Over the past decade, antibiotic resistance has increased substantially in the United States (1–3). In response, many experts have advocated a judicious approach to antibiotic use in both inpatient and outpatient settings (4–6). Such an approach may decrease community rates of antibiotic resistance, even to older drugs with long-standing histories of resistance (7, 8). Similarly, judicious use of potent newer agents may preserve their utility in the treatment of severe or complicated infections, forestalling the emergence of widespread resistance (9, 10).

In a landmark study, McCaig and Hughes (11) documented increasing outpatient use of amoxicillin and the cephalosporins between 1980 and 1992 in the United States. Over the past decade, several studies and interventions have focused on the excess use of antibiotics. However, only recently has increasing attention been paid to the type of agents being prescribed (12–14). As a result, relatively little is known about the impact of antibiotic prescribing choices on quality of care, health care costs, and antibiotic resistance.

In this study, we used a large, nationally representative sample of community-based physicians to evaluate outpatient antibiotic prescribing during the 1990s. First, we examined the ways in which patterns of antibiotic use have changed over the past decade, particularly among broad-spectrum agents such as azithromycin and clarithromycin, quinolones, amoxicillin–clavulanate, and second- and third-generation cephalosporins. Next, we determined the association between these patterns of use and clinical factors related to the need for broad-spectrum therapy.
Changing Use of Antibiotics

Context
Indiscriminate use of antibiotics promotes the development of antibiotic-resistant strains of bacteria.

Contribution
This survey of patient visits to community-based clinics shows that antibiotic use for ambulatory infections, especially upper respiratory tract infections, decreased from 1991–1992 to 1998–1999. However, the use of broad-spectrum antibiotics rose over this period.

Implications
Efforts to encourage rational use of antibiotics should focus on which antibiotic to use as well as whether or not to use antibiotics.

–The Editors

characteristics, were recorded by the physician or by office staff completing the visit encounter form.

Design and Classification
We were interested in the use of oral and intramuscular antibiotics, but the NAMCS does not provide information on the route of drug administration. We therefore excluded patient visits to dermatologists and ophthalmologists because these specialists frequently prescribe topical antibiotics, which we could not distinguish from systemic forms of the same drugs. Visits to these specialists made up approximately 10% of patient encounters in each study period. Among the remaining sample, 60,252 visits were recorded in 1991–1992, 62,169 visits were recorded in 1994–1995, and 37,467 visits were recorded in 1998–1999. The smaller sample size in the last study period reflects a smaller number of visits surveyed by the NAMCS in those years.

We divided the remaining sample into patient visits that did and did not involve an antibiotic. Antimicrobial medications used by outpatients almost exclusively in topical or intravenous form, such as polymyxins and aminoglycosides, were not counted as antibiotics. We also did not count antimycobacterial medications as antibiotics because they are infrequently used for typical bacterial infections. Antibiotic use, according to these criteria, was recorded in 8208 sampled visits in 1991–1992, 7944 visits in 1994–1995, and 4200 visits in 1998–1999. In each study period, 3% to 4% of these visits involved the use of more than one antibiotic. In total, there were 8514 antibiotic prescriptions in 1991–1992, 8308 antibiotic prescriptions in 1994–1995, and 4406 antibiotic prescriptions in 1998–1999.

For the purposes of this study, we defined broad-spectrum agents as azithromycin and clarithromycin, quinolones, amoxicillin–clavulanate, and second- and third-generation cephalosporins (17). Many of the broad-spectrum agents we studied were introduced more recently than narrow-spectrum agents that made up at least 2% of total antibiotic prescriptions in any study period received U.S. Food and Drug Administration approval before 1979. Among broad-spectrum agents that made up at least 2% of total antibiotic prescriptions, Food and Drug Administration approval was granted between 1979 and 1984 for amoxicillin–clavulanate, cefaclor, and cefuroxime; in 1987 for ciprofloxacin; in 1991 for azithromycin, cefprozil, and clarithromycin; and in 1996 for levofloxacin (Bergman E. Personal communication. Publically available data from the Tufts Center for the Study of Drug Development’s approved products database).

