Trends in Antimicrobial Prescribing Rates for Children and Adolescents

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Context Annual rates of antimicrobial prescribing for children by office-based physicians increased from 1980 through 1992. The development of antimicrobial resistance, which increased for many organisms during the 1990s, is associated with antimicrobial use. To combat development of antimicrobial resistance, professional and public health organizations undertook efforts to promote appropriate antimicrobial prescribing.

Objective To assess changes in antimicrobial prescribing rates overall and for respiratory tract infections for children and adolescents younger than 15 years.

Design, Setting, and Participants National Ambulatory Medical Care Survey data provided by 2500 to 3500 office-based physicians for 6500 to 13 600 pediatric visits during 2-year periods from 1989-1990 through 1999-2000.

Main Outcome Measures Population- and visit-based antimicrobial prescribing rates overall and for respiratory tract infections (otitis media, pharyngitis, bronchitis, sinusitis, and upper respiratory tract infection) among children and adolescents younger than 15 years.

Results The average population-based annual rate of overall antimicrobial prescriptions per 1000 children and adolescents younger than 15 years decreased from 838 (95% confidence interval [CI], 711-966) in 1989-1990 to 503 (95% CI, 419-588) in 1999-2000 (P for slope $<.001$). The visit-based rate decreased from 330 antimicrobial prescriptions per 1000 office visits (95% CI, 305-355) to 234 (95% CI, 210-257; P for slope $<.001$). For the 5 respiratory tract infections, the population-based prescribing rate decreased from 674 (95% CI, 568-781) to 379 (95% CI, 311-447; P for slope $<.001$) and the visit-based prescribing rate decreased from 715 (95% CI, 682-748) to 613 (95% CI, 570-657; P for slope $<.001$). Both population- and visit-based prescribing rates decreased for pharyngitis and upper respiratory tract infection; however, for otitis media and bronchitis, declines were only observed in the population-based rate. Prescribing rates for sinusitis remained stable.

Conclusion The rate of antimicrobial prescribing overall and for respiratory tract infections by office-based physicians for children and adolescents younger than 15 years decreased significantly between 1989-1990 and 1999-2000.

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FROM 1980 THROUGH 1992, ANTIMICROBIAL prescribing rates for children by physicians in office-based practice in the United States increased by 48%.[1] The increased use of antimicrobial drugs coincided with the emergence of antimicrobial resistance, an important clinical and public health problem.[2-8] The association of resistance with the use of antimicrobial drugs has been documented in both inpatient[9] and outpatient settings.[10]

Antimicrobial resistance among respiratory pathogens has become a common clinical problem in routine office practice.[11] In recent years, an increase in illness caused by multidrug-resistant *Streptococcus pneumoniae*, a community-acquired pathogen, was observed in the United States.[12] The majority of antimicrobial prescriptions provided by office-based physicians are for respiratory tract infections,[1] and much of this prescribing is for viral conditions for which these drugs are not indicated.[13,14]

Throughout the 1990s, public health and professional organizations, including the Centers for Disease Control and Prevention (CDC), American Academy of Pediatrics, American Academy of Family Practice, American Society for Microbiology, and Alliance for the Prudent Use of Antibiotics, undertook campaigns and interventions to promote appropriate antimicrobial use,[15-18] which is defined as use that maximizes therapeutic impact while minimizing toxicity and the development of resistance.

See also pp 3103 and 3133.

This study analyzed National Ambulatory Medical Care Survey (NAMCS) data from 1989 through 2000 to describe trends in antimicrobial prescribing by US office-based physicians for children and adolescents younger than 15 years overall and for respiratory tract infections. The NAMCS is the only survey of office-based physicians in the United States that produces unbiased national estimates and collects prescribing information. These data pro-

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vide a unique opportunity to evaluate antimicrobial use on a national level over time.

METHODS

The NAMCS is an annual probability sample survey of office-based physicians in the United States conducted by the National Center for Health Statistics of the CDC. The NAMCS was administered continuously from 1973 through 1981, was conducted again in 1985, and resumed continuous administration in 1989. Since 1989, the US Census Bureau has been responsible for field operations and data collection.

