

Treatment of Acute and Chronic Rhinosinusitis in the United States, 1999-2002

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Objective: To generalize the prescribing trends of a statistically defined sample of patient visits because of acute or chronic rhinosinusitis in the United States, using reported diagnostic codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*.

Design: Four-year prospective study.

Setting: Public use data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey collected by the National Center for Health Statistics.

Results: The most frequently recommended medications for treatment of both acute and chronic rhinosinusitis are antibiotic agents, followed by antihistamines;

nasal decongestants; corticosteroids; and antitussive, expectorant, and mucolytic agents, respectively. In addition, corticosteroids are used for the treatment of chronic rhinosinusitis.

Conclusions: The use of prescription antibiotics far outweighs the predicted incidence of bacterial causes of acute and chronic rhinosinusitis. Frequency of antibiotic class used was not congruent with reported antimicrobial efficacy of the respective classes. Despite contradictory efficacies reported in the literature, inhaled corticosteroids were frequently used to treat acute rhinosinusitis. Antibiotics and inhaled nasal corticosteroids are being used more often than their published efficacies would encourage.

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RHINOSINUSITIS IS AN IMPORTANT personal medical problem for patients in the United States. Recently, the disorder was divided into various classifications for acute and chronic rhinosinusitis based on time line and symptoms.¹ Although this classification added clarity, there is still much confusion between patients and physicians about the causes and symptoms that constitute rhinosinusitis and within the medical field about how to treat the different subgroups. Until recently, most studies of rhinosinusitis relied on patient symptom

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responses, and because of the confusion regarding causes, symptoms, and treatment, these results were difficult to interpret. In this study, data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) were used to evaluate patient visits to statistically selected ambulatory care facilities. Although rhinosinusitis has been more

recently favored as a diagnosis because of the combined nasal and paranasal sinus involvement,² the data in NAMCS and NHAMCS relate only to sinusitis. To be consistent with the current guidelines and to avoid confusion, we use the term "rhinosinusitis" throughout this article. Physician-generated clinical information about patient visits because of rhinosinusitis was collected. Using reported *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes and diagnoses, we were able to generalize the prescribing trends of a statistically defined sample of visits in the United States that resulted in a primary diagnosis of acute or chronic rhinosinusitis.

Rhinosinusitis represents a huge financial burden for the US health care system. In 1992, direct medical costs of rhinosinusitis were nearly \$2.4 billion by conservative estimates. With direct and indirect costs calculated, the total expenditure is much larger, which establishes rhinosinusitis as one of the most expensive disorders experienced by the US population.³ Proof can also be found in the number of prescriptions written for antibiotic agents to treat rhinosinusitis; in 2002, rhinosinusitis accounted for 9% of pre-

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scriptions for antibiotics in children and 21% in adults.⁴ Not only cost, but also the effect that rhinosinusitis has on quality of life, makes it a major medical concern.⁵ Without standard protocols, treatment of this varied disorder can be inconsistent between providers and among similar symptom groups.

In this article the various medical treatments used for chronic and acute rhinosinusitis are tabulated. The current classification of rhinosinusitis in adults, from the Sinus and Allergy Health Partnership (SAHP) and the American Rhinologic Society, is as follows: acute rhinosinusitis is manifested with symptoms for up to 4 weeks, with the presence of at least 2 major symptoms, or 1 major and at least 2 minor symptoms or purulence; and chronic rhinosinusitis is defined as the duration of symptoms for 12 weeks or longer, with the same symptom profile as in acute rhinosinusitis.⁴

