Predictors of Broad-Spectrum Antibiotic Prescribing for Acute Respiratory Tract Infections in Adult Primary Care

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Context Broad-spectrum antibiotics are commonly prescribed, but little is known about the physicians who prescribe and the patients who take these agents.

Objective To identify factors associated with prescribing of broad-spectrum antibiotics by physicians caring for patients with nonpneumonic acute respiratory tract infections (ARTIs).

Design, Setting, and Patients Cross-sectional study using data from the National Ambulatory Medical Care Survey between 1997 and 1999. Information was collected on a national sample of 1981 adults seen by physicians for the common cold and nonspecific upper respiratory tract infections (URTIs) (24%), acute sinusitis (24%), acute bronchitis (23%), otitis media (5%), pharyngitis, laryngitis, and tracheitis (11%), or more than 1 of the above diagnoses (13%).

Main Outcome Measure Prescription of broad-spectrum antibiotics, defined for this study as quinolones, amoxicillin/clavulanate, second- and third-generation cephalosporins, and azithromycin and clarithromycin.

Results Antibiotics were prescribed to 63% of patients with an ARTI, ranging from 46% of patients with the common cold or nonspecific URTIs to 69% of patients with acute sinusitis. Broad-spectrum agents were chosen in 54% of patients prescribed an antibiotic, including 51% of patients with the common cold and nonspecific URTIs, 53% with acute sinusitis, 62% with acute bronchitis, and 65% with otitis media. Multivariable analysis identified several clinical and nonclinical factors associated with choice of a broad-spectrum agent. After adjusting for diagnosis and chronic comorbid illnesses, the strongest independent predictors of broad-spectrum antibiotic prescribing were physician specialty (odds ratio [OR], 2.4; 95% confidence interval [CI], 1.6-3.5 for internal medicine physicians compared with general and family physicians) and geographic region (OR, 2.6; 95% CI, 1.4-4.8 for Northeast and OR, 2.4; 95% CI, 1.4-4.2 for South [both compared with West]). Other independent predictors of choosing a broad-spectrum agent included black race, lack of health insurance, and health maintenance organization membership, each of which was associated with lower rates of broad-spectrum prescribing. Patient age, sex, and urban vs rural location were not significantly associated with prescribing choice.

Conclusions Broad-spectrum antibiotics are commonly prescribed for the treatment of ARTIs, especially by internists and physicians in the Northeast and South. These high rates of prescribing, wide variations in practice patterns, and the strong association of nonclinical factors with antibiotic choice suggest opportunities to improve prescribing patterns.

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Antibiotics are commonly prescribed for acute respiratory tract infections (ARTIs).[1-4] Some of this use, such as for the common cold and uncomplicated acute bronchitis, is almost always unnecessary.[5,6] For other infections, such as otitis media and acute sinusitis, antibiotics provide some benefit, but the value of their use as first-line treatment has been debated.[6,7]

Even for conditions in which antibiotic use might be justified, many experts have expressed concern about substantial overuse of newer broad-spectrum antibiotics such as the quinolones, amoxicillin/clavulanate, second- and third-generation cephalosporins, and second-generation macrolides. Recent studies have documented frequent use of nonrecommended and second-line antibiotics for patients with sore throat and sinusitis, and found that nonrecommended antibiotic use increased over the last decade among patients with sore throat.[2,3] These agents, while providing little therapeutic benefit for most patients, add substantially to health care costs. More importantly, frequent use of these agents promotes bacterial resistance.[8-10] As a result, future patients may face high levels of resistance to some of today's most powerful therapies.

A variety of factors affect prescribing behavior, including the clinical characteristics of patients, physician training and local patterns of practice,

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drug cost and formulary restrictions, and pharmaceutical detailing and marketing.[11-17] However, most studies of outpatient antibiotic prescribing have focused on the decision to treat or not to treat, rather than on the choice of a particular antibiotic. Information about which factors affect the choice of a particular drug could help efforts to improve both the quality and the quantity of antibiotic prescribing.

In this study, we sought to identify factors associated with the prescribing of broad-spectrum antibiotics by primary care physicians caring for patients with nonpneumonic ARTIs.

