MAJOR ARTICLE

Adherence to the Infectious Diseases Society of America Guidelines in the Treatment of Uncomplicated Urinary Tract Infection

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(See the editorial commentary by Stamm on pages 775–6)

Background. Uncomplicated urinary tract infection (UTI) is one of the most common infections encountered and treated in outpatients. A set of guidelines published in 1999 by the Infectious Diseases Society of America recommends trimethaprim-sulfamethoxazole as first-line therapy.

Methods. We undertook a study of cross-sectional data describing the use of ambulatory medical services in the United States by women ⩾18 years of age who had uncomplicated UTI. Data from 1996 to 2001 were obtained from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey to (1) examine the prescribing practices for the treatment of uncomplicated UTI and (2) determine whether these practices were influenced by the recommendation in the Infectious Diseases Society of America guidelines. The major outcomes measurement was to evaluate whether antibacterial selection was influenced by the Infectious Diseases Society of America guidelines. Data were analyzed by year, treatment in private offices vs. hospital clinics, race, geographic location, the specialty of the prescribing health care provider, and the payment method of the patient.

Results. We identified 2339 cases of uncomplicated UTI. Trimethaprim-sulfamethoxazole and ciprofloxacin were the most commonly prescribed drugs. Despite the Infectious Diseases Society of America guidelines, the use of trimethaprim-sulfamethoxazole did not change significantly (odds ratio, 0.89; 95% confidence interval, 0.60–1.30; $P = .53$), whereas the use of ciprofloxacin increased significantly (odds ratio, 1.75; 95% confidence interval, 1.11–2.75; $P \leqslant .016$). Similar results were obtained after adjusting for age, geographic region, race, physician specialty, payment method, and whether the visit was by a new or returning patient.

Conclusions. Despite the Infectious Diseases Society of America recommendation of trimethaprim-sulfamethoxazole as first-line therapy for uncomplicated UTI, physicians in the United States have not altered their prescribing practices. Adjustment for age, geographic region, race, physician specialty, and payment method confirmed a lack of adherence to this recommendation.

Acute bacterial urinary tract infection (UTI) is one of the most common infections encountered and treated in outpatients. According to the 1999 Infectious Diseases Society of America (IDSA) *Guidelines for Antimicrobial Treatment of Uncomplicated Acute Bacterial Cystitis and Acute Pyelonephritis in Women* [1], the use of trimethoprim-sulfamethoxazole (TMP-SMX) for 3 days is the current standard therapy for the treatment of uncomplicated bacterial UTI. Fluoroquinolones are not recommended as first-line, empirical therapy because of their cost and concerns over the emergence of bacterial drug resistance.

Since the publication of these guidelines in 1999, there continues to be concern over increasing bacterial resistance to TMP-SMX [2–4]. Despite this concern, more recent reviews have continued to recommend TMP-SMX as first-line therapy for the treatment of uncomplicated urinary tract infection (UTI) [5, 6].

Several studies have examined the prescribing preferences of physicians for the treatment of uncomplicated UTI [7, 8]. These studies suggest that physicians' preference for use of fluoroquinolones over TMP-SMX is increasing. However, these existing studies used

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data obtained prior to 1999, before the IDSA guidelines were published, and report antibiotic choices over short periods of time without evaluating trends in use before and after the release of the IDSA guidelines [1]. Furthermore, these studies examined only the prescribing patterns of office-based practices and excluded the prescribing patterns of hospital-based practices in treating uncomplicated UTI.

More recently, a study by Kallen et al. [9] examined antibacterial use for uncomplicated UTI in women using data from the 2000–2002 National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) to determine predictors of quinolone use [9]. We used expanded data from these 2 surveys to (1) examine the prescribing practices for the treatment of uncomplicated UTI and (2) determine whether these practices were influenced by the IDSA guidelines.

METHODS

The NAMCS and the NHAMCS. Data from the NAMCS and the NHAMCS from 1996 to 2001 were analyzed. Compiled annually by the National Center for Health Statistics of the Centers for Disease Control and Prevention, these surveys describe the use of ambulatory medical care services in the United States. The NAMCS and NHAMCS are cross-sectional studies; patients were not followed longitudinally. Data provided for each patient visit include patient demographic information, reasons for the visit, patient diagnoses, procedures and tests performed, and medications prescribed. The NAMCS provides data on visits to non–federally employed, office-based physicians who are primarily engaged in direct primary care. The NHAMCS provides data on visits to emergency departments and outpatient departments of noninstitutional general and short-stay hospitals, exclusive of federal, military, and Veterans Administration hospitals. For the purposes of this study, data on emergency department visits were not used.