Patients were considered to have a common infectious condition if the corresponding International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code appeared as the first, second, or third diagnosis for that visit (18). Diagnoses included nasopharyngitis (the common cold) or upper respiratory tract infection not otherwise specified (ICD-9-CM codes 460, 465); acute or chronic sinusitis (ICD-9-CM codes 461, 473); pharyngitis and streptococcal sore throat (ICD-9-CM codes 462, 34.0); suppurative or nonsuppurative otitis media (ICD-9-CM codes 381.0–381.4, 382); acute or acute-on-chronic bronchitis and bronchiolitis (ICD-9-CM codes 466, 490, 491.21); acute tonsillitis, laryngitis, and tracheitis (ICD-9-CM codes 463–464); bacterial or unspecified pneumonia (ICD-9-CM codes 481–483, 485–486); urinary tract infection or acute or unspecified cystitis (ICD-9-CM codes 599.0, 595.0, 595.9); cellulitis, carbuncle, or furuncle (ICD-9-CM codes 680–682); prostatitis or pelvic inflammatory disease (ICD-9-CM codes 601, 614); and sexually transmitted diseases, including syphilis, gonococcal infections, and other venereal infections (ICD-9-CM codes 90–99, 647.0–647.2). In each study period, 11% to 13% of patients who were prescribed antibiotics received a diagnosis of more than one of these infectious conditions. To prevent confusion over which disease was treated by the listed antibiotics, we excluded these patients from the diagnosis-specific analyses. Among adults with a single diagnosis of an infectious disease, there were 1657 visits for the common cold and unspecified upper respiratory tract infections, 2652 visits for sinusitis, 963 visits for pharyngitis, 908 visits for otitis media, 1674 visits for acute bronchitis, and 1636 visits for urinary tract infection over the entire study period. Among children, there were 1976 visits for the common cold and unspecified upper respiratory tract infections, 651 visits for sinusitis, 1120 visits for pharyngitis, 3107 visits for otitis media, and 625 visits for acute bronchitis.

Statistical Analysis
We analyzed overall antibiotic use for a given patient at the level of the patient visit. Individual prescriptions were analyzed at the level of the antibiotic prescription. For example, a patient visit involving amoxicillin and cipro-
of antibiotic prescribing decreased from 1991–1992 to 1998–1999 for the common cold and unspecified upper respiratory tract infections (56% vs. 43% of patient visits; \( P = 0.011 \)), pharyngitis (78% vs. 64% of patient visits; \( P = 0.02 \)), and acute bronchitis (76% vs. 59% of patient visits; \( P < 0.001 \)). Among children, the frequency of antibiotic prescribing decreased for the common cold and unspecified upper respiratory tract infections (41% vs. 21% of patient visits; \( P < 0.001 \)) and pharyngitis (73% vs. 54%; \( P = 0.002 \)) and trended toward a decrease for otitis media (78% vs. 72%; \( P = 0.08 \)) and acute bronchitis (78% vs. 68%; \( P = 0.091 \)). However, despite decreases in the frequency of antibiotic treatment of these conditions, nonpneumococcal acute respiratory tract infections (the common cold and nonspecific upper respiratory tract infections, pharyngitis, otitis media, sinusitis, acute bronchitis, laryngitis, acute tonsillitis, and tracheitis) accounted for 47% to 56% of adult and 75% to 80% of pediatric antibiotic prescriptions in each study period.