A report describing sample design, sampling variance, and estimation procedures of the NAMCS has been published.[19] The NAMCS uses a 3-stage probability sampling procedure. The first stage contains 112 geographic primary sampling units. The second stage consists of a probability sample of practicing nonfederally employed physicians (excluding those in the specialties of anesthesiology, radiology, and pathology) selected from the master files maintained by the American Medical Association and the American Osteopathic Association, which are stratified by physician specialty. Physicians who are selected to participate in the NAMCS during a particular calendar year are not eligible to be selected again for at least another 3 years. The third stage involves selecting patient visits to sample physicians during a randomly assigned 1-week reporting period throughout the year.

Response rates and numbers of participating physicians, pediatric patient visit records, and pediatric antimicrobial records for 1989-1990 through 1999-2000 are presented in the TABLE. The NAMCS response rate was defined as the number of eligible physicians who completed the survey plus the number of eligible physicians who saw no patients during the study period (numerator) divided by the sum of the numerator and the number of physicians who refused to participate.

The patient visit record form contained patient demographic data and information about the visit including up to 3 diagnoses coded according to the *International Classification of Diseases, Ninth Revision, Clinical Modification,*[20] and medications prescribed. Physicians were instructed to record all new or continued medications ordered, supplied, or administered at the visit, including prescription and nonprescription preparations, immunizations, desensitizing agents, and anesthetics. From 1989 through 1994, up to 5 medications could be recorded per visit and from 1995 through 2000 up to 6 medications could be recorded per visit. Drugs were coded according to a classification system developed at the National Center for Health Statistics. A report describing the method and instruments used to collect and process drug information has been published.[21] Since data on the route of administration were not collected, an attempt was made to delete topical preparations by reviewing trade names and excluding those intended for topical use.[22-26] For this study, antimicrobial drugs were defined as those belonging to the following groups: azithromycin/clarithromycin, cephalosporins, erythromycins, penicillins, quinolones, tetracyclines, and trimethoprim-sulfamethoxazole.

Table. Physicians, Response Rates, and Pediatric Visit and Antimicrobial Records: National Ambulatory Medical Care Survey

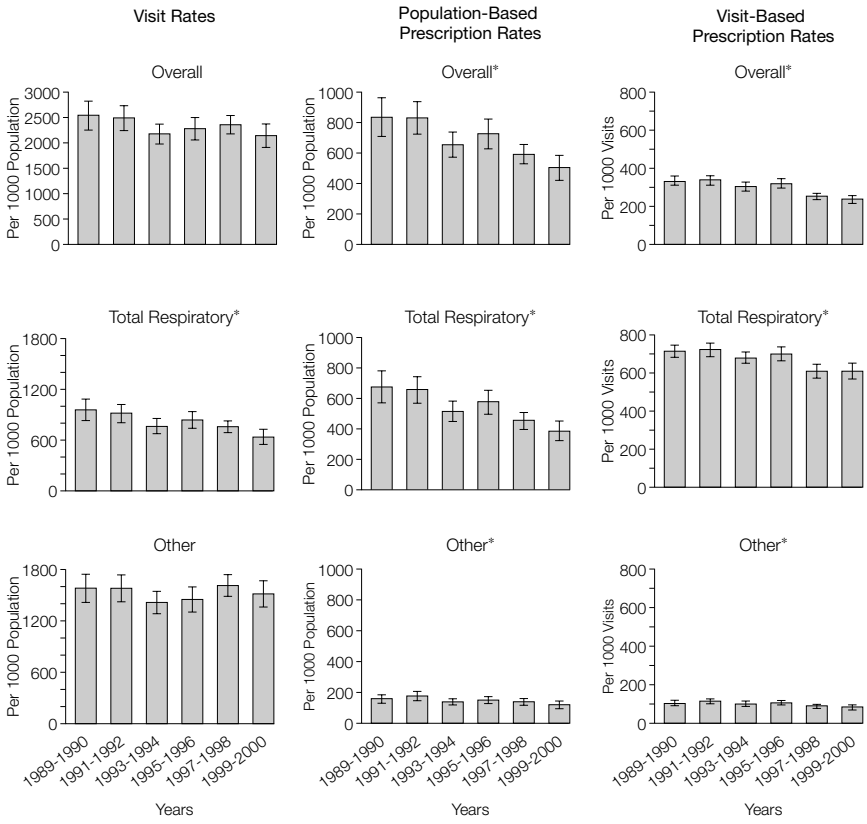
Years	No. of Participating Physicians	Response Rates, %*	No. of Pediatric Records†	
			Total	Antimicrobial
1989-1990	3105	74	13589	4089
1991-1992	2912	72	10570	3098
1993-1994	3506	72	9357	2359
1995-1996	3383	71	9181	2482
1997-1998	2473	69	7717	1712
1999-2000	2474	65	6517	1343

