and cefuroxime axetil have been shown to be effective in CAP and other lower respiratory tract infections,[14-20] neither agent has the in vitro activity of levofloxacin against *atypical* respiratory tract pathogens.[4]

Ceftriaxone is a third-generation cephalosporin and the most frequently prescribed antimicrobial agent for inpatients with CAP.[21-23] Because cefuroxime axetil, a second-generation cephalosporin, has an antimicrobial profile similar to that of ceftriaxone and is frequently prescribed as an oral alternative to ceftriaxone, it is the appropriate choice for the Phase III registration trial (ie, to accommodate switching between intravenous (IV) and po formulations in the emergency department and in inpatient versus outpatient settings). Cefuroxime axetil is the most commonly prescribed cephalosporin for outpatient CAP.[22]

This Phase III trial therefore included relevant comparator products so that useful economic analysis legitimately could proceed concurrently. This paper reports economic outcomes for outpatients receiving either po levofloxacin or po cefuroxime axetil as initial primary treatment in the clinical trial, the results of which were reported in File et al.[4] A separate economic analysis of the inpatient results from the same trial has been reported previously.[24]

··· METHODS ···

Study Design

This clinical study was a multicenter, prospective, randomized, open-label, active-controlled Phase III trial. Patients were randomly assigned to 1 of 2 treatment groups: (1) IV or po levofloxacin; or (2) IV ceftriaxone and/or po cefuroxime axetil. Adult patients with a primary diagnosis of CAP were eligible for enrollment. The inclusion and exclusion criteria for the clinical study have been reported elsewhere.[4] A total of 310 patients were enrolled as outpatients and 280 patients as inpatients. The economic research reported here examines only those enrolled as outpatients.

The clinical study was initiated before the commencement of economic-data collection, which was added to the study through protocol amendment. Therefore, no economic data were collected for the first 82 outpatients in the clinical study whose participation began prior to the amendment. An additional 17 patients were excluded from the economic

evaluation for the following reasons: (1) 3 patients had incomplete data; (2) 7 patients were lost to follow-up; (3) 1 patient received 3 days of IV drug as initial treatment; and (4) 6 patients experienced serious adverse events judged by the investigator to be unrelated to the study drug. The remaining 211 patients, for whom data were complete, were included in the analyses.

With the exception of some patients who were enrolled in the study through the emergency department, all outpatients included in this economic analysis received oral medications as initial treatment. Some patients enrolled through the emergency room received an initial dose of IV antimicrobial agent (levofloxacin in the trial arm and ceftriaxone in the cefuroxime axetil arm). Of the 211 outpatients included in this outpatient economic evaluation, 103 received po levofloxacin 500 mg once daily (qd) for 7 to 14 days and 108 received po cefuroxime axetil 500 mg twice daily (bid) for 7 to 14 days. In addition, patients in the po cefuroxime axetil group in whom atypical respiratory tract pathogens were suspected or confirmed could receive po erythromycin at a dosage of 0.5 to 1 g every 6 hours. Patients who were unable to tolerate erythromycin could be given doxycycline po. Patients whose outpatient treatment was unsuccessful could be hospitalized and switched to IV formulations, with IV ceftriaxone substituting for po cefuroxime axetil with or without erythromycin or doxycycline.

Resource Utilization

During the course of the clinical study, resource utilization data were collected on all medications (ie, the study medication, other antimicrobial agents, and concurrent nonantimicrobial agents), and on outpatient, emergency department, and hospital care (including all laboratory and other procedures). The data were collected from the time of entry into the study until the required poststudy visit, at 21 to 28 days posttherapy. Resource utilization data were collected even after a patient was classified as a "failure" (defined as no response to therapy).

Although CAP was the primary diagnosis for enrolled patients, the likelihood that some significant comorbidities were present suggested that resource utilization data be separated into 2 categories: (1) data related to CAP or respiratory problems; and (2) data unrelated to CAP or respiratory problems. The inherently higher variance associated with resource utilization variables versus clinical ones[25] contributed to the rationale for this type of resource utilization identification. Therefore, including *unrelated* resource use would further increase the variance associated with estimates of total costs from that associated with related resource utilization alone. This variance was already expected to be high relative to the variance in the pooled-sample clinical study because the sample size in the separated outpatient sample (n = 211) was smaller. The sample size in the trial was determined solely with reference to *clinical* outcomes in a *pooled* inpatient and outpatient sample (n = 590). Therefore, the attempt to reduce the variance in the outpatient economic analysis by separating CAP- and respiratory-related resource utilization was deemed necessary to increase the likelihood that we could make statistical inferences about the relative costs of treating CAP in the smaller subsets of separately analyzed inpatients and outpatients. In all cases, the investigating physician determined the "relatedness" of resource utilization to CAP and respiratory problems.