METHODS

Sample and Data Set

We used data from the National Ambulatory Medical Care Survey (NAMCS) between 1997 and 1999. Conducted annually by the National Center for Health Statistics, the NAMCS is a nationally representative probability sample of patient visits to community-based outpatient physicians.[18-20] Upon selection for participation in this survey, physicians were asked to complete a standardized encounter form for each eligible patient visit during a 1-week period. Eligible encounters ranged from each patient encounter in small practices to every fifth encounter in large practices. Visits outside the physician office (eg, in nursing homes), visits to federal facilities, and visits to hospital-based outpatient or emergency departments were not included. Over the study period, approximately 1800 physicians were recruited each year, with approximately 63% to 69% agreeing to participate.[18-20]

All information was recorded by the physician or office staff on a standardized form. This form had space for up to 3 diagnoses and 6 medications, which were converted by NAMCS data entry staff into *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes and a standardized drug coding schema.[21] Using a 4-step process, each patient visit was weighted by the inverse probability of its selection (ie, the number of visits in the population that the sampled visit was taken to represent).[20] Using these weights, data from this survey can be extrapolated to the universe of community-based outpatient visits that occur in the United States each year.

Inclusion Criteria and Definitions

The study sample was drawn from 3151 patient visits made by adults aged 18 years or older who received a primary, secondary, or tertiary diagnosis of a nonpneumonic ARTI. These diagnoses included nasopharyngitis (ie, the common cold) or upper respiratory tract infection (URTI) not otherwise specified (*ICD-9-CM* codes 460 and 465), acute or unspecified sinusitis (*ICD-9-CM* codes 461 and 473.9), suppurative or nonsuppurative otitis media (*ICD-9-CM* codes 381.0-381.4 and 382), acute or unspecified bronchitis and bronchiolitis (*ICD-9-CM* codes 466 and 490), and other URTI including pharyngitis, laryngitis, tracheitis, and streptococcal sore throat (*ICD-9-CM* codes 462, 464, and 34.0). During the study period, these diagnoses accounted for 7% of all adult outpatient visits to community-based physicians in the United States, and for 44% of all visits involving an antibiotic prescription.

We excluded 66 visits that involved a concomitant diagnosis with other common outpatient infections that might be treated with an antibiotic, including chronic sinusitis (*ICD-9-CM* codes 473.0-473.8), influenza (*ICD-9-CM* code 487), bacterial or unspecified pneumonia (*ICD-9-CM* codes 481-483 and 485-486), urinary tract infection or acute/unspecified cystitis (*ICD-9-CM* codes 599.0, 595.0, and 595.9), cellulitis, carbuncle, or furuncle (*ICD-9-CM* codes 680-682), prostatitis or pelvic inflammatory disease (*ICD-9-CM* codes 601 and 614), and sexually transmitted diseases including syphilis, gonococcal infections, and other venereal infections (*ICD-9-CM* codes 90-99 and 647.0-647.2).

We subsequently excluded 1054 visits to pediatricians and nonprimary care physicians (ie, physicians with specialties other than general practice, family practice, or internal medicine). In the NAMCS database, most internal medicine subspecialists were coded separately from generalists and were excluded from this analysis. Finally, we excluded an additional 50 visits for which the patient was referred to the treating physician.

Of the remaining 1981 patient visits, 1257 involved an antibiotic. Antibiotics were defined as antibacterial agents commonly available in oral or intramuscular form for outpatient use. We did not count polymyxins and aminoglycosides in our tally of antibiotics, as these medications are used almost exclusively in topical form for outpatients. Similarly, we did not count antimycobacterial medications as antibiotics, as they are uncommonly used in the treatment of typical ARTIs. Of the remaining agents, we classified the quinolones, amoxicillin/clavulanate, second- and third-generation cephalosporins, and azithromycin and clarithromycin as broad-spectrum antibiotics. All other antibiotics were classified as narrow-spectrum.

Thirty-seven (3%) of 1257 patients received more than 1 antibiotic, for a total of 1298 antibiotic prescriptions. For most of our analyses, the patient was the unit of analysis (ie, patients who received at least 1 broad-spectrum antibiotic were counted in the broad-spectrum antibiotic category). For our analysis evaluating use of specific agents, we made the antibiotic the unit of analysis, such that each antibiotic was counted separately.