Acute rhinosinusitis is most often thought to be caused by an infectious agent. Watchful waiting, lavage with saline solution, and use of a decongestant or proper antimicrobial agents are the treatments of choice.⁶ Despite the 32 million cases of chronic rhinosinusitis occurring annually in the United States, the causes are not so clear as for acute rhinosinusitis.⁷ It is assumed that the chronic process is multifactorial and possibly different in children than in adults. Repeated acute upper respiratory tract infections can lead to mucosal swelling, obstruction of sinus outflow, and, eventually, chronic infection. A number of conditions predispose to rhinosinusitis, including smoking, swimming, decongestant spray abuse (rhinosinusitis medicamentosa), immunoglobulin deficiencies, disorders of mucociliary transport, and changes in glandular secretions.⁸ Allergies, via antigen-antibody reactions and release of vasodilators and mediators of inflammation, can cause mucosal swelling and obstruction.⁹ In addition, anatomical factors such as septal spurs or deviations, hypertrophic middle turbinates, and concha bullosa can affect nasal cavity and sinus ostia airflow.¹⁰ All of these conditions can lead to an environment that is suitable for mucous stasis, bacterial or fungal overgrowth, and chronic inflammation.¹¹ Other proposed causes include hormonal effects, and further research should elucidate a better understanding of these processes.

With a demonstration of the complexity of acute and chronic rhinosinusitis, it is understandable why the approach to treatment has remained controversial. Inasmuch as viruses frequently cause acute rhinosinusitis, many advocate no antibiotic treatment if the symptoms are not severe, wane in 5 to 7 days, and resolve in 10 days.⁶ When antibiotics are used, there are recommendations from the SAHP¹² for calculated clinical efficacy and bacteriologic efficacy, as well as when to change therapy. In 2000 and again in 2004, the SAHP reported the clinical and bacteriologic efficacy of a number of antimicrobial agents, including, in descending order, amoxicillin-clavulanate potassium, amoxicillin, cefpodoxime proxetil, cefuroxime axetil, cefdinir, trimethoprim-sulfamethoxazole, doxycycline, azithromycin or clarithromycin or erythromycin, and telithromycin. The SAHP recommended antibiotic therapy for adults with acute bacterial rhinosinusitis with mild disease and no

antimicrobial use in the past 4 to 6 weeks.⁴ This order will be compared with the descending order of antimicrobial prescribing frequency by physicians in the United States. The effects of antibiotic therapy on chronic rhinosinusitis are questionable, but if an acute infection occurs in the inflamed nasal or sinus cavities, use of a short-term regimen can provide relief.⁴ Decongestants are often used in treatment plans to increase sinus drainage and ventilation and to thin mucosa and mucous secretions, and result in decreasing mucous stasis.¹³

For acute rhinosinusitis, and especially for acute bacterial rhinosinusitis, there are guidelines for treatment. Chronic disorders are not so categorical and are much more complex. This may be why there is no consensus in the medical community about algorithms or protocols for treatment. The goal of resolution of chronic rhinosinusitis is to resolve predisposing factors, but many treatments effective in acute episodes do not have the same efficacy in chronic disorders.⁴ In this article, we examine the national trends in treatment and how they compare with current research.

METHODS

Public use data from the NAMCS and NHAMCS for 1999 through 2002 were combined and used in this analysis. These years were chosen because data were collected similarly during all 4 years. The NAMCS and NHAMCS prospectively collect data from a national probability sample of visits for ambulatory medical care to a physician's office and to hospital outpatient departments and emergency departments. These surveys are conducted annually by the National Center for Health Statistics.

Both surveys use a multistage probability design. The NAMCS uses a 3-stage design that starts with a probability sample of primary sampling units, then samples physician practices within primary sampling units, and finally samples patient visits within practices. Patient visits are randomly selected from a 1-week reporting period. Physicians are identified through membership lists from the American Medical Association and the American Osteopathic Association. Only nonfederally employed physicians are included. Physicians with a specialty of anesthesiology, pathology, or radiology are excluded from the survey. The NHAMCS uses a 4-stage design that also starts with a probability sample of primary sampling units, then samples hospitals within primary sampling units; outpatient clinics and emergency services areas within hospitals; and visits in the outpatient and emergency clinic area. Patient visits are randomly sampled during a 4-week reporting period. Hospitals included are noninstitutional general and short-stay hospitals; federal, military, and Veterans Administration hospitals and hospital units of institutions are excluded.

