Impact of First-Line vs Second-Line Antibiotics for the Treatment of Acute Uncomplicated Sinusitis

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Sinusitis is associated with significant morbidity, anxiety, reduced quality of life, lost time from work, and treatment expense. It is estimated that approximately 35 million US residents have some form of sinusitis, and in 1996 the direct cost of this disorder in the United States was more than $3.3 billion.1 McCaig and Hughes2 analyzed National Ambulatory Medical Care Surveys (NAMCS) data and found that acute and chronic sinusitis was the fifth most common diagnosis for which antibiotics were prescribed and also found an increasing trend of office visits between the years 1980 and 1992. In 1992 alone, sinusitis accounted for 12% of all recorded antibiotic prescriptions. There was a trend over time toward increased use of more expensive broad-spectrum antibiotics and decreased use of less expensive narrow-spectrum antibiotics. Ironically, this trend to prescribe more expensive antibiotics with a broader spectrum of action occurs despite evidence that about two thirds of patients with acute sinusitis improve or are cured without any antibiotics.3,4

Antibiotic selection for initial management of acute sinusitis is controversial, and there is much variation in clinical practice.3,6–8 Recommendations for antibiotics for initial treatment of acute sinusitis vary between older less expensive antibiotics (eg, amoxicillin and trimethoprim-sulfamethoxazole)5,9 and newer more expensive drugs with a broader antimicrobial spectrum (eg, clarithromycin, amoxicillin and clavulanic acid, and more recent macrolides)6,10

Context Studies suggest little benefit in relief of acute sinusitis symptoms from the use of newer and more expensive (second-line) antibiotics instead of older and less expensive (first-line) antibiotics. However, researchers have failed to include development of complications and cost of care in their analyses.

Objective To compare the effectiveness and cost of first-line with second-line antibiotics for the treatment of acute uncomplicated sinusitis in adults.


Main Outcome Measures Absence of additional claim for an antibiotic in the 28 days after the initial antibiotic, presence of a claim for a second antibiotic, serious complications of sinusitis, and direct charges and use for the acute sinusitis treatment.

Results There were 17 different antibiotics prescribed in this study. The majority (59.5%) of patients received 1 of the first-line antibiotics. The overall success rate was 90.4% (95% confidence interval [CI], 90.0%-90.8%). The success rate for the 17,329 patients who received a first-line antibiotic was 90.1% and for the 11,773 patients who received a second-line antibiotic was 90.8%, a difference of 0.7% (95% CI, 0.01%-1.40%; P < .05). There were 2 cases of periorbital cellulitis, one in each treatment group. The average total direct charge for patients receiving a first-line antibiotic was $68.98 and a second-line antibiotic was $135.17, a difference of $66.19 (95% CI, $64.95-$67.43; P < .001). This difference was due entirely to the difference in charge of antibiotics and not other charges, such as professional fees, laboratory tests, or emergency department visits.

Conclusions Patients treated with a first-line antibiotic for acute uncomplicated sinusitis did not have clinically significant differences in outcomes vs those treated with a second-line antibiotic. However, cost of care was significantly higher for patients treated with a second-line antibiotic.

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and cefuroxime). The recent Evidence-Based Practice Center report and the American College of Physicians-American Society of Internal Medicine Position Papers both state that the most cost-effective way to manage acute sinusitis in the community is to initially use symptomatic treatment only (eg, decongestants, nasal steroids). Further treatment, including the use of antibiotics, should be guided by clinical criteria, such as type, duration, and severity of symptoms.

In the ambulatory care setting, the epidemiologic emergence and spread of resistant bacteria are a major problem. Bacterial proliferation is thought to occur as a result of the increasing use of antibiotics, especially in the treatment of viral acute respiratory tract infection. The increase in resistant bacteria has led to the recognition of the need for more prudent use of antibiotics by limiting use to the treatment of bacterial infections. Spontaneous resolution of symptoms, without antibiotics, occurs within 2 weeks in the majority of patients with acute sinusitis. And although the natural history and clinical course of acute sinusitis are quite favorable, serious sequelae and complications (eg, meningitis, brain abscess) do occasionally occur.