*Values are 2-year averages.
†Refers to children and adolescents younger than 15 years.

The *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes[20] for the 5 respiratory tract infections studied were otitis media, 381.0, 381.4, 382.0, 382.4, and 382.9; bronchitis, 466.0 and 490; pharyngitis, 034.0, 462, and 463; sinusitis, 461 and 473; and upper respiratory tract infection, 460 and 465. All listed diagnoses were included. Urinary tract infection (UTI; diagnosis codes 595.0, 595.9, and 599.0) was included in the analysis as an attempt to control for any general changes in prescribing behavior, such as an increase in telephone prescribing or shifts to other health care settings, since UTI is a condition for which antimicrobials are universally indicated.[27] Patient visit records were classified as having a diagnosis of bronchitis or upper respiratory tract infection if bronchitis or upper respiratory tract infection was the sole diagnosis, or if additional diagnoses on the patient record form were for 1 or more noninfectious diseases, or if there was an additional infectious disease diagnosis[28] for which antimicrobials were determined to be inappropriate. In the latter case, records were reviewed by a pediatrician (R.E.B.) to ensure that there were no competing conditions that potentially warranted treatment with an antimicrobial. Therefore, a visit with a diagnosis of both otitis media and upper respiratory tract infection would be classified as having an otitis media diagnosis, not an upper respiratory tract infection diagnosis. A visit with a diagnosis of both bronchitis and a viral infection for which an antimicrobial would be inappropriate was classified as having a bronchitis diagnosis.

Data from the NAMCS sample were weighted to produce national estimates. The weighting from 1989-1994 included selection probability, nonresponse adjustment, and physician-population weighting ratio adjustment. In 1995, a fourth component, weight smoothing, was added. Two

Figure 1. Trends in Visit and Antimicrobial Prescription Rates for Children and Adolescents Younger Than 15 Years



Asterisk indicates *P* for slope ≤.01. Error bars indicate 95% confidence intervals.

years of data were combined to provide more reliable estimates. The data presented reflect average annual estimates for each 2-year period.

Two types of antimicrobial drug prescribing rates were used in the analysis. The population-based rate was defined as the average annual number of antimicrobial drugs recorded for children and adolescents younger than 15 years during the 2-year period divided by the average annual number of US children and adolescents younger than 15 years during the 2-year period. The population denominators were based on US Census Bureau monthly postcensal estimates of the civilian noninstitutional population of the United States as of July of each year.[29] Figures were adjusted for net underenumeration using the 1990 National Population Adjustment Matrix. Changes in population-based antimicrobial prescribing rates reflect changes in physician prescribing behavior and in frequency of office visits. Changes in the frequency of office visits may result from changes in telephone advice and prescribing, in patient education by physicians, in insurance status, or in disease incidence. The visit-based rate was defined as the average annual number of antimicrobial drugs recorded for children and adolescents younger than 15 years during the 2-year period divided by the average annual number of physician office visits by children and adolescents younger than 15 years. The denominator of the visit-based rates for the specific respiratory tract infections was the number of physician office visits by children and adolescents younger than 15 years for that particular diagnosis. The visit-based prescribing rates were used to assess changes in office-based antimicrobial prescribing during encounters over time.

Because NAMCS data show that children younger than 5 years represent the pediatric group for whom physician office visits for otitis media and the common cold are the most frequent (L.F.M., unpublished data, 1999-2000), antimicrobial population- and visit-based prescribing rates were also calculated for this age category.

