Antibiotic Treatment of Adults With Sore Throat by Community Primary Care Physicians
A National Survey, 1989-1999

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SORE THROAT ACCOUNTS FOR 2.1% of ambulatory visits in the United States and is the second most common symptomatic reason for seeking care, after cough. Most sore throats are due to upper respiratory tract viruses such as rhinovirus, coronavirus, and adenovirus. The main bacterial cause of sore throat is group A β-hemolytic streptococci (GABHS), which is cultured in 15% to 36% of children and 5% to 17% of adults with sore throat. Group A β-hemolytic streptococci is the only common cause of sore throat warranting antibiotic treatment.

Ideally, the proportion of patients with sore throat receiving an antibiotic would approximate or perhaps slightly exceed the prevalence of GABHS in those with sore throat. However, 76% of adults and 71% of children diagnosed with pharyngitis in 1992 were treated with an antibiotic. Therefore, pharyngitis represents 5.6 million annual antibiotic prescriptions and is responsible for 9% of all antibiotics used in adults, over half of which are likely unnecessary.

Compared with the frequency of antibiotic prescription, less is known about the classes of antibiotics prescribed for patients with sore throat. The Infectious Diseases Society of America recommends using penicillin or erythromycin (for those who are penicillin allergic) as the first-line agent for patients with sore throat due to GABHS. These recommendations were recently reiterated in the guidelines for the treatment of adults with acute pharyngitis issued by the Centers for Disease Control and Prevention and the American College of Physicians—American Society of Internal Medicine. Penicillin and erythromycin are recommended because of

Context Most sore throats are due to viral upper respiratory tract infections. Group A β-hemolytic streptococci (GABHS), the only common cause of sore throat warranting antibiotics, is cultured in 5% to 17% of adults with sore throat. The frequency of antibiotic use for pharyngitis has greatly exceeded the prevalence of GABHS, but less is known about specific classes of antibiotics used. Only penicillin and erythromycin are recommended as first-line antibiotics against GABHS.

Objectives To measure trends in antibiotic use for adults with sore throat and to determine predictors of antibiotic use and nonrecommended antibiotic use.


Main Outcome Measures Treatment with antibiotics and treatment with nonrecommended antibiotics, extrapolated to US annual national rates.

Results There were an estimated 6.7 million annual visits in the United States by adults with sore throat between 1989 and 1999. Antibiotics were used in 73% (95% confidence interval [CI], 70%-76%) of visits. Patients treated with antibiotics were given nonrecommended antibiotics in 68% (95% CI, 64%-72%) of visits. From 1989 to 1999, there was a significant decrease in use of penicillin and erythromycin and an increase in use of nonrecommended antibiotics, especially extended-spectrum macrolides and extended-spectrum fluoroquinolones (p < .001 for all trends). In multivariable modeling, increasing patient age (odds ratio [OR], 0.86 per decade; 95% CI, 0.79-0.94) and general practice specialty (OR, 1.54 compared with family practice specialty; 95% CI, 1.10-2.14) were independent predictors of antibiotic use. Among patients receiving antibiotics, nonrecommended antibiotic use became more frequent over time (OR, 1.17 per year; 95% CI, 1.11-1.24).

Conclusions More than half of adults are treated with antibiotics for sore throat by community primary care physicians. Use of nonrecommended, more expensive, broad-spectrum antibiotics is frequent.
proven efficacy, narrow spectrum, safety, and low cost.

We used the National Ambulatory Medical Care Survey (NAMCS) to determine if antibiotic prescribing practices for adults with sore throat have changed over time. We tracked changes in the use of different antibiotic classes for sore throat by community primary care physicians from 1989 to 1999. In addition, we evaluated predictors of patients receiving an antibiotic for sore throat and evaluated predictors of receiving nonrecommended antibiotics for sore throat.

METHODS

National Ambulatory Medical Care Survey

The NAMCS has been administered by the National Center for Health Statistics annually since 1989. The NAMCS collects information on patient visits to nonfederally funded, office-based physician practices throughout the United States and has a multistage probability design in which sampling is based on geographic location, physician specialty, and visits within individual physician practices. Each visit is weighted by the National Center for Health Statistics to account for location, specialty, and practice nonparticipation. These weights allow extrapolation to national figures for all aspects of the survey.

The NAMCS has collected information on 355,354 patient visits between 1989 and 1999. The participation rate of physician practices in the NAMCS has declined over the last 11 years from 74% in 1989 to 63% in 1999.16,17

At each visit, patient, physician, and clinical information is collected. Patient information includes demographics, insurance status, and up to 3 reasons for the visit. Physician information includes self-selected specialty, geographic location, and if the practice is in a standard metropolitan statistical area (SMSA). An SMSA approximates an urban region and is defined as an area that includes a city of at least 50,000 people or that has a total area population of at least 100,000 people. Information about SMSAs has been included in the NAMCS since 1990. Visit characteristics include up to 3 diagnoses (coded using the International Classification of Diseases, Ninth Revision, Clinical Modification), 6 entries for medications, and the type of visit (e.g., acute, chronic follow-up).