With several exceptions, which are specified in the Study Design section or in the forthcoming discussion of the sensitivity analysis, all the analyses were based on assumptions made by a contract research organization (Technology Assessment Group, San Francisco, CA). This organization was blinded to the treatment group.

Costs

Utilization data for each resource were converted into resource costs by multiplying unit cost estimates by units of resource utilization observed in the trial. These unit costs were based on the Medicare national fee schedule, if these estimates were available. In cases in which Medicare unit cost estimates were not available, we estimated costs to be 61% of private-payer fees (obtained by a Technology Assessment Group survey), based on the reported average ratio of Medicare payments to private-sector charges.[26] All drug costs were estimated using published average wholesale prices (AWPs).[27] Study drug costs were $7.35 per day for levofloxacin (500 mg po qd) and $13.64 per day for cefuroxime axetil (500 mg po bid). All costs are reported in 1997 US dollars.

Practical and theoretical reasons exist for relying on Medicare cost estimates. Both reasons are important. From a practical point of view, given that most clinical trials are multicentered, assessing actual charges at each center would yield a result that (like the economic results from a pooled inpatient and outpatient sample) would be an arbitrary mix of the

centers' charges. To the extent that these centers had different charges (as is often the case), this mix would be of no relevance to any organization unless it had a mix of similar variety. It would be far more useful to develop a uniform estimate of costs to be applied to all centers.

With respect to the theoretical reason, it is important to establish a measure that is valid, as well as uniform. The validity of any measure of "costs" depends crucially on the purpose the measure is intended to serve. The Medicare fee schedule partly was designed to reflect estimates of the true "economic" costs of resources,[28] whereas accounting entries or charges from claims data tend to be conglomerations of various fees sometimes only loosely associated with the true economic costs of a given activity. To optimize decisions, healthcare providers (but not necessarily third-party payers) should be interested in the true economic costs of an activity, rather than in some other cost concept that is only tangentially related to true costs.[29] The Panel for Cost-Effectiveness in Health and Medicine, which represents a consensus of experts in the evaluation field, endorses the use of Medicare fees in order to approximate true economic activity costs in economic evaluations.[30] This practice both provides a uniform and relevant set of costs and adheres to the standard in the field of economic evaluation.

Statistical Analyses

As the economic sample could not include all outpatients from the trial (see the Study Design section), we compared the demographic characteristics of those in the economic sample and those who were excluded. We made a similar comparison between the treatment groups of those within the economic sample. Discrete variables (sex, race, age category, infection severity, and efficacy) were compared across these groups, using chi-square tests. Two-sided *t*-tests were used for analyses of continuous variables (mean costs and mean age). *P* values of significance levels of estimates are reported for all comparisons.

The sample size for the clinical study was based on power calculations for detecting a statistically significant difference at conventional levels ($P < .05$) in the primary clinical end point (clinical treatment success) for the *pooled* outpatient and inpatient sample. As previously indicated, however, the outpatient sample available for this economic analysis was much smaller than the full sample for the pooled study. The difference in sample size, combined with the knowledge that economic variables tend to exhibit larger variances than do clinical variables,[25] considerably reduced the likelihood of achieving statistical significance in this economic analysis at the conventional levels expected in the clinical research.

··· RESULTS ···

As shown in Table 1, no statistically significant differences were observed between the baseline demographic characteristics of the outpatients included in the economic evaluation and the baseline demographic characteristics of the outpatients included in the clinical study but not in the economic evaluation. In addition, as indicated in Table 2, there were no statistically significant differences in the baseline demographic characteristics of the 2 groups of patients in the economic evaluation (ie, those in the levofloxacin and cefuroxime axetil groups).

The mean total duration of treatment for the outpatients included in the economic analysis sample was 11.7 days in the levofloxacin arm versus 12.3 days in the cefuroxime axetil arm. Nineteen patients (17.6%) in the cefuroxime axetil arm also received IV ceftriaxone. In comparison, only 6 levofloxacin-treated patients (5.8%) received IV levofloxacin, with 1 patient receiving the IV formulation only. Fifteen patients (13.9%) receiving ceftriaxone and/or cefuroxime axetil also received erythromycin or doxycycline therapy for an average of 11.3 days. The mean durations of po and IV levofloxacin therapy were 11.7 and 2.5 days, respectively. In the comparator arm, 94 subjects (87.0%) received po cefuroxime axetil 500 mg bid and 14 subjects (13.0%) received po cefuroxime axetil 250 mg qid. The mean durations of IV ceftriaxone, cefuroxime axetil 500 mg bid, and cefuroxime axetil 250 mg qid treatments were 1.2, 11.9, and 12.4 days, respectively.