Both surveys use a multilevel sampling design. The NAMCS uses a 3-stage probability design with samples of geographically defined areas, physicians' offices within these areas, and patients' visits to these offices. The NHAMCS uses a 4-stage probability design with samples of geographically defined areas, hospitals within these areas, clinics within the outpatient departments of these hospitals, and patients' visits to these departments.

Study population. We identified the cases of women aged ⩾18 years who presented to a health care facility with an uncomplicated UTI. A UTI-related visit was defined as any visit assigned an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code of UTI (599.0) or acute cystitis (595.0 or 595.9). A case was excluded from the study if the patient was pregnant or had a chronic indwelling urinary catheter or a history of recurrent UTI, urinary stones, or urinary neoplasm.

Analysis. National estimates for cases of uncomplicated UTI were calculated. Characteristics of office visits were summarized, including patient demographic information, physician specialty, whether urine samples were sent for culture, and which, if any, antibacterial agent was prescribed. For the most commonly prescribed antibacterial agents, rates of use in cases of uncomplicated UTI were calculated. To assess any differences across various subpopulations, we also examined treatment patterns by outpatient setting (office-based practices vs. hospital-based practices), patient age, patient race, geographic region, method of payment for the visit, and physician specialty.

To determine whether antibacterial treatment choices were affected by the IDSA guidelines, logistic regression was performed on cases in which antibacterials were prescribed, using the guidelines' year of publication (1999) as a binomial predictor for the use of each antibiotic. To control for potential confounding variables, the regression was recalculated after adjusting for age, race, geographic region, physician specialty, payment method, and whether the visit was a follow-up visit for an earlier UTI.

As previously mentioned, patients who received diagnoses that precluded the possibility of an uncomplicated UTI were excluded from analysis. However, there may have been other risk factors that placed a case that should have been considered in analysis in the "complicated" UTI category. As an additional measurement, the regression model was recalculated and compared after the exclusion of patients who were ⩾60 years of age, had diabetes mellitus, and/or were HIV positive or had received a diagnosis of AIDS. To assess any differences across various subpopulations, we examined treatment patterns according to outpatient setting (office-based practices vs. hospital-based practices), patient age, patient race, geographic region, method of payment for the visit, and physician subspecialty.

As mentioned above, the NAMCS and NHAMCS employed a multistage sampling design. Calculation of sampling variance would necessitate a consideration of this design, because the sampling variance would be larger than would be expected for a 1-stage, simple, random sample of equal size. Sampling variances were calculated by approximation from the ultimate cluster variance [10]. In addition, given this sampling design, patient visits were sampled randomly but with unequal probability. Therefore, each visit was weighted accordingly, where the weighting variable was inversely proportional to its probability of being included in the sample. All analyses were performed using Stata software, version 8.0 (Stata Corporation).

RESULTS

The NAMCS and NHAMCS reported 394,472 cases from 1996 to 2001. Of those cases, we identified 2339 that met our criteria for uncomplicated UTI. By extrapolation, we estimate that there were 41.6 million patient visits (95% CI, 37.9–45.4 million patient visits) to a health care provider for uncomplicated UTI in the United States from 1996 to 2001 (and average of ~7 million patient visits per year).

Table 1 shows characteristics of patient visits for uncomplicated UTI. In most of these visits (73%), patients were evaluated by a general medicine physician. A majority of visits (92%) occurred in a private office rather than in a hospital clinic. In most cases (91%), patients were known to the health care provider; in 78% of visits, a urine test was performed, and in 69%, the patient received an antibiotic. Neither the frequency of the use of urine tests nor the administration of an antibiotic changed with time ($P = .096$ and $P = .520$, respectively).

The most common antibacterial agents prescribed for uncomplicated UTI during the study period are listed in table 2. For cases in which antibacterial treatment was given, TMP-SMX and ciprofloxacin were used most frequently, followed by nitrofurantoin.

After the introduction of the IDSA guidelines in 1999 [1], use of TMP-SMX for uncomplicated UTI did not change significantly (table 3). In contrast, use of ciprofloxacin increased by approximately two-thirds. The use of nitrofurantoin also did not change significantly. None of the remaining antibacterials that were studied demonstrated significant changes in rates of use. Similar results were obtained after adjusting for age, race, geographic region, physician specialty, method of payment for the visit, and whether the visit was a follow-up visit for an earlier UTI. Results also did not change significantly after excluding patients aged >60 years and patients who had diabetes mellitus, HIV infection, or AIDS (results not shown).

