lished, nor did we determine whether unpublished trials reported results on ClinicalTrials.gov.

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Author Contributions: Mr Smithy had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Downing, Ross. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: All authors. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Smithy. Study supervision: Downing, Ross.

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Burden of Ambulatory Visits and Antibiotic Prescribing Patterns for Adults With Community-Acquired Pneumonia in the United States, 1998 Through 2009

Community-acquired pneumonia (CAP) is commonly managed in ambulatory settings, yet little is known about trends in ambulatory visit rates or antibiotic prescribing for CAP in adults in the United States. The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS)2 published guidelines for CAP management in 2007. These guidelines recommend a macrolide or doxycycline for previously healthy ambulatory patients with CAP. Fluoroquinolone monotherapy or a β-lactam–macrolide combination are recommended for patients with comorbid conditions or risk factors for drug-resistant Streptococcus pneumoniae infection.

We estimated US adult ambulatory CAP visit rates and described antibiotic prescribing patterns for CAP. We also examined associations between patient and visit characteristics and antibiotic selection to assess concordance with IDSA/ATS guidelines.

Methods | We used 1998 through 2009 data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS), 2 annual surveys of ambulatory patient encounters in the United States.7 Adults at least 18 years of age with a primary International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis of pneumonia or a primary diagnosis of fever or cough and a secondary diagnosis of pneumonia, empyema, or pleurisy were considered to have CAP.7 Patients with concurrent bacterial illnesses and those requiring hospitalization were excluded from the prescribing analysis.

We used adjusted patient weights and age-specific and year-specific census estimates to calculate CAP visit rates for 6 periods of 2 years. We assessed trends in antibiotic selection using logistic regression analysis. To assess whether patient comorbid conditions were associated with receipt of a fluoroquinolone or a β-lactam–macrolide combination, as recommended by the IDSA/ATS guidelines, we used multivariable logistic regression analysis to assess patient and physician visit characteristics associated with receipt of these regimens. All statistical analyses were performed using Stata software, version 11 (StataCorp).

Results | An estimated 37 million visits occurred during the study period. Average annual visit rates were 12.6 to 15.7 visits per 1000 persons (Figure) and were highest among persons 65 years or older.

Figure. Population-Based Rates of Ambulatory Community-Acquired Pneumonia (CAP) Visits, by Age Group—United States, 1998 Through 2009

Individuals aged 18 to 49 years: P for trend, .82; 50 to 64 years: P for trend, .94; 65 years and older: P for trend, .16; all ages: P for trend, .51. Symbols indicate averages, and error bars, 95% confidence intervals.
Antibiotics were prescribed at 61% of CAP visits (Table); a single medication made up 88% of regimens. Fluoroquinolone treatment increased from 18% of regimens during 1998 to 1999 to 35% during 2008 to 2009 (P for trend,.01). Treatment with β-lactams decreased from 36% of regimens in 1998 to 1999 to 18% in 2008 to 2009 (P for trend,.02). No statistically significant associations were found between age, sex, race, presence of chronic comorbid conditions, insurance status, obtaining a chest radiograph, or tobacco use and receipt of fluoroquinolone monotherapy or a β-lactam-macrolide combination.

**Discussion** | We found no significant change in the burden of ambulatory CAP visits in the United States between 1998 and 2009. However, fluoroquinolone prescribing for CAP increased dramatically. Although β-lactams have not been recommended for CAP treatment since 2001, they still constituted 18% of regimens. Selection of fluoroquinolone monotherapy or a β-lactam-macrolide combination was not associated with the presence of comorbid conditions, as recommended by the IDSA/ATS CAP guidelines.

Convenient dosing may contribute to the popularity of fluoroquinolones, which has been documented elsewhere for other conditions. Because CAP treatment decisions are usually made empirically, physician preference may drive antibiotic selection. However, because indiscriminate use of antibiotics may select for resistance, reserving fluoroquinolones for specific indications may be important for preventing the development of resistance to this important class of antibiotics.

Because no specific diagnostic code for CAP exists, some patients may have been misclassified. In addition, we were unable to distinguish between diagnostic and follow-up visits, so both were likely included in our sample. Consideration of all comorbidities was not possible with data from the NAMCS and NHAMCS. Nonetheless, efforts to understand antibiotic selection are needed to inform efforts to promote guideline-concordant therapy. Improving guideline implementation will preserve the utility of fluoroquinolones for the patients who need them most, improving healthcare quality and reducing unnecessary variation in care.