**Broad-Spectrum Antibiotic Use**

Over the decade, use of broad-spectrum agents doubled among adults, from 24% to 48% of antibiotic prescriptions \( (P < 0.001 \)). Azithromycin and clarithromycin increased from 2% to 13% of adult prescriptions \( (P < 0.001 \)), quinolones increased from 8% to 16% \( (P < 0.001 \)), amoxicillin–clavulanate increased from 4% to 6% \( (P < 0.001 \)), and second- and third-generation cephalosporins remained stable at 11% to 12% \( (P > 0.2) \). Among children, broad-spectrum antibiotic use increased from 23% to 40% of antibiotic prescriptions \( (P < 0.001 \)), azithromycin and clarithromycin increased from less than 1% to 13% \( (P < 0.001 \)), amoxicillin–clavulanate increased from 6% to 11% \( (P < 0.001 \)), and second- and third-generation cephalosporins remained stable at 16% to 15% \( (P > 0.2) \). Quinolones, which are usually contraindicated in children because of potential cartilage toxicity, made up 1% or less of pediatric prescriptions.

Use of broad-spectrum agents increased across a range of adult and pediatric age groups. Among adults, use of broad-spectrum agents approximately doubled in all age groups, from 21% to 43% of antibiotic prescriptions in those 18 to 39 years of age, from 25% to 52% in those 40 to 59 years of age, and from 28% to 49% in those 60 years of age and older \( (P < 0.001 \) for each age group). Among children, broad-spectrum antibiotic use increased from 26% to 40% of antibiotic prescriptions in those younger than 1 year of age, from 25% to 44% in those 1 to 5 years of age, and from 19% to 36% in those 6 to 17 years of age \( (P < 0.01 \) for each age group).

Use of broad-spectrum antibiotics also increased across a wide range of infections (Figures 1 and 2). Among adults, use of these agents (as a percentage of total antibiotic use) increased approximately two- to threefold for all diagnoses shown in Figure 1 (for pharyngitis, \( P = 0.002 \); for all other conditions, \( P < 0.001 \)). Among children, use...
Overall use of antibiotics decreased in adult visits for the common cold and unspecified upper respiratory tract infections (URTI) ($P = 0.011$), for pharyngitis ($P = 0.02$), and for acute bronchitis ($P < 0.001$). Among adults receiving an antibiotic, broad-spectrum agents made up an increased proportion of antibiotic prescriptions for each condition shown (for pharyngitis, $P = 0.002$; for all other conditions, $P < 0.001$). (Results are shown at the level of the patient visit: Broad spectrum indicates visits involving at least one broad-spectrum antibiotic; narrow spectrum indicates visits involving only narrow-spectrum agents.) The mean number of visits occurring annually during the study period is shown for each condition. UTI = urinary tract infection.

Of broad-spectrum antibiotics increased for each diagnosis shown in Figure 2 (for common cold and unspecified upper respiratory tract infections; sinusitis, and bronchitis, $P \leq 0.001$; for pharyngitis, $P = 0.004$; for otitis media, $P = 0.044$).

To evaluate the clinical appropriateness of broad-spectrum antibiotic use, we examined a condition for which antibiotic resistance has been well described (urinary tract infections) and a predominantly viral group of conditions for which antibiotics have little utility (colds and unspecified upper respiratory tract infections) (Figure 3). For each infection, adult use of broad-spectrum agents made up more than doubled ($P < 0.001$ for change over time). Quinolone use increased from 17% to 35% of antibiotics used to treat urinary tract infections ($P < 0.001$) and from less than 1% to 13% of antibiotics used to treat the common cold and unspecified upper respiratory tract infections ($P < 0.001$). Use of azithromycin and clarithromycin also increased from 1% to 16% of prescriptions for the common cold and unspecified upper respiratory tract infections ($P < 0.001$). Among children, use of broad-spectrum antibiotics increased for otitis media ($P = 0.044$) and more than doubled for the common cold and unspecified upper respiratory tract infections ($P < 0.001$).