Data are collected on a patient record form that includes patient demographic data and visit information. Visit information includes up to 3 reasons for the visit, a primary diagnosis and 1 or 2 secondary diagnoses, projected visit payment type, and a list of medications ordered, supplied, administered, or continued at the visit. As many as 6 medications can be listed on the survey, and each drug is referred to as a drug mention. These medications were assigned therapeutic classifications from the *National Drug Code Directory*, 1995 edition. An overall antibiotic category was created by combining the following therapeutic classes: penicillins; cephalosporins; erythromycins, lincosamides, and macrolides; tetracyclines; sulfonamides and trimethoprim; and quinolones and their derivatives.

Table 1. ICD-9-CM Codes Used to Evaluate Frequency of Chronic and Acute Rhinosinusitis Visits in the United States, 1999-2002*

Chronic Rhinosinusitis ICD-9-CM Code	No. of Visits in Database	Acute Rhinosinusitis ICD-9-CM Code	No. of Visits in Database
471.0, Polyp of nasal cavity	8	461.0, Maxillary acute sinusitis	51
471.1, Polypoid sinus degeneration	0	461.1, Frontal acute sinusitis	18
471.8, Other polyp of sinus	18	461.2, Ethmoidal acute sinusitis	10
471.9, Unspecified nasal polyp	89	461.3, Sphenoidal acute sinusitis	1
473.0, Maxillary chronic sinusitis	168	461.8, Other acute sinusitis	16
473.1, Frontal chronic sinusitis	31	461.9, Acute sinusitis, unspecified	850
473.2, Ethmoidal chronic sinusitis	61		
473.3, Sphenoidal chronic sinusitis	11		
473.8, Other chronic sinusitis	39		
473.9, Unspecified sinusitis (chronic)	4508		

Abbreviation: ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*.

*Of the codes included, any one listed as the primary diagnosis qualified the visit for the respective category of diagnosis, chronic or acute rhinosinusitis.

Table 2. Medication Classes With Frequency per Visit*

Medication Class†	Chronic Rhinosinusitis	Acute Rhinosinusitis
Antibiotics		
Penicillins	30.35 (27.44-33.26)	27.18 (21.04-33.32)
Cephalosporins	13.80 (11.15-16.45)	17.98 (13.26-22.70)
Erythromycins, lincosamides, and macrolides	14.03 (11.69-16.37)	24.32 (16.39-32.25)
Tetracyclines	NE	NE
Sulfonamides and trimethoprim	4.19 (2.74-5.64)	4.77 (1.85-7.69)
Quinolones and derivatives	7.37 (5.50-9.24)	9.43 (5.85-13.01)
All antibiotics combined	69.95 (66.91-72.99)	82.74 (76.17-89.31)
Adrenal corticosteroids	4.00 (2.75-5.25)	NE
Nasal decongestants	16.79 (14.09-19.49)	24.03 (15.46-32.60)
Antitussives, expectorants, and mucolytics	9.58 (7.62-11.54)	13.61 (8.02-19.20)
Antihistamines	20.93 (18.16-23.70)	25.26 (20.19-30.33)
Corticosteroids, nasal or inhalation	16.44 (14.13-18.75)	15.05 (9.75-20.35)

Abbreviation: NE, not reliably estimable because of fewer than 30 observations or a relative standard error greater than 30%.

*Data are given as number of visits (95% confidence interval).

†Up to 6 medications could be listed per visit. Medication classes of interest that met the requirement of 30 subjects and less than 30% relative standard error for either chronic or acute rhinosinusitis are given in Table 3.

STUDY SAMPLE SELECTION

In this study, we selected only those visits that resulted in a primary diagnosis of chronic or acute rhinosinusitis. As many as 3 diagnoses could be listed at each visit. The first diagnosis was considered primary and the other diagnoses were considered secondary.

If a visit included 1 of the ICD-9-CM codes given in **Table 1** for the primary diagnosis, it was selected as a visit because of chronic or acute rhinosinusitis. We excluded those visits with a diagnosis of both chronic and acute rhinosinusitis because there were fewer than 30 such visits in the database.