The goal of this study was to use a large and comprehensive pharmaceutical database to compare the effectiveness of first-line and second-line antibiotics for the treatment of acute uncomplicated sinusitis. The primary end point was the clinical response to initial treatment with an antibiotic. The secondary end points were the development of serious complications and cost of care. The implication of this research is that if there is no difference in clinical response and development of complications between patients treated with first-line antibiotics compared with those treated with second-line antibiotics, then the least expensive (ie, first-line) antibiotics should be chosen. Because of the large size of the database and the inclusion of accurate clinical and charge data, all 3 important end points were studied. The findings from this study will assist in the management of patients with acute uncomplicated sinusitis.

### METHODS

#### Study Population

For this study, we used data from the Express Scripts Patient Treatment Episode (PTE) registry, a relational database with more than 2.1 million covered lives from several large health maintenance organizations. The PTE registry includes integrated medical claims and pharmaceutical data. The study population included insurance plan members who had an office visit with an accompanying International Classification of Diseases, Ninth Revision (ICD-9) code for acute sinusitis (461.0-461.3, 461.8, or 461.9) between July 1, 1996, and June 30, 1997, and who also had 60 days of enrollment prior to and 365 days after the first sinusitis-associated office visit (TABLE 1). Subjects were excluded if they were younger than 18 years, had an earlier diagnosis of acute sinusitis in the 60 days prior to the index office visit, received a prescription for an antibiotic in the 60 days prior to the index office visit for a concurrent infectious disease, or had received a diagnosis for chronic sinusitis (ICD-9, 473.0-473.9) in the study focus year. Subjects with a diagnosis of cystic fibrosis, human immunodeficiency virus (HIV) infection, or any other immunodeficiency were excluded. Subjects with complications of acute sinusitis, including periorbital cellulitis, orbital cellulitis, meningitis, and intracranial abscess, prior to the index office visit were also excluded. Patients who received a prescription for an antibiotic in the 60 days prior to the index office visit were also excluded because the subsequent antibiotic use during the study period may have been for the comorbid condition and not for sinusitis. This concurrent use of antibiotic would lead to mislabeling of the indication for and evaluation of the success of the antibiotic. Finally, patients for whom no antibiotic was prescribed after the index office visit were excluded. Given the structure of the database, we could not conclude with certainty that patients who did not have a claim for an antibiotic did not receive an antibiotic as an office sample.
Physician Type
The physician type was determined by the physician type code attached to each office visit claim. Physician type was categorized as primary care if the code indicated the physician was a primary care or internal medicine physician, specialist if the physician was an otolaryngologist, allergist, or pulmonologist, and other was selected for all other physician types.

Antibiotics
The name and frequency of the antibiotics that were prescribed in association with the index office visit are listed in Table 2. The antibiotics are grouped into 2 categories: first line or second line based on accepted treatment guidelines.1,9

Sinusitis Classification, Treatment, and Outcome
The classification of a sinusitis episode was determined retrospectively by the investigators based on guidelines from the American Academy of Otolaryngology-Head and Neck Surgery Foundation Inc19 and from previously published standards.25,26 Patients with asthma, allergic rhinitis, or nasal polyps were classified as having comorbidity. The primary treatment for the index acute sinusitis episode was either a first-line or second-line antibiotic. Information on adjuvant symptomatic therapy, consisting of decongestants, antihistamines, nasal steroids, or a combination of these medications, was also included. The sinusitis episode began with the first antibiotic prescription in a 6-day window period around the index office visit (ie, 3 days before and 3 days after).

Treatment success was defined as the absence of an additional claim for an antibiotic in the 28 days after the initial claim. Treatment failure was defined as the presence of an additional claim for a second antibiotic in the first 28 days after the initial claim. Based on clinical experience and the published literature,1,14,27 the investigators thought that a majority of episodes of additional antibiotics within the 28-day period represent failure of symptoms to improve. A minority of episodes reflect the development of an of the episode adverse reaction to the first antibiotic. Relapse was defined as the presence of a claim for a second antibiotic in the 15- through 28-day period after the initial claim.