In 1998–1999, nonpneumonic acute respiratory tract infections accounted for 54% of adult and 77% of pediatric prescriptions for broad-spectrum antibiotics. Among adults, the common cold and unspecified upper respiratory tract infections accounted for 7% of broad-spectrum antibiotic prescriptions, and sinusitis and acute bronchitis accounted for another 15% each. Among children, 8% of broad-spectrum agents were given for the common cold and unspecified upper respiratory tract infections; in addition, 9% were given for sinusitis, 6% were given for acute bronchitis, and 27% were given for otitis media. In both adults and children, nonpneumonic acute respiratory tract infections accounted for at least two thirds of prescriptions for azithromycin and clarithromycin, amoxicillin–clavulanate, and second- and third-generation cephalosporins. Nonpneumonic acute respiratory tract infections accounted for only 31% of adult quinolone use, although the proportion of adult quinolone use accounted for by urinary tract infections was even lower (17%).

In 1991–1992, broad-spectrum antibiotics made up 21% to 26% of antibiotic prescriptions in all regions of the United States ($P > 0.2$ for difference between regions). By 1998–1999, use of these agents varied substantially by region, making up 37% of antibiotic prescriptions in the Midwest, 40% in the West, 49% in the Northeast, and 52% in the South ($P < 0.001$). Similarly, rates of broad-
spectrum antibiotic use were almost identical in urban versus rural settings in 1991–1992 (23% vs. 24% of prescriptions) but diverged substantially by the end of the decade (47% vs. 38% of prescriptions).

DISCUSSION

Antibiotics are among medicine’s most powerful tools. However, their popularity is their Achilles’ heel. The more frequently antibiotics are used, the more they promote the bacterial resistance that undercuts their effectiveness (9). As a result, physicians can be tempted to use newer and broader-spectrum agents, thereby fueling the expanding cycle of resistance (2, 14, 20).

Our study shows some encouraging signs. Overall, community-based outpatient physicians prescribed substantially fewer antibiotics over the course of the 1990s, particularly among children. Moreover, antibiotics are being used less often for illnesses for which they have limited utility, such as upper respiratory tract infections and acute bronchitis. This may reflect the success of many recent educational interventions to discourage unnecessary antibiotic use.

However, there is also reason for concern. When community-based physicians decide to use an antibiotic, they increasingly turn to broad-spectrum agents, such as azithromycin and clarithromycin, quinolones, and amoxicillin–clavulanate, and have maintained steady use of second- and third-generation cephalosporins. By 1998–1999, these broad-spectrum agents made up 5 of the 10 most commonly prescribed antibiotics in community-based outpatient practice. For many nonpneumonic acute respiratory tract infections, broad-spectrum antibiotics provide little clinical advantage over narrow-spectrum agents or no antibiotic therapy at all (21–29). However, these are the conditions for which broad-spectrum agents are most often used.

Because they are largely protected by patent and exclusivity laws that prevent generic competition, broad-spectrum antibiotics have substantial direct costs. In 1999, the average wholesale price of the five most common broad-spectrum drugs exceeded $50 for a typical 7-day adult course. In contrast, the price of the five most common narrow-spectrum drugs (all of which had generic competition) averaged less than $5 per 7-day course (30).

Increasing use of broad-spectrum antibiotics also has important implications for bacterial resistance. In addition to their broad-spectrum activity, quinolones, amoxicillin–clavulanate, and second- and third-generation cephalospo-
rins are widely used for empirical treatment of severe or complicated infections and for directed treatment of otherwise resistant organisms (31–34). The expanding use of these agents, which by the late 1990s made up more than one third of all adult antibiotic prescriptions, can promote escalating antimicrobial resistance within both individuals and communities (35–37). As a result, the medical profession risks losing some of its most potent therapies for patients with the greatest need (38).

Several clinical factors may help explain the increasing use of broad-spectrum antibiotics. Community-based physicians are prescribing fewer antibiotics overall, perhaps selecting sicker patients for treatment. At the same time, the number of elderly persons is growing rapidly, creating a cohort of patients who are more susceptible to invasive infections and antibiotic-resistant pathogens (35–37). As a result, the medical profession risks losing some of its most potent therapies for patients with the greatest need (38).