SUDAAN statistical software was used for all statistical analyses.[30] The SEs used to calculate the 95% confidence intervals (CIs) around the rates took into account the complex sample design of the NAMCS.[30] All estimates in this analysis had less than a 30% relative SE (ie, the SE divided by the estimate expressed as a percentage of the estimate) and were based on 30 cases or more in the sample data. Significance of trends was based on a weighted least-squares regression analysis at the .05 level of significance.[31] The 2-tailed *t* test was used to compare the slopes of trend lines (.05 level of significance).[31]

RESULTS

The number of participating sample physicians in each 2-year period of the study ranged from 2500 to 3500 and the annual response rates ranged from 65% to 74% (Table). The number of completed pediatric patient record forms ranged from 6500 to 13 600 per 2-year period, and the number of these records that had an antimicrobial prescribed ranged from 1300 to 4000 per 2-year period.

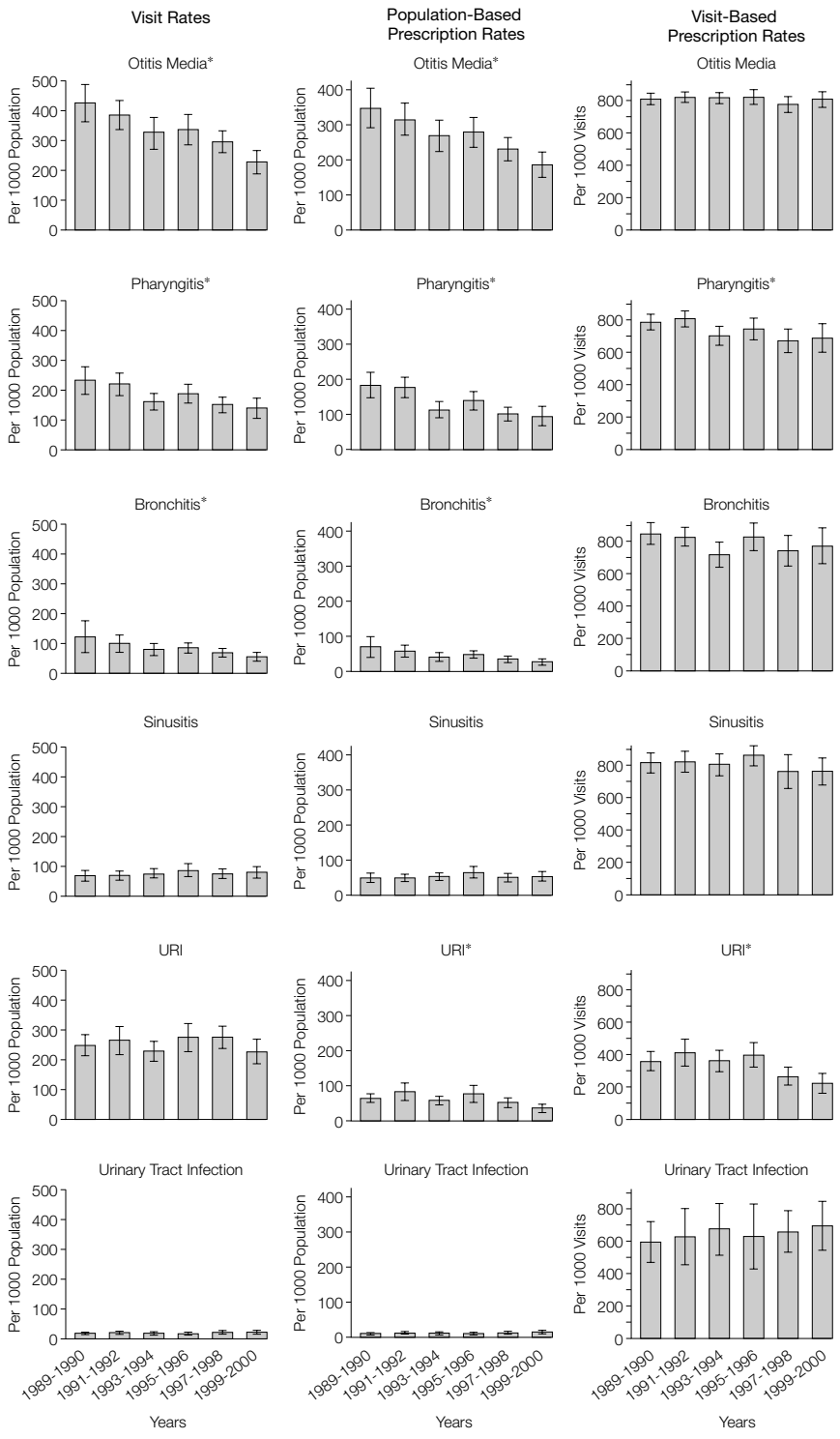
There was no significant change in the overall office visit rate, regardless of antimicrobial prescribing, from 1989-1990 to 1999-2000 (from 2541 [95% CI, 2254-2828] per 1000 children and adolescents <15 years to 2152 [95% CI, 1919-2384]; *P* for slope = .08; FIGURE 1). The number of visits for the 5 respiratory tract infections combined declined 34% from 1989-1990 to 1999-2000 from 961 (95% CI, 828-1094) visits per 1000 children and adolescents younger than 15 years to 635 (95% CI, 542-728; *P* for slope <.001). During the 12-year study period, the average annual