Analysis

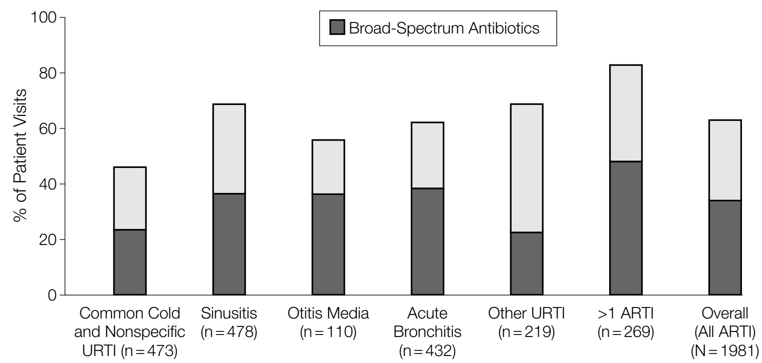
To identify patients with active comorbid conditions, we searched the 3 diagnosis fields for common chronic diseases that were listed alongside the ARTI diagnosis. These included chronic obstructive pulmonary disease or asthma (*ICD-9-CM* codes 491-493 and 496), congestive heart failure (*ICD-9-CM* code 428), ischemic or hypertensive heart disease (*ICD-9-CM* codes 410-414, 402, and 404), diabetes mellitus (*ICD-9-CM* code 250), malignant neoplasms and neoplasms of uncertain or unspecified behavior (*ICD-9-CM* codes 140-208 and 235-239), cerebrovascular disease (*ICD-9-CM* codes 430-438), acute or chronic renal disease (*ICD-9-CM* codes 403 and 580-588), and human immunodeficiency virus infection (*ICD-9-CM* code 042). Comorbid conditions were recorded in 96 (8%) of 1257 patients receiving an antibiotic.

In each analysis, we adjusted for patient weights to make our point estimates of antibiotic prescriptions nationally representative.[20] These weights are assigned in inverse proportion to the probability of a visit being selected from the universe of patient visits. As such, they denote the number of visits in the US population that are represented by the sampled visit. To account for the sample's hierarchical design, we adjusted for clustering at the level of the individual physician, thus increasing the variance around our point estimates to account for nonindependence of observations within the sampling frame. The 1981 visits in our sample were conducted by 558 physicians, with a mean (SD) of 3.6 (2.8) visits per physician. The intracluster correlation coefficient for broad-spectrum antibiotic prescriptions among these physicians was 0.31. Additional cluster identifiers based on the local geographic sampling unit were not available in the public-use data set at the time of this analysis, and could not be used in our calculations.

Adjusting for patient weights and physician-level clustering, we performed bivariate analyses with the design-based F test, which is analogous to a χ^2 test for complexly sampled data. Multivariable analyses were performed with generalized estimating equations, using forward stepwise regression with $P<.10$ to stay and $P<.05$ to report. We checked for potential interactions, none of which added significantly to the model.

All analyses were performed using STATA statistical software (Intercooled Version 6.0; STATA Corp, College Station, Tex). All results except raw numbers are presented after adjustment for patient weights. $P<.05$ was considered significant. This research was approved by the Committee on Human Research of the University of California, San Francisco.

Figure 1. Antibiotic Prescriptions for Adults With Nonpneumonic Acute Respiratory Tract Infections, by Diagnosis



Overall, 63% of all patients with an acute respiratory tract infection (ARTI) received an antibiotic, including 29% who received narrow-spectrum therapy and 34% who received broad-spectrum therapy. Broad-spectrum antibiotics included the quinolones, amoxicillin/clavulanate, the second- and third-generation cephalosporins, and azithromycin and clarithromycin. Other upper respiratory tract infection (URTI) includes pharyngitis, laryngitis, and tracheitis.

RESULTS

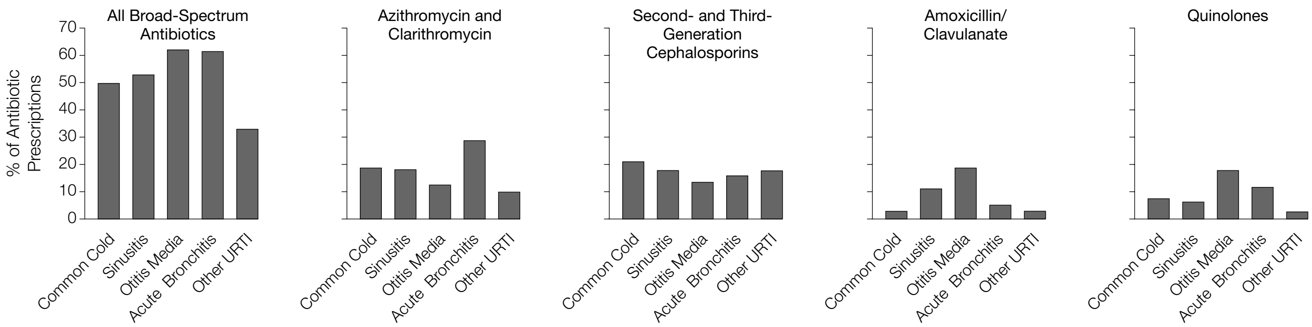
Of 1981 adults with nonpneumonic ARTIs that participated in the NAMCS, the most common diagnoses were sinusitis (24% of patient visits), the common cold and nonspecific URTIs (24%), and acute bronchitis (23%). Less common diagnoses were pharyngitis, laryngitis, or tracheitis (11%), otitis media (5%), and combinations of more than 1 ARTI (13%).