Data Extraction

We limited our analysis to adults with a primary reason for their visit of “symptom referable to the throat” (reason for visit code, 1455; over 97% complained of “soreness” or “pain” in the throat). We included only visits to primary care physicians, including those who identified themselves as belonging to the specialties of family practice, general practice, internal medicine, adolescent medicine, geriatrics, and general preventive medicine. In all analyses, adolescent medicine physicians were included with family practice physicians; geriatric and general preventive medicine physicians were included with internal medicine physicians.

We excluded patients younger than 18 years and patients immunosuppressed with diabetes mellitus, human immunodeficiency virus infection, or cancer. We also excluded patients with a primary diagnosis of sinusitis, an alternate cause of sore throat that might prompt antibiotic treatment (7% of the sample in a preliminary analysis). We excluded visits described as nonacute; chronic, flare-up; chronic, routine; preoperative; postoperative; or visits that were the result of an injury. This final sample consisted of 2244 patient visits.

Data Analysis

We calculated annual national rates of antibiotic prescriptions for patients with sore throat and the rate of nonrecommended treatment for patients with sore throat. We assessed changes in the distribution of different antibiotic classes over 11 years. For ease of interpretability, we also grouped changes in the use of antibiotics and nonrecommended antibiotics into the periods of 1989-1992, 1993-1996, and 1997-1999.

Antibiotics were identified according to the National Drug Code Directory.18 classification of “antimicrobial agents.” We included only nontopical antibacterial agents in the analysis. Because the National Drug Code Directory has only 8 categories for antimicrobial agents, we further subdivided antibiotics into 37 different classes based on pharmacology and route of administration.

Recommended treatment was defined as the use of penicillin, including intramuscular preparations, or erythromycin for patients who received antibiotics. If more than 1 antibiotic was used in a single visit (2.5% of visits), each antibiotic was considered prescribed in its respective class. For all other calculations and statistical tests, use of multiple antibiotics within a single visit was counted as a single antibiotic use. If a patient received both a recommended and a nonrecommended antibiotic, they were considered to have received only a recommended antibiotic.

To ensure the validity of our main analysis, all weights and analyses were recalculated after excluding any diagnosis—primary, secondary, or tertiary—that could account for an antibiotic prescription other than pharyngitis. Excluded diagnoses included acute bronchitis, acute exacerbation of chronic bronchitis, staphylococcal infection, bacterial infection, gonococcal infection, lymphadenitis, otitis media, otitis externa, pneumonia, urinary tract infections, and skin infections. Exclusion of these diagnoses reduced the sample size by 17.5% from 2244 to 1852 for this secondary analysis.

Statistical Analysis

Ninety-five percent confidence intervals (CIs) for percentage estimates were obtained by calculating relative SEs for these calculations are dependent on physician specialty and year. Because our analysis spans 11 years and 3 specialties, we used the single largest relative SE available. We used modified sample weights, according to the method of Potthoff et al.,16 to derive effective sample sizes that account for clustering by physician practice.
We used linear trends to assess changes in antibiotic use over time. Multivariable logistic regression was used to evaluate independent predictors of antibiotic prescription and use of nonrecommended treatments. In the first model, the use of any antibiotic was the dependent variable. In the second model, use of a nonrecommended antibiotic among those receiving an antibiotic was the dependent variable. Because patient age had a roughly linear effect on these 2 outcomes, we modeled patient age as the odds ratio (OR) associated with each increasing decade of age. We evaluated interaction terms, none of which were significant or included in the final models.

All analyses were done with SAS statistical software, version 8.01 (SAS Institute Inc, Cary, NC). P values less than .05 were considered significant, except for univariate trend tests by year, where, because of multiple comparisons, P values less than .001 were considered significant.

RESULTS

There were an estimated 6.7 million (range by year, 5.1 million to 8.7 million) annual visits to office-based, community physicians by adult patients with sore throat between 1989 and 1999 that met our inclusion and exclusion criteria. There was no significant change in the number of estimated annual visits over 11 years. The most frequent physician-reported diagnoses were acute pharyngitis (41%), upper respiratory infection (21%), acute tonsillitis (8%), streptococcal infection (6%), acute bronchitis (5%), and acute laryngitis (2%).

The sample had a mean age of 38 years (SD,13) and was 35% male and 79% white, non-Hispanic (Table 1). Forty-one percent of patients had private insurance, 29% made some type of self-payment at their visit, and 23% belonged to a health maintenance organization. Family practice physicians, internal medicine physicians, and general practice physicians accounted for 45%, 29%, and 25% of visits, respectively. Twenty-three percent of visits occurred in non-SMSA areas.