visit rates also significantly decreased for otitis media (from 428 [95% CI, 364-492] to 230 [95% CI, 190-270]; *P* for slope <.001), pharyngitis (from 233 [95% CI, 186-279] to 140 [95% CI, 107-174]; *P* for slope <.001), and bronchitis (from 123 [95% CI, 68-178] to 55 [95% CI, 38-72]; *P* for slope <.001; FIGURE 2). However, there was no significant change in visit rates for sinusitis (*P* for slope=.27), upper respiratory tract infection (*P* for slope >.99), or UTI (*P* for slope=.39).

Population-Based Prescribing Rates

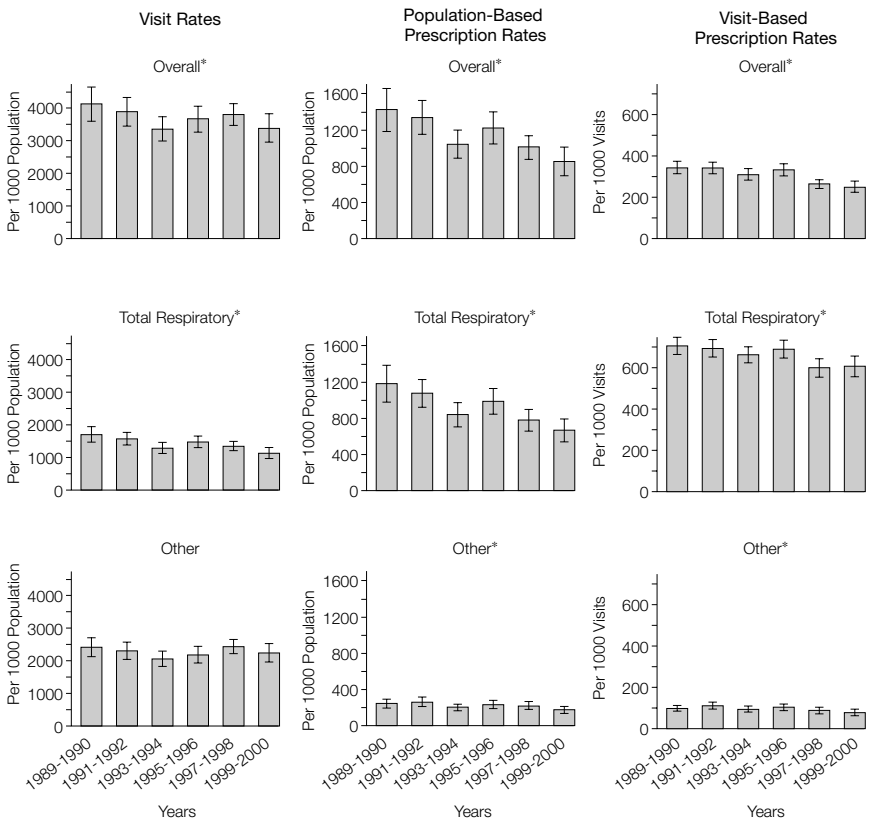
In 1989-1990, the average annual number of antimicrobial drugs prescribed in physician offices for children and adolescents younger than 15 years was 45.5 million compared with 30.3 million in 1999-2000. The average population-based annual rate of overall antimicrobial prescriptions decreased 40% from 838 (95% CI, 711-966) per 1000 children and adolescents younger than 15 years in 1989-1990 to 503 (95% CI, 419-588) in 1999-2000 (*P* for slope <.001; Figure 1). For the 5 respiratory tract infections combined, the average annual rate decreased 44% from 674 (95% CI, 568-781) antimicrobial prescriptions per 1000 children and adolescents younger than 15 years in 1989-1990 to 379 (95% CI, 311-447) in 1999-2000 (*P* for slope <.001). From 1989-1990 through 1999-2000, decreasing trends in antimicrobial drug prescriptions per 1000 children and adolescents younger than 15 years were observed for otitis media (47% decrease from 347 [95% CI, 289-404] to 184 [95% CI, 148-220]; *P* for slope <.001), pharyngitis (47% decrease from 183 [95% CI, 145-220] to 96 [95% CI, 67-126]; *P* for slope <.001), bronchitis (61% decrease from 69 [95% CI, 38-101] to 27 [95% CI, 18-37]; *P* for slope <.001), and upper respiratory tract infection (45% decrease from 65 [95% CI, 52-78] to 36 [95% CI, 23-48]; *P* for slope <.001; Figure 2). No significant change in the population-based rates of antimicrobial prescribing was found for sinusitis (*P* for slope=.61) or for UTI (*P* for slope=.19).