Antibiotics were prescribed to 63% of patients with an ARTI, ranging from 46% of patients with the common cold or nonspecific URTI to 69% of patients with sinusitis and 83% of patients with more than 1 ARTI (FIGURE 1). Similarly, prescriptions for broad-spectrum antibiotics were common, but varied across conditions. Broad-spectrum agents were chosen in 54% of patients prescribed an antibiotic, ranging from 33% of patients with pharyngitis, laryngitis, or tracheitis to 65% of patients with otitis media. Overall, broad-spectrum therapy was ordered for more than half of patients prescribed an antibiotic for each type of ARTI except pharyngitis, laryngitis, or tracheitis (Figure 1).

Azithromycin and clarithromycin were the most commonly prescribed broad-spectrum agents, comprising 21% of all antibiotic prescriptions for patients with ARTIs. These were followed by second- and third-generation cephalosporins (17% of prescriptions), amoxicillin/clavulanate (8%), and the quinolones (7%). Prescriptions for these agents varied substantially across diagnoses (FIGURE 2).

Among patients prescribed antibiotics, several factors were associated with choice of a broad-spectrum agent (TABLE). On unadjusted analyses, there was substantial variation by diagnosis, comorbidity, sex, national region, and physician specialty ($P<.05$ for each). On multivariable analysis controlling for diagnosis and comorbidity, the strongest independent predictors of broad-spectrum antibiotic choice were national region and physician specialty, with physicians in the Northeast and South and internists prescribing at particularly high rates. Other independent predictors included black (non-Hispanic) patient race, patient health maintenance organization membership, and lack of patient health insurance for the visit, each of which was associated with lower rates of broad-spectrum antibiotic prescribing.

Figure 2. Type of Broad-Spectrum Antibiotic Prescribed for Adults With Nonpneumonic Acute Respiratory Tract Infections, by Diagnosis



The total number of antibiotic prescriptions by diagnostic category is common cold, 228; sinusitis, 332; otitis media, 67; acute bronchitis, 286; and other URTI, 157. Prescriptions for narrow-spectrum antibiotics are not shown. URTI indicates upper respiratory tract infection.

The association between prescribing behavior and physician specialty and region appeared additive. The percentage of patients whose antibiotic regimen included a broad-spectrum agent ranged from 41% for general and family physicians in the Midwest and West, to 50% for general and family physicians in the Northeast and South, to 56% for internists in the Midwest and West, to 76% for internists in the Northeast and South.

The total volume of broad-spectrum antibiotic prescriptions depends on overall rates of antibiotic prescribing and the proportion of those prescriptions that are for broad-spectrum agents. Our primary analysis measured only the proportion of broad-spectrum prescriptions among patients who received an antibiotic. To control for overall rates of antibiotic prescribing, we rebuilt our multivariable analysis to compare patients who received a broad-spectrum antibiotic with all other patients (ie, those who received either a narrow-spectrum agent or no antibiotic at all). After controlling for diagnosis and comorbidity, broad-spectrum antibiotic prescribing was still significantly predicted by internal medicine specialty (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.2-2.3) compared with general and family physicians and region (Northeast: OR, 2.3; 95% CI, 1.4-3.8 and South: OR, 2.0; 95% CI, 1.3-3.2 [both compared with West]). Other variables from the original model remained generally stable as well.

COMMENT

Our study has 2 principal findings. First, when primary care physicians prescribe antibiotics for ARTIs, they choose a broad-spectrum agent more than half the time. Second, there is wide variation in prescribing of broad-spectrum agents among different groups of patients and physicians, even after controlling for diagnosis and comorbidities. Internists and physicians in the Northeast and South were particularly likely to prescribe broad-spectrum antibiotics. More than three quarters of antibiotic regimens among patients seen by internists in these 2 regions involved a broad-spectrum agent. Other factors including patient race, health maintenance organization membership, and insurance status were also significantly associated with choice of a broad-spectrum agent.