STATISTICAL ANALYSIS

Sample weights from the National Center for Health Statistics were used for each visit in both the NAMCS and NHAMCS data to obtain unbiased national estimates based on various patient characteristics and to adjust for nonresponse. Standard errors were calculated using an ultimate cluster variance estimation design using Survey Data Analysis software (SUDAAN, version 8.0; Research Triangle Institute, Cary, NC). This accounts for the multistage sampling design to estimate unbiased standard errors and 95% confidence intervals (CIs). Estimates were considered unreliable if they were based on fewer

than 30 visits in the database or if their relative standard error was greater than 30%.¹⁴

RESULTS

Extrapolations of data from the NAMCS and NHAMCS show that in 1999 through 2002 in the United States there were an estimated 14 277 026 visits annually because of chronic rhinosinusitis and an estimated 3 116 142 visits annually because of acute rhinosinusitis. These visits represented 1.39% (95% CI, 1.26-1.52) and 0.30% (95% CI, 0.22-0.38), respectively, of all visits for ambulatory care.

Antibiotic agents were mentioned in visits because of both acute and chronic rhinosinusitis. Penicillins were the most frequently recommended class of antibiotics mentioned (**Table 2**), and in this group, most mentions were specifically for amoxicillin or amoxicillin-clavulanate potassium (**Table 3**). The grouping of erythromycin, lincosamides, and macrolides was the second most frequent class of antibiotics mentioned at visits because of rhinosinusitis.

Among other drug classes, inhaled or nasal corticosteroidal agents and antihistamines were mentioned in visits because of both acute and chronic rhinosinusitis. Additional drug class uses are given in Table 2.

COMMENT

The use of prescription antibiotics to treat acute rhinosinusitis far outweighs the predicted incidence of bacterial causes. The literature repeatedly shows that viruses are by far the most frequent cause of acute rhinosinusitis. However, in practice, physicians ordered, supplied, administered, or continued at least 1 prescription antibiotic in 82.74% of visits because of acute rhinosinusitis. With etiologies less understood for chronic rhinosinusitis, a comparison cannot be made between research and practice. However, with inflammation the most likely cause, the use of at least 1 antibiotic in 69.95% of visits because of chronic rhinosinusitis is a surprising number.

Penicillins, mainly amoxicillin and amoxicillin-clavulanate potassium, were the most commonly used medication class for both chronic and acute rhinosinusitis. A penicillin drug was mentioned in 30.35% of all visits with a primary diagnosis of chronic rhinosinusitis and in 27.18% visits with a primary diagnosis of acute rhinosinusitis. This is intuitive, inasmuch as recent studies have shown penicillins to be highly effective against the bacteria in nasal and sinus areas. Amoxicillin-clavulanate potassium (875/125 mg twice a day for 14 days) has a 95% clinical response rate in acute bacterial rhinosinusitis and acute exacerbations of chronic rhinosinusitis.¹⁵

Penicillins are mentioned more often in visits because of chronic rhinosinusitis compared with acute rhinosinusitis. When the SAHP published antimicrobial guidelines for acute bacterial rhinosinusitis in 2004, they discussed all antimicrobial agents with β -lactam activity en bloc. This class topped the list of efficacious agents, and, when subdivided, amoxicillin-clavulanate potassium had the highest calculated clinical efficacy in both the groups that had or had not recently received antimicrobial agents.⁴

The group including erythromycins, lincosamides, and macrolides was second in frequency of antibiotic mentions in visits because of acute rhinosinusitis. A mention in 24.32% of visits puts the use of this class of antibiotics ahead of cephalosporins, sulfonamides and trimethoprim, and tetracyclines, in that order. The Acute Bacterial Rhinosinusitis protocol issued by the SAHP in January 2004 listed efficacies of these classes in an order different from that reported in our studies. In the SAHP data, the erythromycin, lincosamides, and macrolides group had the lowest calculated clinical efficacy and bacteriologic efficacy, behind the cephalosporins and the sulfonamides and trimethoprim. This higher than expected ranking in clinical practice could be owing to an anti-inflammatory benefit that macrolides possess.¹⁶ Based on the number of visits with an antibiotic mention (69.95% for chronic rhinosinusitis and 82.74% for acute rhinosinusitis) and the suspected low number of rhinosinusitis episodes caused by a bacterium, one must en-

Table 3. Frequency of Amoxicillin vs Amoxicillin-Clavulanate Potassium for Treatment of Both Chronic and Acute Rhinosinusitis*

Medication†	Chronic Rhinosinusitis	Acute Rhinosinusitis
Amoxicillin‡	18.56 (15.83-21.29)	14.75 (8.90-20.61)
Amoxicillin-clavulanate potassium§	11.80 (9.78-13.82)	11.78 (7.69-15.87)

*Data are given as number of visits (95% confidence interval).