Figure 2. Trends in Visit and Antimicrobial Prescription Rates for Specific Respiratory Tract and Urinary Tract Infections for Children and Adolescents Younger Than 15 Years



Asterisk indicates *P* for slope ≤.001. Error bars indicate 95% confidence intervals. URI indicates upper respiratory infection.

Figure 3. Trends in Visit and Antimicrobial Prescription Rates for Children Younger Than 5 Years



Asterisk indicates *P* for slope ≤.04. Error bars indicate 95% confidence intervals.

For children younger than 5 years, similar trends in population-based rates of antimicrobial prescribing were found as those observed in children and adolescents younger than 15 years. The average annual rate of overall antimicrobial prescribing decreased 40% from 1422 (95% CI, 1182-1663) antimicrobial prescriptions per 1000 children younger than 5 years in 1989-1990 to 851 (95% CI, 694-1008) in 1999-2000 (*P* for slope <.001; FIGURE 3). Decreasing trends were also found from 1989-1990 to 1999-2000 for the 5 respiratory tract infections combined (43% decrease from 1184 [95% CI, 977-1391] to 678 [95% CI, 548-808]; *P* for slope <.001), otitis media (42% decrease from 722 [95% CI, 590-854] to 418 [95% CI, 335-500]; *P* for slope <.001), pharyngitis (51% decrease from 224 [95% CI, 164-285] to 109 [95% CI, 73-145]; *P* for slope <.001), bronchitis (71% decrease from 112 [95% CI, 51-173] to 32 [95% CI, 13-51]; *P* for slope <.001), and upper respiratory tract infection (40% decrease from 120 [95% CI, 94-147] to 72 [95% CI, 41-102]; *P* for slope=.009). No significant differences in the slopes of the trend lines were found between children younger than 5 years and children and adolescents younger than 15 years for the overall population-based antimicrobial prescribing rate or the prescribing rates for the 5 individual or combined respiratory tract infections.