When comparing antibacterials given to treat uncomplicated UTI, health care providers in hospital clinics were more likely than those in private offices to treat uncomplicated UTI with TMP-SMX (54.7% vs. 27.6%; $P < .001$), whereas providers in private offices were more likely than those in hospital clinics to use ciprofloxacin (24.8% vs. 18.1%; $P = .038$). Patients aged <50 years were more likely to be treated with TMP-SMX than were older patients (36.1% vs. 22.9%; $P = .001$). Antibacterial preferences did not vary significantly across different geographic regions. White patients were significantly less likely to receive TMP-SMX than were nonwhite patients (27.8% vs. 40.8%; $P = .015$). However, race was not a significant predictor of ciprofloxacin or nitrofurantoin use. General medicine physicians were more likely to prescribe TMP-SMX than were other physicians (32.4% vs. 21.5%; $P = .01$), and physicians who practiced obstetrics and gynecology were more likely to prescribe nitrofurantoin than were other physicians (39.1% vs. 16.6%; $P < .001$). Self-paying patients were most likely to be given TMP-SMX than were patients who had private insurance, Medicare, or Medicaid coverage (42.4% vs. 27.9%; $P = .047$). There were no significant differences in prescribing patterns among patients who had private insurance coverage and patients who had Medicare or Medicaid coverage. Finally, there were no significant differences in antibacterial selection for patients who were known to the physician, compared with new patients.

DISCUSSION

The IDSA's recommendations [1] were published in 1999 to provide physicians with a standard protocol for the treatment of uncomplicated UTI. Our study demonstrates that physicians in the United States have not altered their prescribing patterns in response to these guidelines. We observed that TMP-SMX is not the preferred agent in the treatment of uncomplicated UTI, although its use is suggested by the IDSA guidelines, and that ciprofloxacin is not only preferred, but its rate of prescription is increasing.

In general, the rates of antibacterial use that we report are consistent with those previously reported. In our study, 30% of uncomplicated UTIs were treated with TMP-SMX from 1996 through 2001. Other studies have reported a rate of 37% from 1996 through 1999 [7], 24% from 1997 through 1998 [8], and 30% in 2002 [9]. On the basis of these studies, as well as on the basis of our study, the 3 most commonly prescribed antibacterial agents for the treatment of uncomplicated UTI are TMP-SMX, fluoroquinolones, and nitrofurantoin. Furthermore, all studies demonstrated that antibacterial preference was significantly influenced by race, payment method, and physician specialty.

McEwen et al. [7] analyzed treatment preferences for both acute and chronic UTIs using the insurance claims from 1996 to 1999 of employees of a company that had preferred provider organization health care insurance coverage. Trends were not analyzed. Duration of therapy, which could not be ascertained with our data, was reported in the study by McEwan et al. [7]. Average duration of therapy for acute UTI was 8.6 days, which exceeded the recommended 3-day course. It should be noted that acute UTI was defined as "not recurrent" and that the study was unable to identify visits as "uncomplicated" because data about comorbid conditions and pregnancy were unavailable.

Huang and Stafford [8] examined the NAMCS data from 1989 to 1998. They reported a statistically significant increase in the use of fluoroquinolones, as well as a decrease in the use of TMP-SMX. Because NHAMCS data were not included in this study, prescribing patterns for hospital clinics were un-

Table 1. Characteristics of visits to health care providers for urinary tract infection, 1996–2001.

Characteristic	No. of visits (n = 2339)	Weighted percentage of visits (95% CI)
Patient age, years		
18–39	897	33.4 (29.8–37.0)
40–59	662	27.8 (24.0–31.7)
60–79	582	27.8 (25.7–32.9)
⩾80	198	9.5 (7.1–11.9)
Patient race/ethnicity		
White	1927	86.1 (83.3–89.0)
Black	332	9.8 (7.5–12.2)
Other	80	4.0 (2.1–6.0)
Physician specialty		
General medicine	1572	72.7 (69.3–76.1)
General surgery	98	1.4 (0.8–2.0)
OB/GYN	241	10.5 (8.2–12.9)
Other	428	15.3 (12.8–17.9)
Outpatient setting		
Private office	1059	91.5 (90.2–92.8)
Hospital clinic	1280	8.5 (7.2–9.8)
Returning patient		
Yes	1887	90.5 (88.7–92.3)
No	421	9.5 (7.7–11.3)
Urine test performed		
Yes	1804	77.7 (74.5–81.0)
No	535	22.3 (19.0–25.5)
Patient given antibiotics		
Yes	1575	69.5 (65.7–73.2)
No	764	30.5 (26.8–34.3)
Geographic region of the United States		
Northeast	485	16.0 (13.0–19.1)
Midwest	539	22.2 (18.6–25.8)
South	866	40.5 (35.9–45.1)
West	449	21.2 (17.4–25.1)
Type of payment		
Private	968	49.9 (45.9–53.9)
Medicare/Medicaid	925	37.4 (33.7–41.1)
Self-pay	225	5.6 (4.0–7.2)
Other	221	7.1 (5.0–9.1)