†Some visits listed both medications. While this is unlikely accurate and more likely a mistake in reporting, the data must be evaluated.

‡Includes amoxicillin, Amoxil (SmithKline Beecham Pharmaceuticals, Philadelphia, Pa), Polymox (Apothecon, a Bristol-Myers Squibb Co, Shawnee Mission, Kan), and Trimox (Apothecon).

§Includes Augmentin, Augmentin 125, Augmentin 250, Augmentin 500, and Augmentin ES (all produced by SmithKline Beecham Pharmaceuticals).

tain the secondary efficacy of these drugs. Perhaps these physicians were treating a secondary infection or using the anti-inflammatory effects of antibiotic treatments. While keeping the goals of treatment in mind, there are concerns about the overuse of antibiotics and the resultant problems, including drug resistance and increasingly virulent bacteria. When two thirds of patients with sinus symptoms expect or receive an antibiotic and as many as one fifth of antibiotic prescriptions for adults are written for a drug to treat rhinosinusitis, these disorders hold special pertinence on the topic.

Inhaled or nasal corticosteroids were mentioned in 15.05% of visits because of acute rhinosinusitis. Prescribed in a significant number of visits, it is important to discuss what has previously been reported about the role of corticosteroids in rhinosinusitis. Dolor et al¹⁷ showed that the concomitant use of cefuroxime and intranasal fluticasone for 21 days had a higher clinical success rate than use of cefuroxime with placebo (93.5% and 73.9%, respectively; $P = .009$). Lack of objective criteria for measuring improvement, data based on patient reports of improvement, and funding of the study by the manufacturer of fluticasone all proved limitations of that publication. In a different double-blind, placebo-controlled trial,² the use of flunisolide as an adjunct to amoxicillin-clavulanate potassium therapy was studied. Despite use of flunisolide vs placebo 3 times daily for 3 weeks, many patients continued to have symptoms and recurrences were common in both groups.² As our data show and as many practicing clinicians can report, the use of inhaled corticosteroids as adjunctive treatment in acute rhinosinusitis is not rare but is of undetermined benefit.

In chronic rhinosinusitis, even more intranasal and oral corticosteroid use was reported. Inasmuch as many consider chronic rhinosinusitis both an infectious and an inflammatory disease, it is understandable that clinicians are, in many cases, attempting to treat both. Two studies used to evaluate treatment approaches in chronic rhinosinusitis have been published. One focused on symptomatic improvement only, while a more recent study coupled symptomatic and radiographic changes due to medical treatment. In the earlier study, McNally et al¹⁸ showed that treatment with antibiotics, decongestants, and intranasal steroids can decrease symptoms of chronic rhinosinusitis. In that study,

however, patients were not followed up for occurrence of relapse.¹⁶ In a 2002 retrospective study, chronic rhinosinusitis was treated with an antibiotic (most commonly, trovafloxacin, amoxicillin-clavulanate potassium, levofloxacin, or metronidazole), oral prednisone for 10 days, intranasal steroids, and nasal irrigation with saline solution.¹⁹ Statistically significant improvement in both symptoms and findings at computed tomography from baseline to the end of the study were demonstrated.¹⁹ However, neither of these studies included a concurrent control group. Based on current understanding of the pathogenesis of chronic rhinosinusitis and these findings, it is understandable why some physicians prescribe corticosteroids to treat the disorder.