Visit-Based Prescribing Rates

The average visit-based annual rate for overall antimicrobial prescribing decreased 29% from 330 (95% CI, 305-355) antimicrobials per 1000 visits among children and adolescents younger than 15 years in 1989-1990 to 234 (95% CI, 210-257) in 1999-2000 (*P* for slope <.001; Figure 1). For the 5 respiratory tract infections combined, the average annual rate decreased 14% from 715 (95% CI, 682-748) antimicrobial prescriptions per 1000 visits among children and adolescents younger than 15 years in 1989-1990 to 613 (95% CI, 570-657) in 1999-2000 (*P* for slope <.001; Figure 1). Declining trends were also found during this period for pharyngitis (13% decrease from 785 [95% CI, 736-834] to 686 [95% CI, 598-774]; *P* for slope=.001) and upper respiratory tract infection (38% decrease from 359 [95% CI, 299-418] to 221 [95% CI, 159-283]; *P* for slope <.001; Figure 2). However, no significant changes were observed for otitis media (809 [95% CI, 772-847] to 802 [95% CI, 752-852]; *P* for slope=.42); bronchitis (850 [95% CI, 780-919] to 773 [95% CI, 663-883]; *P* for slope=.08); sinusitis (819 [95% CI, 753-885] to 766 [95% CI, 679-853]; *P* for slope=.45); or UTI (593 [95% CI, 465-722] to 695 [95% CI, 543-847]; *P* for slope=.33).

For children younger than 5 years, similar trends in visit-based rates of antimicrobial prescribing were found as those observed in children and adolescents younger than 15 years. The average annual visit-based rate of overall antimicrobial prescribing decreased 27% from 345 (95% CI, 315-374) antimicrobial prescriptions per 1000 visits among children younger than 5 years in 1989-1990 to 252 (95% CI, 224-279) in 1999-2000 (*P* for slope <.001; Figure 3). Decreasing trends were also found from 1989-1990 to 1999-2000 for the 5 respiratory tract infections combined (14% decrease from 706 [95% CI, 664-749] to 610 [95% CI, 558-662]; *P* for slope <.001), pharyngitis (11% decrease from 828 [95% CI, 765-891] to 738 [95% CI, 621-855]; *P* for slope=.03), and upper respiratory tract infection (36% decrease from 324 [95% CI, 264-385] to 207 [95% CI, 134-280]; *P* for slope=.002). No significant differences in the slopes of the trend lines were found between children younger than 5 years

and children and adolescents younger than 15 years for the overall visit-based antimicrobial prescribing rate or the prescribing rates for the 5 individual or combined respiratory tract infections.

COMMENT

This analysis of 1989-2000 NAMCS data found decreasing trends in both the population- and visit-based antimicrobial prescription rates, overall and for respiratory tract infections for children and adolescents seen by office-based physicians over a 12-year period, in contrast to the previously reported increasing trend in annual population-based rates from 1980 through 1992.[1] The population-based prescribing rate indicates the number of antimicrobials prescribed per child in the United States and was used to assess changes over time that may be due to variations in visiting an office-based physician. Changes in population-based rates may reflect changes in the visit or prescribing threshold, or both. For example, one of the efforts to promote the appropriate use of antimicrobials included educating clinicians and patients about which infections might have a viral origin. Therefore, patients may have been less likely to make a physician office visit if they had a cold or bronchitis or knew that their physician would not prescribe an antimicrobial for their condition. Also, clinicians might have been less inclined to see a child during the first few weeks after treatment of otitis media, since antimicrobials are no longer recommended for the management of an uncomplicated posttreatment middle ear effusion.[32]

Visit-based antimicrobial prescribing rates reflect prescribing behavior once a visit has occurred. Trends in population- and visit-based antimicrobial prescribing rates for the 5 specific respiratory tract infections were concordant for pharyngitis, sinusitis, and upper respiratory tract infection. For otitis media and bronchitis, however, decreases were found in the population-based but not visit-based antimicrobial prescribing rates, which indicates that there was no change in antimicrobial prescribing for patients who came into the office. Several factors may explain why there was no change in the visit-based prescribing rate: only patients with more serious infections for which antimicrobials might be appropriate came into the office; diagnostic accuracy was improved, for example, through use of pneumatic otoscopy to diagnose middle ear effusion; or the incidence of otitis media and bronchitis may have decreased with no change in prescribing practices.