Complications of acute sinusitis (ICD-9 code) include orbital cellulitis (376.01), periorbital cellulitis (682.0), meningitis-bacterial (320.81-320.9), subdural abscess (324.0), intracranial abscess (324.0), subperiosteal abscess (730.18, 730.08), orbital abscess (376.01), and cavernous sinus thrombosis (325). A complication was recorded if a claim containing an ICD-9 code corresponding to 1 of the conditions listed above was received within the 28-day follow-up period.

Direct Charges and Utilization
Direct charges and utilization were determined for the index episode of sinusitis and the 28-day follow-up period. All medical claims for charges and services attached to the ICD-9 acute sinusitis code claim were included in the direct charges and utilization analyses. Direct prescription charges for each patient were calculated by summing the charges for all of the study antibiotic drugs used by a patient in the 28-day period.

Statistical Analysis
The analysis of treatment effectiveness first proceeded with an analysis of the relationship between cogent demographic and clinical subgroups (ie, existence of comorbidity) and category of antibiotic use (first-line or second-line) and rate of the outcome event (success of antibiotic treatment). A t test, χ² test, and analysis of variance (ANOVA) were performed to test the statistical significance of the observed relationships. To adjust for inflated P values due to multiple comparisons in the ANOVA, the Bonferroni correction was used. Two-tailed tests of significance were used and P<.05 was selected for the level of statistical significance. Stepwise logistic regression analysis was used to assess the impact of treatment on outcome while controlling for the impact of baseline demographic and clinical factors.

Results are presented as differences in outcome between treatment groups, and 95% confidence intervals (CIs) are used to indicate the precision of the observed differences. Due to the extremely large number of patients contained within the database and the observational nature of the study, sample size calculations and determination of power to detect a clinically meaningful difference were not performed prior to the start of this study. All analyses were performed using SAS software, version 6.12 (SAS Institute, Cary, NC).

Unfortunately, multiple logistic regression techniques cannot discriminate between the effects of treatment and the effects of baseline features if these features are related to both treatment selection and outcome.28,29 In an attempt to control for significant factors related to treatment and outcome, Rubin28,29 proposed the use of propensity score technology. Propensity scores adjust for significant characteristics of the patient or provider that are related to the choice of a particular treatment (eg, antibiotic) and outcome. In this study, multivariable analysis was used to determine the factors related to the use of antibiotics (first

### Table 2. List of Antibiotics

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>No. (%) of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line</strong></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin*</td>
<td>11 528 (39.6)</td>
</tr>
<tr>
<td>Trimethoprim*</td>
<td>4629 (15.9)</td>
</tr>
<tr>
<td>Cefuroxime axetil*</td>
<td>1615 (5.5)</td>
</tr>
<tr>
<td>Cefprozil*</td>
<td>862 (3.0)</td>
</tr>
<tr>
<td>Cefclor†</td>
<td>585 (2.0)</td>
</tr>
<tr>
<td>Loracarbef*</td>
<td>455 (1.6)</td>
</tr>
<tr>
<td>Ciprofloxacin*</td>
<td>231 (0.8)</td>
</tr>
<tr>
<td>Ceftaxime</td>
<td>132 (0.4)</td>
</tr>
<tr>
<td>Cefpodoxime proxetil</td>
<td>74 (0.3)</td>
</tr>
<tr>
<td>Cephalexin†</td>
<td>51 (0.2)</td>
</tr>
<tr>
<td>Levofloxacin†</td>
<td>24 (0.05)</td>
</tr>
<tr>
<td>Clindamycin†</td>
<td>13 (0.04)</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>11 (0.03)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>29 102 (100.0)</td>
</tr>
</tbody>
</table>

*Has received US Food and Drug Administration approval for the treatment of acute sinusitis.  