Over the 11-year period studied, antibiotics were prescribed in 73% (95% CI, 70%-76%) of visits (Table 2). Recommended antibiotics were prescribed in 23% (95% CI, 20%-26%) of visits. Nonrecommended antibiotics were prescribed in 49% (95% CI, 46%-52%) of visits. Among those receiving antibiotics, 68% (95% CI, 64%-72%) received nonrecommended antibiotics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Proportion of Sample With Characteristic, %</th>
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<tr>
<td>Age, mean (SD), y</td>
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<td>Sex, % male</td>
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<tr>
<td>Race/ethnicity</td>
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<tr>
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<td>South</td>
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<td>21</td>
</tr>
<tr>
<td>Non-SMSA‡</td>
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*Data for some variables do not equal 100% due to rounding.
†Insurance categories are not mutually exclusive.
‡SMSA indicates standard metropolitan statistical area.
Because SMSA was not available in 1989, n = 1950 for this characteristic only.

Table 2. Distribution of Antibiotic Classes Prescribed Each Year by Primary Care Physicians to Adults With Sore Throat, 1989-1999*  

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<tr>
<td>Recommended antibiotics, % of visits†</td>
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<td>Penicillin, oral and intramuscular</td>
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<td>15</td>
<td>13</td>
<td>12</td>
<td>9</td>
<td>7</td>
<td>5</td>
<td>10</td>
<td>9</td>
<td>6</td>
<td>12‡</td>
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<tr>
<td>Erythromycin</td>
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<td>16</td>
<td>14</td>
<td>16</td>
<td>15</td>
<td>11</td>
<td>6</td>
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<td>7</td>
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<td>12‡</td>
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<td>29</td>
<td>29</td>
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<td>20</td>
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<td>13</td>
<td>14</td>
<td>16</td>
<td>11</td>
<td>23‡</td>
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<td>Nonrecommended antibiotics, % of visits</td>
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<td>Aminopenicillins</td>
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<td>Cephalosporins, oral</td>
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<td>9</td>
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<td>13</td>
<td>12</td>
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<td>4‡</td>
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<td>Tetracyclines</td>
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<td>7</td>
<td>4</td>
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<td>3</td>
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<td>4</td>
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<td>2</td>
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<tr>
<td>Trimethoprim/sulfamethoxazole</td>
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<td>2</td>
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<td>1</td>
<td>1</td>
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<td>Fluoroquinolones¶</td>
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<td>Other antibiotic classes¶</td>
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<td>49</td>
<td>42</td>
<td>51</td>
<td>61</td>
<td>53</td>
<td>61</td>
<td>56</td>
<td>46</td>
<td>49‡</td>
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</table>

*Columns may not add up exactly due to rounding and individuals receiving multiple antibiotics.
†Recommended first-line antibiotics for adults with sore throat are penicillin or erythromycin according to the Infectious Diseases Society of America.
‡P for trend, <.001.
§Extended macrodiloids prescribed were azithromycin, clarithromycin, and dirithromycin.
¶Fluoroquinolones prescribed were ciprofloxacin and ofloxacin.
¶Extended fluoroquinolones prescribed were levofloxacin and trovafloxacin.
*Other antibiotic classes include intravenous penicillins, parenteral cephalosporins, lincomycin, trimethoprim, sulfonamides, clindamycin, aminoglycosides, nitrofurantoin, and entires labeled as "antibiotic agent." Each of these antibiotic classes was used in less than 1% of visits overall.

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Recommended antibiotic use decreased from 32% of visits in 1989 to 11% of visits in 1999 (P for trend, <.001). There was a significant decrease in the use of both penicillin (17% of visits in 1989 to 6% in 1999; P for trend, <.001), and erythromycin (15% of visits in 1989 to 5% in 1999; P for trend, <.001).

Nonrecommended antibiotic use increased from 45% of visits in 1989 to 56% of visits in 1998, but decreased to 46% of visits in 1999 (P for trend, <.001). There was a significant increase in the use of extended-spectrum macrolides (P for trend, <.001) and extended-spectrum fluoroquinolones (P for trend, <.001).

Antibiotics were prescribed in 76% of visits in 1989-1992, 71% of visits in 1993-1996, and 69% of visits in 1997-1999 (P for trend, <.001; TABLE 3). The proportion of visits in which nonrecommended antibiotics were given to patients who received an antibiotic increased from 60% in 1989-1992, to 74% in 1993-1996, to 80% in 1997-1999 (P for trend, <.001).

Internal medicine physicians significantly decreased the proportion of visits in which an antibiotic was prescribed from 74% of visits in 1989-1992, to 64% in 1993-1996, to 60% in 1997-1999 (P for trend, .01). However, when prescribing an antibiotic, internal medicine physicians significantly increased their use of nonrecommended antibiotics: from 66% of visits 1989-1992, to 73% in 1993-1996, to 88% in 1997-1999 (P for trend, .003).