Table 3 indicates the mean total cost estimates, by treatment, as well as those for several component cost categories. The levofloxacin treatment group demonstrated a total cost advantage over cefuroxime axetil (mean advantage, $169); the total cost for cefuroxime axetil treatment was 24% higher than that for levofloxacin ($P = .094$; not statistically significant at a conventional *P*-value threshold for clinical analysis). Study medications were less expensive in the levofloxacin group than in the cefuroxime axetil group (mean advantage, $86), and the result achieved statistical significance ($P = .0001$). Mean

cost estimates for 3 of the other 5 cost categories also indicated advantages for the levofloxacin treatment group, but not at statistically significant levels.

In economic analysis, it is necessary to make assumptions, as well as to account for the uncertainty surrounding sampling variation by testing the statistical significance of results. This type of analysis therefore commonly includes a sensitivity analysis that changes 1 or more assumptions about which there is some uncertainty in order to determine the sensitivity of results to the change. To increase the statistical power to detect differences between treatment arms, our base-case analysis excluded costs unrelated to CAP or respiratory problems. Under the study protocol, the clinical investigators determined, a priori, whether resource utilization was related or unrelated to CAP or respiratory problems. We tested the sensitivity of our results to including unrelated resource utilization costs. The inclusion was expected to increase total costs in each treatment group without greatly affecting the estimated difference in treatment costs. Statistical significance was expected to decrease. Total treatment costs increased to $906 and $736 for cefuroxime axetil and levofloxacin, respectively, with the cost savings due to levofloxacin increasing by $1 to $170. Surprisingly, the statistical significance was unaffected (P = .093).

We conducted a second sensitivity analysis to account for the effect of duration on treatment. A therapy spell of less than 48 hours' duration is sufficiently short such that one may question whether it is possible to make valid conclusions about the effect of treatments evaluated in a study. We therefore performed a sensitivity analysis that excluded from the analysis any subject who did not receive at least 48 hours of the assigned study medication.

Only 1 patient included in this economic evaluation received fewer than 48 hours of therapy with the assigned study medication. The patient received 1 dose of po levofloxacin as an outpatient and, the following day, was admitted to a hospital and switched from levofloxacin to erythromycin. The patient did not have any reported adverse experiences related to the study drug;

Table 1. Baseline Characteristics of Patients Included in the Economic Sample Evaluation Compared with Those Excluded from the Evaluation

	Included in Economic Sample (n = 211)	Not Included in Economic Sample (n = 99)	*P*
Age			
<45	110 (52.1%)	58 (58.6%)	.525
45-64	58 (27.5%)	22 (22.2%)	.269
65+	43 (20.4%)	19 (19.2%)	
Mean	48.2	45.8	
Sex			
Male	112 (53.1%)	53 (53.5%)	.940
Race			
White	149 (70.6%)	71 (71.7%)	.480
Black	59 (28.0%)	25 (25.3%)	
Hispanic	3 (1.4%)	2 (2.0%)	
Other	0 (0.0%)	1 (1.0%)	
Severity of Infection			
Mild or moderate	194 (91.9%)	89 (89.9%)	.552
Severe	17 (8.1%)	10 (10.0%)	

Table 2. Baseline Characteristics of Patients in Economic Sample Receiving Oral Levofloxacin Versus Those Receiving Oral Cefuroxime Axetil

	Levofloxacin (n = 103)	Cefuroxime Axetil (n = 108)	*P*
Age			
<45	55 (53.4%)	51 (47.2%)	.233
45-64	32 (31.1%)	30 (27.8%)	.126
65+	16 (15.5%)	27 (25.0%)	
Mean	46.3	50.0	
Sex			
Male	52 (50.5%)	60 (55.6%)	.461
Race			
White	74 (71.8%)	75 (69.4%)	.724
Black	27 (26.2%)	32 (29.6%)	
Hispanic	2 (1.9%)	1 (0.9%)	
Severity of Infection			
Mild or moderate	95 (92.2%)	99 (91.7%)	.880
Severe	8 (7.8%)	9 (8.3%)	

Table 3. Per-Patient Mean Costs of Oral Levofloxacin Versus Oral Cefuroxime Axetil*

	Levofloxacin (L) (n = 103)	Cefuroxime Axetil (C) (n = 108)	Difference (L—C)	*P*
Costs ($)				
Study medications	92 (3.7)	178 (13.0)	-86	.0001
Other antimicrobial agents	7 (2.6)	9 (2.4)	-2	.463
Concurrent medications	7 (1.5)	5 (1.2)	2	.307
Outpatient visits	448 (13.9)	419 (13.9)	29	.135
Emergency department visits	101 (17.3)	131 (20.7)	-30	.263
Hospitalizations	61 (60.2)	141 (79.1)	-80	.425
Total Costs	716 (59.0)	883 (80.2)	-169	.094

*Standard errors are shown in parentheses.