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Table 3. Sample Characteristics by Treatment Class*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participants (N = 29,102)</th>
<th>Taking First-Line Antibiotics</th>
<th>Taking Second-Line Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td>29,102</td>
<td>17,329 (59.5)</td>
<td>11,773 (40.5)</td>
</tr>
<tr>
<td>Men</td>
<td>9,752 (33.5)</td>
<td>5,772 (59.2)</td>
<td>3,980 (40.8)</td>
</tr>
<tr>
<td>Women</td>
<td>19,350 (66.5)</td>
<td>11,557 (59.7)</td>
<td>7,793 (40.3)</td>
</tr>
<tr>
<td>Age, mean (SD), y†</td>
<td>38.6 (11.07)</td>
<td>38.1 (10.88)</td>
<td>38.9 (10.70)</td>
</tr>
<tr>
<td>Physician type‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary care physician†</td>
<td>23,435 (80.5)</td>
<td>14,139 (60.3)</td>
<td>9,296 (39.7)</td>
</tr>
<tr>
<td>Specialist‡</td>
<td>540 (1.9)</td>
<td>197 (36.5)</td>
<td>343 (63.5)</td>
</tr>
<tr>
<td>Other</td>
<td>5,127 (17.6)</td>
<td>2,993 (58.4)</td>
<td>2,134 (41.6)</td>
</tr>
<tr>
<td>Symptomatic therapy‡§</td>
<td>4,325 (14.9)</td>
<td>2,234 (51.2)</td>
<td>2,091 (48.4)</td>
</tr>
<tr>
<td>Comorbidity††</td>
<td>1,392 (4.8)</td>
<td>681 (48.9)</td>
<td>711 (51.1)</td>
</tr>
</tbody>
</table>

*Data are presented as number (percentage) unless otherwise indicated. †P < .001. ‡Otolaryngologist, allergist, pulmonologist. §Nasal steroids, decongestants, antihistamines. †Comorbid ailments: asthma, allergic rhinitis, or nasal polyps.

The propensity scores analysis was performed by examining a stepwise multivariable logistic regression analysis of the association between comorbidity (eg, patient preference), significant number of subjects within each quintile did not receive the treatment suggested by the propensity score. This variation in treatment within each quintile allowed for the comparison of success rates between subjects who received first-line antibiotics and those who received second-line antibiotics (ie, treatment effectiveness).

RESULTS

Description of the Population

The study population of 29,102 adults with an ICD-9 diagnosis code of acute sinusitis was drawn from a larger sample of 88,403 subjects. The largest numbers of patients were excluded either because they did not have a claim for receiving an antibiotic during the episode period (17,627) or had received an antibiotic during the 60-day preperiod (12,092) (Table 1). The use of office antibiotic samples is 1 reason a patient with a diagnosis of acute sinusitis may not have an associated claims record for an antibiotic prescription.

Distribution of First-Line and Second-Line Antibiotics

The list of 17 different antibiotics that the study subjects received and the frequency of use is shown in Table 2. The antibiotics are divided into first-line and second-line therapy. Amoxicillin was the most frequently prescribed (39.6%), trimethoprim-sulfamethoxazole was the second most frequently prescribed (15.9%), and clarithromycin was the third most frequently prescribed (9.8%). The majority of patients (59.5%) received 1 of the first-line antibiotic agents. Surprisingly, a large number of patients (32%) received 1 of the antibiotics that are not approved for the treatment of sinusitis by the US Food and Drug Administration (FDA).

There was large variation in the frequency of antibiotic prescriptions throughout the year. As expected, the number of antibiotic prescriptions was greatest between the months of November and March. The frequency of antibiotic prescriptions throughout the year was similar between first- and second-line antibiotics.

Relationship Between Patient and Provider Characteristics and Treatment

The relationship between patient and provider characteristics and use of first- or second-line antibiotic is shown in Table 3. The relationship between the first-line vs second-line antibiotic use was approximately the same for men (59.2% vs 40.8%) as for women (59.7% vs 40.3%). The mean age was approximately the same within the 2 antibiotic groups (first-line, 38.1 vs second-line, 38.9).