It is difficult to quantify the correct amount of broad-spectrum antibiotic prescribing, yet several features suggest that the rates we observed are too high. Many of the diseases we studied do not require any antibiotic therapy at all, such as the common cold and acute bronchitis.[5,6] It has been estimated that 55% of all antibiotic prescriptions for ARTIs are unnecessary.[22] Moreover, even for ARTIs that may benefit from antibiotics, there is little evidence of clinically meaningful differences in cure rates between broad- and narrow-spectrum agents.[3,23]

Overall rates of medication use and variation in prescribing between physicians stem from a wide array of factors that affect clinical decisions.[13,17,24] Traditional biomedical factors (characteristics of diseases, drugs, and physician knowledge) form one important set of inputs to the prescribing decision.[25] However, a host of other factors ranging from physician and patient attitudes to environmental constraints can play an equal or greater role in physician decision making.[13,17,25] Physicians with a similar knowledge base may make different judgments about the relative importance of various characteristics of a drug, such as its efficacy, ease of use, adverse effect profile, cost, and potential effect on resistance in the community.[26-28] Numerous studies document that patient expectations, driven by explanatory models of illness and increasingly by direct-to-consumer advertising, can be a major driver of prescribing behavior.[17,25,29-31] For example, physicians are far more likely to prescribe an antibiotic when they think their patient expects a drug, even though these perceptions often do not match the reality of patients' wishes.[32,33] Drug samples can also influence prescribing decisions for individual patients, as do the wide range of other marketing efforts such as advertisements, gifts, and promotional detailing.[34-40] Finally, formulary restrictions and other external constraints can promote the use of certain drugs over others.[41-43]

Variation in prescribing behavior between different geographic regions and specialties may reflect an asymmetrical distribution of this wide range of factors. For example, knowledge of recommended treatment strategies for ARTIs may vary between groups of physicians. Perhaps more importantly, the medical culture in which physicians practice (ie, within a specialty or geographic region) may impart different values to therapeutic decisions.[27,44-46] Highlighting this point, Metlay et al[26] demonstrated that infectious disease specialists are more likely than generalists to incorporate public health concerns into their choice of antibiotic. In addition, the distribution of environmental factors may have substantial heterogeneity. For example, different degrees of managed care penetration (and attendant formulary restrictions) may help explain regional differences in patterns of care,[47-49] and pharmaceutical marketing efforts may be greater in areas where the perceived reward is higher.

Other studies of antibiotic choice confirm the complex interplay of these influences and highlight the role of factors other than a standardized application of accurate clinical knowledge. In a recent study of nonrecommended antibiotic use among patients with pharyngitis, only nonclinical characteristics (ie, calendar year and type of health plan) were associated with medication choice.[2] In contrast, another study of patients with sinusitis found that prescribing of second-line antibiotics was predicted by older age, comorbidity, and specialist care.[3] Other research about whether patients receive an antibiotic has documented a similar mix of clinical and nonclinical inputs into the prescribing decision, including the patient's clinical presentation, age, and perceived patient expectation for antibiotics, as well as physician factors such as clinician age, specialty, method of renumeration, and practice volume.[1,2,12,32,50-53]

It is difficult to disentangle the web of factors that contribute to variation in broad-spectrum antibiotic prescribing. However, cultural factors shared within physician specialties and geographic regions that impact prescribing could serve as important targets for intervention efforts.[13,17] The use of opinion leaders, clinical champions, and one-on-one education (termed *academic detailing*) have been among the most effective strategies for modifying

Table. Predictors of Broad-Spectrum Antibiotic Choice Among Patients Prescribed an Antibiotic*

Characteristic	Unweighted Sample (N = 1257)	Patients Prescribed a Broad-Spectrum Antibiotic, %†	Adjusted OR (95% CI) of Broad-Spectrum Antibiotic Prescription
Diagnosis			
Common cold and nonspecific URTI	222	51	Referent
Sinusitis	325	53	1.1 (0.6-1.8)
Otitis media	64	65	1.9 (0.9-3.7)‡
Acute bronchitis	276	62	1.5 (0.9-2.5)
Other URTI§	153	33	0.4 (0.2-0.7)‖
>1 of the above	217	58	1.4 (0.8-2.3)
Comorbidity			
Absent	1161	53	Referent
Present	96	69	1.7 (1.0-3.0)‖
Age category, y¶			
18-39	522	50	
40-59	454	56	
≥60	281	58	
Sex¶			
Men	501	50	
Women	756	57	
Race/ethnicity			
White non-Hispanic	1073	55	Referent
Black non-Hispanic	98	43	0.5 (0.3-0.9)‖
Other race non-Hispanic	27	51	1.1 (0.5-2.4)
Hispanic, any race	59	51	0.7 (0.3-1.5)
Primary source of payment			
Private insurance	787	55	Referent
Medicare	171	59	0.8 (0.5-1.2)
Medicaid	64	47	0.8 (0.4-1.7)
Self-pay	144	42	0.5 (0.3-0.8)‖
Other	91	53	0.8 (0.4-1.7)
Health maintenance organization membership			
No	800	55	Referent
Yes	370	51	0.6 (0.5-0.9)‖
Region			
West	193	49	Referent
Midwest	379	44	1.3 (0.7-2.3)
Northeast	245	63	2.6 (1.4-4.8)‖
South	440	59	2.4 (1.4-4.2)‖
Location			
Urban	959	56	Referent
Rural	298	48	0.7 (0.4-1.0)‡
Physician specialty			
General practice/family practice	868	46	Referent
Internal medicine	389	68	2.4 (1.6-3.5)‖