Table 4. Sensitivity Analysis Results: Per-Patient Mean Costs of Oral Levofloxacin Versus Oral Cefuroxime Axetil (patients receiving >1 dose of study medication*)†

	Levofloxacin (L) (n = 102)	Cefuroxime Axetil (C) (n = 108)	Difference (L—C)	*P*
Costs ($)				
Study medications	92 (3.6)	178 (13.0)	-86	.0001
Other antimicrobial agents	7 (2.6)	9 (2.4)	-2	.473
Concurrent medications	7 (1.5)	5 (1.2)	2	.294
Outpatient visits	451 (13.8)	419 (13.9)	32	.100
Emergency department visits	102 (17.5)	131 (20.7)	-29	.280
Hospitalizations	1 (0.4)	141 (79.1)	-140	.080
Total Costs	660 (20.1)	883 (80.2)	-223	.008

*One patient, enrolled as an outpatient and who received only 1 dose of study medication before hospitalization for additional treatment, was excluded from this analysis. (The patient was not hospitalized because of an adverse reaction; see the text for a more detailed explanation.)
†Standard errors are shown in parentheses.

because of the switch to inpatient status 1 day into the trial, however, this patient had the highest total healthcare cost among those included in the economic evaluation ($6376). Although the patient was retained in our initial analysis, the minimal dose of drug given, the virtually immediate change to inpatient status, and the nature of the patient as a statistical outlier in terms of costs suggests that the patient would be excluded in a reasonable sensitivity analysis.

When this patient is excluded from the economic evaluation, the cost advantage in favor of levofloxacin increases from the base-case estimate of a mean difference of $169 to a difference in mean total cost of $223. In this sensitivity analysis, the total healthcare costs in the cefuroxime axetil group ($883) are 34% higher than those in the levofloxacin group ($660). The *P* value drops from .094 to .008, indicating statistical significance at the conventional level of 5%. Results from the sensitivity analysis are presented in Table 4.

··· DISCUSSION ···

This economic evaluation indicated that total treatment costs in the group of outpatients receiving levofloxacin as initial treatment for CAP are lower than those in the group receiving cefuroxime axetil as initial treatment. This finding was true for both the base-case analysis and the sensitivity analysis. The expected cost savings per patient from using levofloxacin is $169 (a mean of $223 per patient in the sensitivity analysis).

In the broader base-case analysis, in which the *P* value for the total cost difference was .09, the conventional statistical significance threshold for clinical research of $P < .05$ was not attained. This result was

not surprising, as it was obtained from a trial in which the sample size was based on power calculations for detecting a significant difference in clinical (rather than economic) outcome variables in a much larger pooled analysis of outpatients and inpatients (n = 590), rather than in an analysis of outpatients alone (n = 211). Given this sample size problem, it is particularly noteworthy that the *P* value for the difference in total costs in the sensitivity analysis (.008) surpassed the conventional statistical significance threshold.

Readers should note that economic analysis frequently requires consideration of clinical outcomes as well as costs.[31] Safety and clinical outcome measures from this Phase III study have been reported previously.[4] Those results indicated that more patients achieved successful clinical outcomes (cure or improvement) with levofloxacin than with the comparator treatment (96% versus 90%; $P < .05$). If a product achieves equal or better efficacy than does another product, but at a lower overall cost, it is not necessary to consider cost-effectiveness thresholds.

Lower study medication costs explain approximately half the total cost savings associated with levofloxacin. The lower cost per day of levofloxacin treatment, which is largely the result of once-daily dosing of po levofloxacin compared with twice-daily dosing of po cefuroxime axetil, partly accounts for this finding. In the sensitivity analysis, a substantial, although not statistically significant, difference in estimated costs of hospitalization (mean difference in favor of levofloxacin, $140 per patient; $P = .08$) further supports the cost advantage of levofloxacin in the other cost categories

This research used AWPs to estimate pharmaceutical costs. Institutions frequently obtain discounts from the AWP, which can differ by institution and manufacturer. It is not possible here to include a comprehensive analysis incorporating the range of discounts offered in the market. Nevertheless, even if those discounts were to imply that the mean study drug costs did not differ between the 2 treatment arms, levofloxacin would continue to exhibit a mean cost advantage of $83 per patient.