Several clinical factors may help explain the increasing use of broad-spectrum antibiotics. Community-based physicians are prescribing fewer antibiotics overall, perhaps selecting sicker patients for treatment. At the same time, the number of elderly persons is growing rapidly, creating a cohort of patients who are more susceptible to invasive infections and antibiotic-resistant pathogens (35–37). In recent years, some treatment guidelines have endorsed broad-spectrum antibiotics for the treatment of outpatient conditions, such as community-acquired pneumonia and urinary tract infections (41, 42).

However, these reasons fail to fully account for the increasing use of broad-spectrum agents. By the end of our observation period, broad-spectrum antibiotics made up half of all antibiotic prescriptions for adults and 40% of prescriptions for children. Our findings suggest that only a minority of patients receiving these drugs were likely to have a resistant or complicated infection that mandated their use. These drugs were used almost as frequently in young, generally low-risk adults as in older patients. Moreover, they were often prescribed in situations for which they provide little antimicrobial benefit over older antibiotics. For example, azithromycin and clarithromycin were commonly used for pediatric otitis media despite having no established therapeutic superiority to amoxicillin for uncomplicated acute infections and limited utility in the treatment of complicated infections (43–45).

Broad-spectrum antibiotics are also being extensively used for conditions that often require no antibiotic treatment at all. Diseases with predominantly viral causes (the common cold, unspecified upper respiratory tract infections, and acute bronchitis) accounted for 22% of adult and 14% of pediatric prescriptions for broad-spectrum antibiotics. An additional one third of adult and two thirds of pediatric broad-spectrum prescriptions were for other non-pneumonic acute respiratory tract infections, for which the effectiveness of antibiotic treatment has been debated. Finally, the widening regional and geographic variation in antibiotic choice, which is inconsistent with known patterns of microbial resistance, suggests that prescribing decisions may be largely driven by forces other than microbiological characteristics of disease (1, 2, 40, 46).

Numerous other factors may influence prescribing behavior (20, 47). Once the decision to prescribe has been made, physicians and patients may believe that “newer is better” (48). They may also be attracted by the easy dosing schedules and the low rates of short-term side effects believed to be associated with some new agents (49). Physicians may not fully understand the bacteriologic characteristics of common infections and local resistance patterns and thus may be excessively skeptical about the likelihood and consequences of treatment failure (50, 51). Moreover, antibiotics may often be seen as a way to meet patient needs that are not really infections or that are not likely to benefit from treatment. For example, azithromycin and clarithromycin are commonly used for pediatric otitis media despite having no established therapeutic superiority to amoxicillin for uncomplicated acute infections and limited utility in the treatment of complicated infections (43–45).

Among adults, use of broad-spectrum agents increased for urinary tract infections (UTIs) and for the common cold and unspecified upper respiratory tract infections (URTI) (P < 0.001 for both conditions). Among children, use of broad-spectrum agents increased for otitis media (P = 0.044) and for the common cold and URTIs (P < 0.001).
expectations and terminate an office visit (52). Although motivated by perceived clinical benefits, physicians also face strong personal, economic, and legal incentives to reduce repeated visits, improve patient satisfaction, and maximize physician efficiency (20, 52, 53).

Pharmaceutical marketing to both physicians and patients can substantially influence attitudes, beliefs, and behaviors toward prescribing (54–61). Such marketing promotes the use of patented, and thus lucrative, medications. Over the study period, five of the six most prescribed antibiotics that gained at least 1% market share did so in the absence of generic competition. In contrast, every medication that lost at least 1% market share had generic competition before or during the decade. This includes cefaclor, whose use gradually decreased from 8% to 1% of prescriptions after being challenged by generic competition in the mid-1990s.