Abbreviations: CI, confidence interval; OR, odds ratio; URTI, upper respiratory tract infection.
*Broad-spectrum antibiotics included the quinolones, amoxicillin/clavulanate, second- and third-generation cephalosporins, and azithromycin and clarithromycin.
†As a percentage of the total number of patients prescribed an antibiotic, adjusted for sample weights.
‡$P<.10$.
§Includes pharyngitis, laryngitis, and tracheitis.
‖$P<.05$.
¶Age and sex did not meet prespecified statistical criteria for inclusion in the final multivariate model.

physician prescribing.[54,55] The success of these interventions has been attributed to their ability to address local cultures of practice by modeling approaches to drug use in a context that resonates with the audience.[56,57] Similarly, other successful interventions have accounted for the unique patient, physician, and system influences that impact a discrete group of physicians, simultaneously addressing multiple targets to change the local culture of practice and thereby improve prescribing.[58]

Our findings should be interpreted in light of this study's limitations. Although better than most surveys of its kind, the response rate of the NAMCS was incomplete, and like all surveys there was potential for inaccurate data collection. Our data included little clinical information. For instance, there was no indication if the study visit was an initial or follow-up appointment. Also, our comorbidity variable likely missed many patients with quiescent comorbid conditions, although by preferentially capturing patients with active comorbidities, we likely overestimated the association between comorbidity and broad-spectrum antibiotic prescribing. Although we were unable to completely eliminate other clinical confounders (eg, specialty-based differences in illness severity and regional differences in microbiological resistance), these confounders are unlikely to fully account for the intergroup variation that we observed. Other important clinical variables such as age did not predict broad-spectrum antibiotic choice, even when comorbidity was not included in the multivariate model. Moreover, our findings persisted after expanding the analysis to include patients who did not receive an antibiotic, thus making it unlikely that physicians with the highest proportion of broad-spectrum agents were merely reserving antibiotic therapy for their sickest patients.

In summary, our findings show high rates of broad-spectrum antibiotic prescribing, even among conditions for which antibiotic therapy is not indicated at all. After controlling for clinical characteristics, physician specialty and region were strongly associated with choice of broad-spectrum agents. Further investigation, both globally and locally, is needed to more clearly delineate the forces that contribute to this variation. Whatever these reasons, past experience shows that interventions relying on passive education or a one-size-fits-all approach are not enough. Instead, interventions that focus on understanding and changing shared cultures of practice will be most likely to improve the quality of medication prescribing.

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Study concept and design: Steinman, Gonzales.
Acquisition of data: Steinman.
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Drafting of the manuscript: Steinman, Gonzales.
Critical revision of the manuscript for important intellectual content: Steinman, Landefeld, Gonzales.
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REFERENCES

1. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA.* 1997;278:901-904.
2. Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: a national survey, 1989-1999. *JAMA.* 2001;286:1181-1186.
3. Piccirillo JF, Mager DE, Frisse ME, Brophy RH, Goggin A. Impact of first-line vs second-line antibiotics for the treatment of acute uncomplicated sinusitis. *JAMA.* 2001;286:1849-1856.
4. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA.* 2002;287:3096-3102.
5. Snow V, Mottur-Pilson C, Gonzales R. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults. *Ann Intern Med.* 2001;134:487-489.
6. Snow V, Mottur-Pilson C, Gonzales R. Principles of appropriate antibiotic use for treatment of acute bronchitis in adults. *Ann Intern Med.* 2001;134:518-520.
7. Takata GS, Chan LS, Shekelle P, Morton SC, Mason W, Marcy SM. Evidence assessment of management of acute otitis media, I: the role of antibiotics in treatment of uncomplicated acute otitis media. *Pediatrics.* 2001;108:239-247.
8. Austin DJ, Kristinsson KG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. *Proc Natl Acad Sci U S A.* 1999;96:1152-1156.
9. Resistance of *Streptococcus pneumoniae* to fluoroquinolones—United States, 1995-1999. *MMWR Morb Mortal Wkly Rep.* 2001;50:800-804.
10. Hyde TB, Gay K, Stephens DS, et al. Macrolide resistance among invasive *Streptococcus pneumoniae* isolates. *JAMA.* 2001;286:1857-1862.
11. Gonzales R, Barrett PH Jr, Crane LA, Steiner JF. Factors associated with antibiotic use for acute bronchitis. *J Gen Intern Med.* 1998;13:541-548.
12. Gonzales R, Barrett PH Jr, Steiner JF. The relation between purulent manifestations and antibiotic treatment of upper respiratory tract infections. *J Gen Intern Med.* 1999;14:151-156.
13. Hemminki E. Review of literature on the factors affecting drug prescribing. *Soc Sci Med.* 1975;9:111-116.
14. Soumerai SB, Ross-Degnan D, Avorn J, McLaughlin T, Choodnovskiy I. Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med.* 1991;325:1072-1077.
15. Wazana A. Physicians and the pharmaceutical industry: is a gift ever just a gift? *JAMA.* 2000;283:373-380.
16. Avorn J, Soumerai SB. Improving drug-therapy decisions through educational outreach: a randomized controlled trial of academically based "detailing." *N Engl J Med.* 1983;308:1457-1463.
17. Avorn J, Solomon DH. Cultural and economic factors that (mis)shape antibiotic use: the nonpharmacologic basis of therapeutics. *Ann Intern Med.* 2000;133:128-135.
18. National Center for Health Statistics. *Public Use Microdata File Documentation, National Ambulatory Medical Care Survey, 1997.* Hyattsville, Md: National Technical Information Service; 1999.
19. National Center for Health Statistics. *Public Use Microdata File Documentation, National Ambulatory Medical Care Survey, 1998.* Hyattsville, Md: National Technical Information Service; 2000.
20. National Center for Health Statistics. *Public Use Microdata File Documentation, National Ambulatory Medical Care Survey, 1999.* Hyattsville, Md: National Technical Information Service; 2001.
21. *International Classification of Diseases, Ninth Revision, Clinical Modification.* Washington, DC: Public Health Service, US Dept of Health and Human Services; 1988.
22. Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis.* 2001;33:757-762.
23. Ioannidis JP, Contopoulos-Ioannidis DG, Chew P, Lau J. Meta-analysis of randomized controlled trials on the comparative efficacy and safety of azithromycin against other antibiotics for upper respiratory tract infections. *J Antimicrob Chemother.* 2001;48:677-689.
24. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? a framework for improvement. *JAMA.* 1999;282:1458-1465.
25. Schwartz RK, Soumerai SB, Avorn J. Physician motivations for nonscientific drug prescribing. *Soc Sci Med.* 1989;28:577-582.
26. Metlay JP, Shea JA, Crossette LB, Asch DA. Tensions in antibiotic prescribing: pitting social concerns against the interests of individual patients. *J Gen Intern Med.* 2002;17:87-94.
27. Epstein AM, Read JL, Winickoff R. Physician beliefs, attitudes, and prescribing behavior for anti-inflammatory drugs. *Am J Med.* 1984;77:313-318.