Although we use data from a clinical study that evaluated levofloxacin in both inpatients and outpatients, we limited this analysis to the subgroup of patients for whom treatment was initiated on an outpatient basis. From an analytic perspective, separate economic analyses for inpatients and outpatients are appropriate and necessary for the following reasons: (1) different comparators (both drug and formulation) were used in inpatients and outpatients (IV ceftriaxone and po cefuroxime axetil, respectively); (2) differences in the magnitude of costs between inpatient and outpatient treatment would increase the variance in the pooled sample and would reduce the statistical power of the economic analysis; and (3) the difference in treatment setting is likely to reflect a difference in disease severity. From a healthcare decision maker's perspective, only separate analyses are meaningful because drug formulary decisions for inpatients and outpatients reflect different comparators and decision criteria and may even involve different decision makers. Perhaps most important, pooling the samples potentially would allow the somewhat arbitrary trial recruitment mix of inpatients and outpatients to influence the conclusions. Consequently, at best, the results would be meaningful for an organization that had an identical mix of patient types. Separate analyses therefore substantially increase the utility of the results for decision making.

Differences in treatment setting and comparator easily could lead to differences in both qualitative conclusions and quantitative conclusions between the economic analyses of the inpatient and outpatient samples. Table 5 shows the results of the economic evaluation of the subgroup of inpatients, which we have published previously.[24] Relative to ceftriaxone, levofloxacin is associated with lower treatment costs in both inpatients and outpatients, although overall costs and the reduction in costs due to levofloxacin treatment are considerably larger in the group of inpatients.

The fact that our analysis is based on a Phase III registration trial raises the question of whether our results can be generalized to routine medical practice. Both patient selection and protocol-driven patient management can affect the ability to generalize economic results obtained from clinical trials.[32]

Patient selection for clinical studies takes into account comorbidities as well as the willingness and ability of patients to comply with study procedures. Patients with serious comorbidities often are excluded from these studies. It may not be possible to generalize our results to patients with comorbidities that were excluded from the clinical study.[4]

Patient selection and the controlled environment of a clinical trial generally imply higher drug compliance than can be expected in clinical practice. Reduced compliance may lead to a lower cure rate and could result in increased resource utilization because of the additional care required for treatment failures. This would be the case for both treatment

arms. Empirical evidence has demonstrated that a reduced frequency of dosing is associated with higher rates of compliance.[33] Switching from a clinical trial setting to clinical practice may therefore have less effect on compliance with levofloxacin, a once-daily treatment, than on compliance with cefuroxime axetil, a twice-daily treatment, especially given that the latter regimen may require the addition of erythromycin or doxycycline. It is therefore likely that our trial-based estimates underestimate the expected savings to be obtained by using levofloxacin in clinical practice.

Protocol-mandated visits and procedures can result in overestimation of resource utilization in each treatment arm in a study. More important, if 1 treatment is more efficacious, cost differences between treatment arms may be underestimated because study protocols generally require the same study visits and procedures regardless of whether a patient was treated successfully. Levofloxacin showed superior efficacy in the clinical study on which our economic analysis is based.[4] Therefore, the influence of this protocol, like that of compliance, likely produces an underestimate of the economic advantages of levofloxacin.

Recent clinical studies[4-7,12] have shown that doubts about the efficacy of the older fluoroquinolones against pneumococci that could limit the use of these agents in respiratory indications do not apply to levofloxacin. In the indication for CAP, levofloxacin appears not only to be an efficacious fluoroquinolone, but one that has been shown in a pivotal clinical trial[4] to have a higher treatment success rate than its cephalosporin comparators. The current economic study indicates that po levofloxacin in CAP is also likely to be cost-saving when compared with cefuroxime axetil. The availability of a product with greater efficacy at both lower expected drug cost and lower expected total cost is a considerable benefit to organizations responsible for healthcare delivery. Whether one is motivated solely by considerations of drug efficacy or drug cost or by total treatment costs, the results of this study point to levofloxacin as a superior product in the adult outpatient treatment of CAP.

Table 5. Per-Patient Mean Costs of IV Levofloxacin Versus IV Ceftriaxone in an Inpatient Treatment Setting (previously published results[24])

	Levofloxacin (L) (n = 89)	Ceftriaxone (C) (n = 89)	Difference (L—C)	*P*
Costs ($)				
Study medications	195	388	-193	.0001
Total Costs*	6072	7422	-1410	.048

*Total inpatient costs reported here are the sum of the same categories of costs as reported in Tables 3 and 4 for outpatients.

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