The use of first-line and second-line antibiotics was different based on physician type (primary care vs specialty), use of adjuvant symptomatic therapy, and presence of concurrent diagnosis comorbidity. Primary care physicians were more likely to prescribe first-line antibiotics (60%) while specialists were more likely to prescribe second-line antibiotics (63.5%). Patients who received adjuvant symptomatic therapy were more likely to receive first-line antibiotics. Patients who had comorbidity were also more likely to receive second-line antibiotics.

Treatment Outcomes

The overall treatment outcomes and outcomes according to patient charac-
teristics and antibiotic group are shown in Table 4. The overall success rate was 90.4%, (95% CI, 90.0%-90.8%), failure rate was 3.4%, and relapse rate was 6.3%. Men had a statistically significantly higher success rate than women (91.9% vs 89.6%; difference, 2.3%; 95% CI, 1.6%-3.0%; P<.001) and lower relapse rate (4.9% vs 6.9%) than women. The mean age of the patients classified as a success was statistically significantly lower than the mean age of the patients classified as a failure (38.5 vs 39.5 years; difference, 1.1 years; 95% CI, 0.7-1.5; P<.001). Patients who had a concurrent diagnosis of a comorbid ailment had a significantly lower success rate than those patients without a comorbid ailment (85.1% vs 90.6%; difference, 5.5%; 95% CI, 3.8%-7.2%; P<.001).

The success rate for the 17329 patients who had received first-line antibiotics was 90.1%, and for the 11773 patients who received a second-line antibiotic, it was 90.8%, a difference of 0.7% (95% CI, 0.0%-1.4%; P<.05). Among patients who received first-line antibiotics, the relapse rate was 3.3% and for patients who received second-line antibiotics, the rate was 3.5%. Given this small absolute difference in success rates between patients treated with a first-line vs a second-line antibiotic, 131 patients must be treated with a second-line antibiotic to obtain 1 additional cure had all 29102 patients received a first-line antibiotic.

Direct Charges
The average total direct charges and breakdown of charges by setting according to antibiotic class are shown in Table 5. As can be seen, the average total direct charges for patients who received first-line antibiotics was $68.98 while the amount for patients who received second-line therapy was $135.17. The difference in charges was $66.19 (95% CI, $64.95-$67.43; P<.001). Based on the average charges for patients treated with first-line and second-line antibiotics, an additional $8737 per success is spent when a second-line antibiotic is chosen rather than a first-line antibiotic. As shown in the breakdown of charges, this large difference is due entirely to differences in the cost of prescription therapy and not for other services, such as professional visits, tests, laboratory or pathology, medical or surgical, or emergency department visits.

Propensity Scores Analysis
In Table 6, the results of propensity scores analysis are shown. As described in the “Methods” section, the propensity scores analysis used logistic regression analysis to divide the patients into quintiles based on the propensity to receive a particular category of antibiotic (eg, first-line or second-line). The probability that a patient would receive a first-line antibiotic (as opposed to second-line antibiotic) increased from quintile 1 to quintile 5. Success, failure, and relapse rates for patients treated with first-line and second-line antibiotics were determined within each quintile group. Average direct charges for patients receiving first-line and second-line antibiotics were compared within quintile group and are also presented in Table 6.

There is no consistent pattern of difference in success, failure, or relapse rates between first-line and second-line antibiotics across the different quintiles. With the exception of the second quintile, the success rates between first-line and second-line antibiotics are

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Table 4. Relationship Between Patient Characteristics, Type of Provider, and Treatment and Success Rate