Family practice and general practice physicians also increased their use of nonrecommended antibiotics, but without a significant change in their overall use of antibiotics.

In multivariable modeling, antibiotic use was independently predicted by patient age (OR, 0.86 per increasing decade; 95% CI, 0.79-0.94) and general practice specialty (OR, 1.54 compared with family practice specialty; 95% CI, 1.10-2.14; TABLE 4). Among patients who received antibiotics, nonrecommended antibiotic use was predicted by calendar year (OR, 1.17 per year; 95% CI, 1.11-1.24). Nonrecommended antibiotic use was less likely with health maintenance organization coverage (OR, 0.66; 95% CI, 0.44-1.00).

To ensure the validity of our findings, we reanalyzed the data after removing 392 visits with alternate diag-
noses that could potentially account for antibiotic use. The percentage of visits in which antibiotics were used decreased from 73% to 71% (95% CI, 68%-74%). The trend in use of extended fluoroquinolones no longer met our criteria for significance (P = .002). In the multivariable models, the results changed modestly from the main analysis to the reanalysis. In the first model, age (OR, 0.83 per decade; 95% CI, 0.75-0.91), general practice specialty (OR, 1.45 compared with family practice specialty; 95% CI, 1.01-2.07), and self-payment (OR, 1.62; 95% CI, 1.07-2.47) were significant predictors of antibiotic use. In the second model, calendar year (OR, 1.18; 95% CI, 1.10-1.25) was the sole significant predictor of nonrecommended antibiotic use.

COMMENT

In a national community sample of adults presenting to primary care physicians with a chief complaint of sore throat, 73% were treated with antibiotics. This greatly exceeds the 5% to 17% prevalence of GABHS in adults with sore throat. From 1989 to 1999, there has been a marginally significant decrease in the use of antibiotics overall, but an increase in the use of more expensive, broader-spectrum antibiotics. Encouragingly, there was a decrease in the use of almost all antibiotic classes in 1999.

Predictors of antibiotic use for sore throat were younger patient age and general practice specialty. Prescribing antibiotics more frequently for younger patients makes biologic sense. Younger patients make biologic sense. Younger patients are more likely to be infected with GABHS, and some treatment algorithms for sore throat incorporate antibiotics for upper respiratory tract infections.

The only predictor for the use of nonrecommended antibiotics was calendar year. This effect persisted despite controlling for patient demographics, location, physician specialty, and after eliminating potential competing diagnoses in our reanalysis. We found a significant increase in the use of the extended-spectrum macrolides and a small, but statistically significant increase in the use of the extended-spectrum fluoroquinolones.

While many broad-spectrum antibiotics are effective in eradicating GABHS from the throat, there are 2 main concerns in the use of these agents. The first is cost. A course of azithromycin is roughly 20 times more expensive than a course of penicillin ($39.32 vs $2.31), and a course of oral cephalosporins ranges in price from $4.41 to $80.05.

The second concern with the use of broad-spectrum agents is development of bacterial resistance. Extended-spectrum fluoroquinolones are capable of inducing resistance among GABHS isolates in vitro. In vivo, macrolide resistance among GABHS isolates varies between 2% and 17% and is proportional to local macrolide use. Fortunately, interventions aimed at lowering macrolide use decreases the prevalence of macrolide-resistant GABHS isolates.

In contrast, GABHS has remained exquisitely sensitive to penicillin. Over the past 80 years, there has never been a GABHS isolate resistant to penicillin found in Europe or North America. Despite a small risk of serious allergic reaction, penicillin is generally well tolerated, inexpensive, and effective. Penicillin reduces the duration of symptoms and is the only antibiotic proven to prevent rheumatic fever in patients with sore throat.

Our analysis has limitations that deserve comment. Detailed historical information such as duration of symptoms or history of allergy is not available. We also do not have access to detailed clinical information, such as vital signs, physical examination signs, or the test results for GABHS. As such, we cannot definitively assess the appropriateness of antibiotic use for any individual visit. Despite these limitations, the disparity between the known prevalence of GABHS among adults with sore throat and the proportion of visits in which an antibiotic was used is striking. This disparity persisted in a reanalysis of our data after removing 17.5% of visits that had a potential alternative reason for antibiotic use.

Our analysis of the NAMCS shows that over half of adult patients with sore throat are treated with antibiotics by community primary care physicians. Educational and policy efforts to reduce unnecessary antibiotic use may be having some effect, as evidenced by a decrease in the proportion of patients receiving antibiotics in 1999. However, the use of expensive, broad-spectrum antibiotics that can induce resistance is still frequent. Efforts should be continued to encourage appropriate antibiotic use by both patients and physicians.

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REFERENCES

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