Our study can only raise, not answer, questions about the factors that influence prescribing behavior. Moreover, our results should be interpreted in light of our study’s limitations. Inaccurate survey completion, including failure to record antibiotics prescribed after the visit (for example, after chest radiography or throat culture results became available), may have led us to underestimate antibiotic use. We were also unable to distinguish initial visits from follow-up visits that may have occurred after a course of antibiotics was completed. Together, these factors may explain why patients with illnesses such as pneumonia and urinary tract infections received fewer antibiotics than would be expected. Data were collected on prescribed medications and therefore may not reflect which medications were actually taken. Finally, some patient diagnoses may have been inaccurately or imprecisely reported. This may include diagnosis shifting, in which physicians implicitly justify their choice of antibiotics by recording a modified diagnosis. However, because use of newer antibiotics increased across a wide variety of diagnoses, only extreme degrees of random misclassification would change our conclusions. Moreover, diagnosis shifting would probably underestimate the use of broad-spectrum antibiotics in clinically inappropriate settings.

Throughout the 1990s, many efforts were made to reduce the volume of unnecessary antibiotic prescribing. Physicians seem to have responded, but their increasing reliance on newer, largely broad-spectrum antibiotics may be breeding a new crisis in antibiotic resistance. Broad-spectrum agents have an important role in clinical care. However, their common use across many diagnoses, including predominantly viral illnesses, suggests that they are often prescribed unnecessarily. Improving the quality, not just the quantity, of medication prescribing will require better diagnostic tests, clinical trials, and new types of education (62, 63). Yet this will not be enough. Patients, providers, and health care leaders must make a serious commitment to changing the dynamics of outpatient prescribing. If this is done, the care of individual patients and the health of the community at large can be substantially improved.

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References
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[PMID: 11136263]
32. Sable CA, Schild WM. Fluoroquinolones: how to use (but not overuse) these antibiotics. Geriatrics. 1993;48:41-4, 49-51. [PMID: 8580773]
39. Resident Population Estimates of the United States by Age and Sex: April 1, 1990 to July 1, 1999, with Short-Term Projection to November 1, 2000. Ac-
51. Gonzales R, Barrett PH Jr, Steiner JF. The relationship between purulent manifesta-
54. Avorn J, Chen M, Hartley R. Scientific versus commercial sources of influ-
56. Steinman MA, Shlipak MG, McPhee SJ. Of principles and penicillins.
About a dozen beds away from me was numero 57—I think that was his number—a cirrhosis of the liver case. Everyone on the ward knew him by sight because he was sometimes the subject of a medical lecture. On two afternoons a week the tall, grave doctor would lecture in the ward to a party of students, and on more than one occasion old numero 57 was wheeled on a sort of trolley into the middle of the ward, where the doctor would roll back his nightshirt, dilate with his fingers a huge, flabby protuberance on the man’s belly—the diseased liver, I suppose—and explain solemnly that this was a disease attributable to alcoholism, commoner in the wine-drinking countries. As usual he neither spoke to his patient nor gave him a smile, a nod of any kind of recognition. While he talked, very grave and upright, he would roll the wasted body between his two hands, sometimes giving it a gentle roll to and fro, in just the attitude of a woman handling a rolling-pin. Not that numero 57 minded that kind of thing. Obviously he was an old hospital inmate, a regular exhibit at lectures, his liver long since marked down for a bottle in some pathological museum. Utterly uninterested in what was said about him, he would lie with his colourless eyes gazing at nothing, while the doctor showed him off like a piece of antique china.

George Orwell
“How the Poor Die”
*Essays*

Submitted by:
Stephen J. Williams, MD
Bologna, Italy

Submissions from readers are welcomed. If the quotation is published, the sender’s name will be acknowledged. Please include a complete citation (along with page number on which the quotation was found), as done for any reference.—The Editor
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OBJECTIVES To study patterns of outpatient antibiotic use in the Great Tehran, in order to develop interventional strategies in rationalizing drug and especially antibiotic use. MATERIALS AND METHODS Ten-percent random sample of all prescription belonging to practitioners in south of Tehran and kept in a data bank was sampled.