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%) Successfully Treated</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>26 295 (90.4)</td>
<td>(86.5 to 94.3)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>8957 (91.9)</td>
<td>2.3 (1.6 to 3.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Women</td>
<td>17 338 (89.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>38.3 (10.8)</td>
<td>1.1 (0.7 to 1.5)†</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1184 (85.1)</td>
<td>5.5 (3.8 to 7.2)‡</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No</td>
<td>25 111 (90.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician type‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary care</td>
<td>21 134 (90.2)</td>
<td>0.9 (0.04 to 1.8)</td>
<td>&lt;.11</td>
</tr>
<tr>
<td>Other</td>
<td>4673 (91.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist</td>
<td>488 (90.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3928 (90.8)</td>
<td>0.5 (−0.5 to 1.5)</td>
<td>.26</td>
</tr>
<tr>
<td>No</td>
<td>22 367 (90.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line</td>
<td>15 604 (90.1)</td>
<td>0.7 (0.0 to 1.4)‡</td>
<td>&lt;.03</td>
</tr>
<tr>
<td>Second line</td>
<td>10 691 (90.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as number (percentage) unless otherwise indicated. CI indicates confidence interval.
†Difference in years between successfully and unsuccessfully treated patients.
‡Difference calculated between primary care and other.

Table 5. Average Direct Charges by Antibiotic Group

<table>
<thead>
<tr>
<th>Antibiotic Group</th>
<th>Total Direct Charges</th>
<th>Professional Visits</th>
<th>Tests</th>
<th>Laboratory or Pathology Tests</th>
<th>Medical or Surgical Interventions</th>
<th>Prescriptions</th>
<th>Emergency Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line, $</td>
<td>68.98</td>
<td>47.04</td>
<td>1.26</td>
<td>1.41</td>
<td>0.48</td>
<td>18.19</td>
<td>0.61</td>
</tr>
<tr>
<td>Second line, $</td>
<td>135.17</td>
<td>47.57</td>
<td>2.75</td>
<td>1.80</td>
<td>0.58</td>
<td>81.21</td>
<td>1.26</td>
</tr>
</tbody>
</table>

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not statistically different within each quintile. However, within each quintile, the average direct charges are very different between patients receiving first-line or second-line therapy. In each quintile, patients who received first-line therapy had a statistically significant lower average charge.

**Complication Rates**

There were 2 patients who developed a complication of acute sinusitis in the 28-day follow-up period. In both cases, the complication was periorbital cellulitis. One patient had received a first-line antibiotic while the other received second-line therapy.

**COMMENT**

In this study, patients with acute uncomplicated sinusitis were prescribed a wide range of different antibiotics, many without FDA approval for use in acute sinusitis. The overall success rate was quite high and there was no clinically significant difference in success rates among patients treated with first-line and second-line antibiotics. Two patients developed periorbital cellulitis. One patient had received a first-line antibiotic while the other received second-line therapy.

The findings of this study agree with the recent recommendations of the American College of Physicians-American Society of Internal Medicine Clinical Practice Guideline15,16 and the Agency for Health Care Policy and Research report on the diagnosis and treatment of acute bacterial rhinosinusitis. Both the guideline and the report state that symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms. Antibiotics should be reserved for patients with moderately severe symptoms that have lasted more than 7 days and for those with severe symptoms, regardless of duration of illness. Indiscriminate use of antibiotics in ambulatory practice has contributed to the emergence and spread of antibiotic-resistant bacteria,18,22 allergic reactions, and drug-drug interactions. Antibiotics with the most narrow spectrum and are active against the likely pathogens, Streptococcus pneumoniae and Haemophilus influenzae, should be used.20 The duration of antibiotic use will also affect the development of resistance, and a recently published study suggests that short-course high-dose amoxicillin therapy may minimize the impact of antibiotic use on the spread of resistant pneumococci. These recommendations are based on the fact that most cases of acute, community-acquired sinusitis are preceded by vi-
ral upper respiratory tract infections and only 0.2% to 2% of viral infections are complicated by bacterial sinusitis.35,36

The analysis of the effectiveness of different treatments from an observational database is challenging due to the potential for bias and confounding, both of which are more likely to occur in observational research than in controlled clinical trials.37 In this study, potential sources of error included the inability to classify the severity of the index sinusitis episode, the variation in the treatment patterns of physicians regardless of the severity of illness of the patient, associated comorbidities, and seasonal patterns. These factors may be related both to the choice of antibiotics and the success of treatment. Using propensity scores analysis to control for features that were related to the use of a particular type of antibiotic, there was no significant difference in success rates for patients treated with first-line or second-line antibiotics. However, the large differences in charges between patients receiving first-line and second-line antibiotics remained.