Allergic rhinosinusitis is a common disease that affects approximately 20% of the US population.²⁰ Because corticosteroids are effective in the treatment of this disorder, higher numbers of drug mentions for this chronic class might be expected. Inasmuch as a patient could have acute or chronic sinus complications from allergies, it further clouds the assumptions about use of corticosteroids to treat acute or chronic rhinosinusitis.²¹

The use of antihistamines demonstrated by our data seems logical; 20.93% of visits because of chronic rhinosinusitis and 25.26% of visits because of acute rhinosinusitis is near the prevalence of allergic rhinosinusitis in the population. Antihistamines are clearly indicated in the treatment of allergy-related disease. Some of the older, generally over-the-counter antihistamines are considered detrimental to the nose and sinus mucosa because their cholinergic effects cause dryness of the mucous secretions and resolution of infections can be slowed.²² Most of the antihistamines in this study were prescription drugs, and these newer antihistamines have fewer adverse effects and cause much less drying than their predecessors, which may explain their high usage rates.^{21,23}

Decongestants were mentioned in as many as a fourth of visits because of rhinosinusitis, and more often acute rhinosinusitis than chronic rhinosinusitis. The high use of this class of drugs (evaluated separately from antihistamine combination agents) is understandable considering the efficacy reports in the literature. In reviewing 5 studies, Arroll²⁴ reports a reduction in nasal airway resistance in patients using these drugs compared with placebo. The same study stated that mucolytic agents were less reported but that such treatment decreased symptom scores when compared with placebo.²⁴ The conclusions of this review rely on primary studies of variable quality. The reviewers were clear about the lack of efficacy except in the high-quality studies in which global improvement in symptoms was noted. With limited quantifiable data and supportive anecdotal evidence, the high use of decongestant and mucolytic agents is logical. Further, both decongestant and mucolytic agents are available over the counter; thus, it can be assumed that usage is even higher than reflected by physician reports.

CONCLUSIONS

In evaluating the trends of rhinosinusitis treatment in the United States, many points became apparent. Prescrip-

tion antibiotic drugs are being used far more than bacterial causes studies would indicate. Within the class of antibiotics, the penicillins are, appropriately, at the top of the prescription list for both acute and chronic rhinosinusitis. Questionable is the frequent use of the class that includes erythromycins, lincosamides, and macrolides, with other classes having higher antibacterial efficacy. Nasal and inhaled corticosteroids are prescribed more frequently to treat acute rhinosinusitis than published studies imply is necessary. Despite current theories of causes of chronic rhinosinusitis, the use of corticosteroids remains low in this setting. An area where our findings fit nicely with current information is use of antihistamines, which roughly matched the prevalence of their major indication, allergic rhinosinusitis.

A limitation of this study is that the databases used only data for medications ordered, supplied, administered, or continued by attending physicians. Because these data were not based on patient responses, the use of over-the-counter medicines or home remedies was not recorded. We wonder whether the percentages of medications used would be much smaller when compared with the number of patients who use hot packs to relieve the symptoms of chronic rhinosinusitis or whether physicians recommend irrigation with saline solution and steam, as often as antihistamine prescriptions.

The use of antibiotics and corticosteroids, inhaled and oral, needs more investigation in the treating of rhinosinusitis. Current theories and contradicting evidence in the literature makes the findings of our study all the more compelling. Could their use be more efficacious than proved? Can it be assumed that practicing physicians in the United States base their decisions on experienced success? Evidence-based medicine means incorporating the best evidence into treatment decisions. With limited or no literature addressing the efficacy of each drug class with the separate diagnoses, evidence-based medicine would indicate that it is appropriate to use personal or accumulated clinical experience.

The vast use of these agents makes the statement that they seem to be effective in reducing symptoms or preventing relapse, or they would have been abandoned. Another important possibility is that many patients have self-limited disease that will resolve regardless of treatment, and their physicians could be prescribing what they think will work. With time, many infectious processes are resolved by the patient's immune system. To attribute efficacy or curative credit to a drug class based solely on resolution of symptoms without comparison with non-treated control subjects, physicians could be oversatisfied with their own prescribing habits.

Many physicians might use an ICD-9-CM code to ensure that a patient's insurance will pay for a particular medication and not necessarily because the code is for the disease they believe they are treating. The coding could be questioned if the physician, nurse, or billing clerk may simply be in the habit of using a few ICD-9-CM codes, regardless of the actual findings or symptoms. Follow-up studies might reveal how these trends change.

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