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**Daniel J. Shapiro, BA**

**Adam L. Hersh, MD, PhD**

**Lauri A. Hicks, DO**

**Table. Frequency of Prescribing for Antibiotic Regimens for Community-Acquired Pneumonia, 1998 Through 2009**

<table>
<thead>
<tr>
<th>Antibiotic Regimen</th>
<th>Frequency of Antibiotic Prescribing for Pneumonia, %</th>
<th>P Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any antibiotic</td>
<td>61 56 58 62 67 63 59 .51</td>
<td></td>
</tr>
<tr>
<td>Specific regimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolone alone</td>
<td>34 18 32 26 48 46 35 .01</td>
<td></td>
</tr>
<tr>
<td>Macrolide alone</td>
<td>32 32 35 47 27 26 28 .13</td>
<td></td>
</tr>
<tr>
<td>β-Lactam alone</td>
<td>19 36 23 16 11 9 18 .02</td>
<td></td>
</tr>
<tr>
<td>β-Lactam plus macrolide</td>
<td>6 d d dd 12 12 12 dd .13</td>
<td></td>
</tr>
<tr>
<td>Tetracycline alone</td>
<td>3 d d d d d d d .13</td>
<td></td>
</tr>
<tr>
<td>Other regimens</td>
<td>6 d d d d d d d .02</td>
<td></td>
</tr>
</tbody>
</table>

* Antibiotic prescribing was considered in patients with pneumonia who did not have concomitant urinary tract infection (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 595.0, 595.9, 599.0), meningitis (ICD-9-CM code 320), or skin and soft-tissue infections (ICD-9-CM codes 680–686). The analysis excluded patients who were admitted to the hospital, admitted to the intensive care unit, admitted to an observation unit, transferred, or dead on arrival at the hospital. Trends were assessed for regimens appearing at least 30 times in each time interval during the study period.

† Trends were assessed using logistic regression analysis with time period as a predictor variable.

‡ Data for specific regimens are reported as a proportion of visits in which antibiotics were prescribed.

§ Estimate relies on fewer than 30 raw observations and is therefore unreliable.
COMMENT & RESPONSE

Progression to Hepatitis and Fibrosis Secondary to Lomitapide Use: Selecting the Next Course of Action

To the Editor Sacks and colleagues report an excellent case of severe hypertriglyceridemia-associated pancreatitis depicting the progressive hepatoxic consequences of long-term lomitapide use. Although the authors portray a comprehensive case, there are several aspects that warrant additional clarification. First, though the authors clearly explain the significant deterioration to steatohepatitis and fibrosis with elevated alkaline phosphatase levels over time, there is no mention of the forthcoming therapeutic plan. Because current Food and Drug Administration labeling for lomitapide recommends discontinuing use in patients with this presentation type, should consideration of cessation of therapy be realized? Furthermore, despite observations of worsening liver disease, no discussion exists as to why lomitapide therapy was continued for 13 years, rather than considering other modalities such as use of apheresis alone or in combination. In addition, because hepatic steatosis greater than 5% will develop in 78% of those who use lomitapide, other treatment options (eg, apheresis) should be regarded in case adverse effects support discontinuing lomitapide therapy.

Although lomitapide was used off label for hypertriglyceridemia-associated pancreatitis, it would be worthy to note the low-density lipoprotein cholesterol (LDL-C) level reductions achieved at different time intervals, since studies have revealed LDL-C level reductions of approximately 65% with lomitapide use. The patient’s mean serum fasting LDL-C level was 63 mg/dL (to convert to millimoles per liter, multiply by 0.0259) prior to initiating lomitapide therapy. Because very low levels of LDL-C have been sporadically associated with increased cancer risk, hemorrhagic stroke, and other complications in cohort studies and clinical trials, should this medication be reserved for patients with elevated baseline LDL-C levels in addition to hypertriglyceridemia?

Before making conclusions, the cost of lomitapide should be stated. At a cost of greater than $250 000 yearly, most patients will not be able to afford this medication. Obtaining lomitapide on a compassionate use basis at no cost to the patient will have to be the norm.

Because severe hepatoxic effects were observed with lomitapide use, albeit significant reductions in triglyceride levels, a careful assessment of patients who meet the stated criteria for this off-label indication should be performed prior to treatment initiation and at regular time intervals thereafter.

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In Reply We appreciate the opportunity to comment on the points raised by Miyares. First, we emphasize that use of lomitapide for any type of hyperlipidemia requires careful monitoring for hepatotoxicity. In the case of familial chylomicronemia that we reported, changes in enzymes and biopsy specimens associated with hepatotoxicity began to occur after about 9 years of use and became moderate to severe after 13 years. No other approved effective treatments could have been used, and lomitapide was made available under compassionate use. Currently, the patient is being followed up closely by a hepatologist and her clinical team.

The American Academy of Apheresis systematically reviewed the literature on plasmapheresis for hypertriglyceridemia, assigned plasmapheresis the lowest grade of 2C, “very weak recommendations,” and recommended that institutional review board approval be obtained for clinical use. In 2 case series in a total of 8 patients, plasmapheresis (total plasma exchange) reportedly reduced the frequency of episodes of acute pancreatitis in various types of severe hypertriglyceridemia, although these treatments were uncontrolled, with variable intervals and durations of plasmapheresis.

Low-density lipoprotein cholesterol (LDL-C) level is low in chylomicronemia because the defective lipoprotein lipase impairs conversion of very-low-density lipoprotein cholesterol to LDL-C; indeed, it is extremely uncommon to observe coincident chylomicronemia and elevated LDL-C level clinically. Thus, we do not agree that hypercholesterolemia should be a criterion for treatment of chylomicronemia with lomitapide because that would render all such patients ineligible. Furthermore, pooled analysis of high-intensity statin trials have not shown a relation between an achieved low LDL-C level and either cancer incidence or mortality from cancer or other nonvascular causes of death. Certainly, full consideration needs...