There are several limitations to this research. First, the cohort was defined based on the ICD-9 code assigned at the time of office visit. The accuracy of this diagnosis was not confirmed, and it is possible that patients with other conditions, such as viral upper respiratory illness, may be included in this study. In fact, given the higher success rate observed in this study than in studies in which the diagnosis of acute bacterial sinusitis is confirmed38,39 suggests that patients with viral illness were included in this study. We were unable to estimate the magnitude of this misclassification in this study, although van Buchem et al40 found that approximately 45% of 488 patients presenting to general practitioners with symptoms suggestive of acute maxillary sinusitis had normal sinus radiographs. Furthermore, it is possible, although unlikely, that physicians used first-line antibiotics for patients suspected of viral illness while reserving second-line therapy for patients suspected of bacterial sinusitis. If this selective use of antibiotics did occur, then it is possible that a true antibiotic treatment effect was missed. Unfortunately, in this study, we were unable to investigate the outcomes of patients who did not receive an antibiotic because we could not be certain that those patients for whom an antibiotic claim was not attached to an office visit claim had not in fact received an office antibiotic sample. Information about the use of office antibiotic sample or adjuvant therapy samples was not obtained, and this failure could have led to underreporting of medication use.

The clinical severity of sinusitis is defined by the frequency and severity of symptoms, past history of response to antibiotics, recent use of antibiotics, severity of structural abnormalities within the nasal cavity, severity of abnormalities as defined by computed tomography, presence of concomitant diseases such as allergic rhinitis, nasal polyps, and asthma, and use of tobacco products or exposure to nasal irritants. Some, but not all, of these features were captured by the ICD-9 coding available for this study. Important clinical features of the patient not included in this study affected the accuracy of the prognostic stratification obtained through the propensity analysis. Imprecision in the definition of clinical severity will decrease the ability to detect true clinical effects of first-line and second-line antibiotics. Differences in clinical severity may explain the differences in the use of first-line and second-line antibiotics between primary care and specialty physicians. The patients who seek care from a specialist may, in one or more ways, be more ill than patients who seek care from a primary care physician.

There are no widely agreed on standard ways, at present, to assess treatment success, failure, or relapse for acute sinusitis. For most patients, the main effect of acute sinusitis is the production of symptoms that decrease quality of life, interfere with work or school, and may, in rare circumstances, result in hospitalization. The ideal outcome measure would incorporate patient-based measures of disease-specific functional status and quality of life.40,41 All outcome measures used in this study (success, failure, cost of care, and complications) were derived from claim records contained within the PTE database. No measures of symptoms, functional status, or quality of life were used. Although these outcome measures are clinically important, the authors do not believe that the incorporation of these measures in this study would undermine the central conclusions. Since sinusitis symptoms usually persist over a matter of weeks with gradual diminution over time, an analysis that reflected the impact of symptoms over time (eg, life table or Kaplan-Meier analysis) would be better than relying on a one-time snapshot of clinical response.

In conclusion, it appears that there is no incremental clinical benefit of newer, more expensive second-line antibiotics over older less expensive first-line antibiotics for patients with acute uncomplicated sinusitis. Due to the higher expense and potential for the development of resistant bacteria, physicians should avoid prescribing second-line antibiotics as the initial antibiotic treatment. Health departments, physician specialty organizations, managed care organizations, pharmacy benefits managers, and industry should promote recommendations for the use of narrower-spectrum, less expensive antibiotics (eg, amoxicillin, trimethoprim/sulfamethoxazole, or erythromycin) rather than broader-spectrum, more expensive antibiotics. It seems that there is a significant opportunity to improve patient care and decrease costs through more judicious use and selection of antibiotics.

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