High rates of antimicrobial use for upper respiratory tract infections reported in several studies using NAMCS data[13,14,33] raise concern about appropriateness of antimicrobial prescribing. In a study of pediatric office visits, antimicrobials were prescribed at 44% of visits for the common cold and at 75% of visits for bronchitis.[13] Findings from a study of adult patients seeking care for acute respiratory tract infections at primary care practices in a group-model health maintenance organization suggested that clinicians use the diagnosis of acute bronchitis as an indication for antimicrobial treatment, despite clinical trials and expert recommendations to the contrary.[34] Antimicrobial treatment of uncomplicated acute bronchitis was reduced by up to 40% in a large community practice setting using a multidimensional intervention strategy.[35]

The results of a survey of pediatricians found that parental pressure, rather than concerns about legal liability or the need to be efficient in practice, was the major reason that oral antimicrobials are prescribed inappropriately.[36] The majority of pediatricians surveyed indicated that educating parents about appropriate antimicrobial use is the single most important factor in reducing unnecessary antimicrobial use. Other concerns expressed by physicians are time pressures, inadequate diagnostic criteria for identifying bacterial infections, and concern about lack of patient follow-up.[37]

A major limitation of this study is that diagnoses cannot be associated with a particular drug, dose, or duration of therapy; therefore, the appropriateness of an antimicrobial prescription could not be assessed. Also, we could not assess whether antimicrobial prescribing shifted from office-based to telephone-based because patient visits recorded in the NAMCS do not include telephone encounters. However, the rate of office-based antimicrobial prescriptions for UTI remained stable during the study period, suggesting that no shift from office-based to telephone-based prescribing occurred. For example, if there had been an increase in antimicrobial prescribing for UTIs over the telephone, then the population-based rates for office-based prescribing would have decreased. In addition, antimicrobial prescribing does not appear to have shifted to other health care settings. From 1992 through 1999, the trend in the percentage of hospital emergency department visits among children and adolescents younger than 15 years at which an antimicrobial was prescribed decreased.[38] Also, without incidence data for the respiratory tract infections examined in this study, we could not determine the extent to which changes in disease incidence may have affected physician office visit rates and population-based prescribing rates for these conditions. Finally, although the number of physicians who participated in the NAMCS and the number of patient visit record forms completed during the study period decreased, there was not a corresponding increase in the relative SEs of the estimates.

There is general agreement that antimicrobial use leads to drug resistance.[10,39-43] Some of the efforts of the CDC, its partners, and other professional organizations to address the important clinical and public health problem of emerging antimicrobial resistance are to enhance surveillance systems that track human antimicrobial drug use; to develop educational and behavioral interventions to modify drug prescribing practices and educate patients and parents on the appropriate use of antimicrobials[11,43]; to develop guidelines for the appropriate use of antimicrobials; to evaluate the impact of vaccine use in preventing

drug-resistant infections[12]; to develop and evaluate new laboratory tests to improve the accuracy and timeliness of detecting antimicrobial resistance in clinical settings; and to implement infection-control strategies.[44] The Public Health Action Plan to Combat Antimicrobial Resistance has been developed by a 10-agency task force co-chaired by CDC, the Food and Drug Administration, and the National Institutes of Health.[45] In its report on antimicrobial resistance, the Institute of Medicine proposed the following fundamental questions for addressing antimicrobial misuse and overuse: does use affect resistance and is unnecessary use common?[46] The NAMCS data can assist in providing answers to these questions; however, an increase in sample size and timeliness would enhance the value of the data.

The decline in pediatric antimicrobial prescribing by office-based physicians, especially the significant decline in overall visit-based prescribing rates observed from 1995-1996 through 1999-2000, coincides with increased attention by the media to the problem of antimicrobial resistance and with efforts by many organizations to promote the appropriate use of antimicrobials. Despite the decline in antimicrobial prescribing for children, pneumococcal resistance has increased through the 1990s.[12] It is important to continue efforts to improve appropriate antimicrobial prescribing and to use data from surveys, such as the NAMCS, for the evaluation of ongoing efforts.

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Acquisition of data: McCaig.
Analysis and interpretation of data: McCaig, Besser, Hughes.
Drafting of the manuscript: McCaig.
Critical revision of the manuscript for important intellectual content: McCaig, Besser, Hughes.
Statistical expertise: McCaig.
Administrative, technical, or material support: McCaig, Besser, Hughes.
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