28. Carrin G. Drug prescribing: a discussion of its variability and (ir)rationality. *Health Policy.* 1987;7:73-94.
29. Cockburn J, Pit S. Prescribing behaviour in clinical practice: patients' expectations and doctors' perceptions of patients' expectations—a questionnaire study. *BMJ.* 1997;315:520-523.
30. Macfarlane J, Holmes W, Macfarlane R, Britten N. Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. *BMJ.* 1997;315:1211-1214.
31. Wilkes MS, Bell RA, Kravitz RL. Direct-to-consumer prescription drug advertising: trends, impact, and implications. *Health Aff (Millwood).* 2000;19:110-128.
32. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? *J Fam Pract.* 1996;43:56-62.
33. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. *BMJ.* 1998;317:637-642.
34. Chew LD, O'Young TS, Hazlet TK, Bradley KA, Maynard C, Lessler DS. A physician survey of the effect of drug sample availability on physicians' behavior. *J Gen Intern Med.* 2000;15:478-483.
35. Bell RA, Wilkes MS, Kravitz RL. Advertisement-induced prescription drug requests: patients' anticipated reactions to a physician who refuses. *J Fam Pract.* 1999;48:446-452.
36. Rosenthal MB, Berndt ER, Donohue JM, Frank RG, Epstein AM. Promotion of prescription drugs to consumers. *N Engl J Med.* 2002;346:498-505.
37. Chren MM, Landefeld CS, Murray TH. Doctors, drug companies, and gifts. *JAMA.* 1989;262:3448-3451.
38. Chren MM, Landefeld CS. Physicians' behavior and their interactions with drug companies: a controlled study of physicians who requested additions to a hospital drug formulary. *JAMA.* 1994;271:684-689.
39. Lurie N, Rich EC, Simpson DE, et al. Pharmaceutical representatives in academic medical centers: interaction with faculty and housestaff. *J Gen Intern Med.* 1990;5:240-243.
40. Ziegler MG, Lew P, Singer BC. The accuracy of drug information from pharmaceutical sales representatives. *JAMA.* 1995;273:1296-1298.
41. Lambert BL, Salmon JW, Stubbings J, Gilomen-Study G, Valuck RJ, Kezlarian K. Factors associated with antibiotic prescribing in a managed care setting: an exploratory investigation. *Soc Sci Med.* 1997;45:1767-1779.
42. Avery AJ, Walker B, Heron T, Teasdale SJ. Do prescribing formularies help GPs prescribe from a narrower range of drugs? a controlled trial of the introduction of prescribing formularies for NSAIDs. *Br J Gen Pract.* 1997;47:810-814.
43. Mather JL, Bayliff CD, Reider MJ, Hussain Z, Colby WD. The impact of formulary reservations on drug utilization: a controlled trial. *Can J Hosp Pharm.* 1994;47:111-116.
44. Harrold LR, Field TS, Gurwitz JH. Knowledge, patterns of care, and outcomes of care for generalists and specialists. *J Gen Intern Med.* 1999;14:499-511.
45. Walker S, McGeer A, Simor AE, Armstrong-Evans M, Loeb M. Why are antibiotics prescribed for asymptomatic bacteriuria in institutionalized elderly people? a qualitative study of physicians' and nurses' perceptions. *CMAJ.* 2000;163:273-277.
46. Safavi KT, Hayward RA. Choosing between apples and apples: physicians' choices of prescription drugs that have similar side effects and efficacies. *J Gen Intern Med.* 1992;7:32-37.
47. Hasty M, Schrager J, Wrenn K. Physicians' perceptions about managed care restrictions on antibiotic prescribing. *J Gen Intern Med.* 1999;14:756-758.
48. Hadley J, Mitchell JM, Sulmasy DP, Bloche MG. Perceived financial incentives, HMO market penetration, and physicians' practice styles and satisfaction. *Health Serv Res.* 1999;34:307-321.
49. Reschovsky J, Reed M, Blumenthal D, Landon B. Physicians' assessments of their ability to provide high-quality care in a changing health care system. *Med Care.* 2001;39:254-269.
50. Mainous AG III, Hueston WJ, Eberlein C. Colour of respiratory discharge and antibiotic use. *Lancet.* 1997;350:1077.
51. Metlay JP, Stafford RS, Singer DE. National trends in the use of antibiotics by primary care physicians for adult patients with cough. *Arch Intern Med.* 1998;158:1813-1818.
52. Mainous AG III, Hueston WJ, Love MM. Antibiotics for colds in children: who are the high prescribers? *Arch Pediatr Adolesc Med.* 1998;152:349-352.
53. Hutchinson JM, Foley RN. Method of physician remuneration and rates of antibiotic prescription. *CMAJ.* 1999;160:1013-1017.
54. Oxman AD, Thomson MA, Davis DA, Haynes RB. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *CMAJ.* 1995;153:1423-1431.
55. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD, Thomson MA, for the Cochrane Effective Practice and Organization of Care Review Group. Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ.* 1998;317:465-468.
56. Soumerai SB, Majdumar S, Lipton HL. Evaluating and improving physician prescribing. In: Strom BL, ed. *Pharmacoepidemiology.* New York, NY: John Wiley & Sons Inc; 2000:483-503.
57. Soumerai SB, Avorn J. Principles of educational outreach ("academic detailing") to improve clinical decision making. *JAMA.* 1990;263:549-556.
58. Gonzales R, Steiner JF, Lum A, Barrett PH Jr. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. *JAMA.* 1999;281:1512-1519.