NOTE. No. of visits are not directly proportional to percentages because of weighting of visits. In particular, visits to hospital-based practices (from the National Hospital Ambulatory Medical Care Survey [NHAMCS]) were weighted much less than those to office-based practices (from the National Ambulatory Medical Care Survey [NAMCS]). OB/GYN, obstetrics and gynecology.

available, and conclusions were drawn only from data obtained from private offices.

Kallen et al. [9] examined NAMCS and NHAMCS data from 2000 to 2002. They reported a "nonsignificant trend" toward increasing fluoroquinolone use. This was likely caused by the smaller number of study years included in the analysis. Our study, which spanned a longer period of time, and the study by Huang and Stafford [8] were able to demonstrate statistically significant trends in antibacterial use.

McEwen et al. [7] and Huang and Stafford [8] incorporated data obtained prior to 1999, before the publication of the IDSA guidelines [1]. These studies were, therefore, unable to evaluate physicians' compliance with the guidelines. An analysis performed by Kallen et al. [9] using more-recent data from the NAMCS and the NHAMCS corroborated that quinolones were used more frequently than sulfa agents [9], but it made no comparison with data from years prior to the publication of the IDSA guidelines [1]. Our study is unique, in that we eval-

Table 2. Antibacterial drugs given for urinary tract infection, 1996–2001.

Drug	No. of visits	Weighted percentage of visits (95% CI)
TMP-SMX	620	29.8 (25.9–33.7)
Ciprofloxacin	328	24.2 (20.1–28.4)
Nitrofurantoin	259	18.8 (15.0–22.6)
Fluoroquinolones (except ciprofloxacin)	130	11.2 (8.6–13.8)
Amoxicillin	49	2.6 (1.3–3.8)

NOTE. No. of visits are not directly proportional to percentages because of weighting of visits. In particular, visits to hospital-based practices (from the National Hospital Ambulatory Medical Care Survey [NHAMCS]) were weighted much less than those to office-based practices (from the National Ambulatory Medical Care Survey [NAMCS]). TMP-SMX, trimethoprim-sulfamethoxazole.

uated physicians' compliance with the IDSA guidelines by analyzing and modeling trends of antibacterial use for uncomplicated UTI with data compiled from the NAMCS and NHAMCS both before and after publication of the guidelines.

The deviation from the IDSA guidelines may be explained, in part, by many physicians' lack of awareness of them. Of greater concern, however, are physicians who are aware of the guidelines but who continue to prescribe independently of the published recommendations. It is possible that these physicians are influenced by external factors, including substantial marketing—with attendant perquisites—from pharmaceutical companies that promote the use of the company's drugs. Differences in cost are not trivial. During the study period, a 3-day course of TMP-SMX cost approximately US$1.83, whereas a 3-day course of ciprofloxacin cost approximately US$53.56 [6]. Other possible explanations for physicians' nonadherence to the guidelines may include an unwillingness to change because of greater familiarity with ciprofloxacin and personal bias against TMP-SMX because of its adverse effect profile.

Physicians in hospital clinics exercised much greater compliance with the IDSA guidelines [1] than physicians in private offices. Providers from hospital clinics may be more conscientious in practicing evidence-based medicine. A greater number of uninsured patients (who cannot afford more-expensive medications) or fewer external influences (such as pharmaceutical marketing) may explain better compliance with the guidelines by hospital-based clinic practitioners.

Our observation that nonwhite and uninsured patients were more likely to receive TMP-SMX may also reflect the impact of economic status on treatment preferences. These patient populations may be more likely to be affected by differences in antibacterial costs. Interestingly, the treatment prescribed to patients who had Medicare or Medicaid coverage was similar to that prescribed to patients who had private medical insurance coverage. These populations would unlikely be affected by differences in drug price, because their treatment regimens would be covered by their respective health care plans.

The preference of general surgeons for TMP-SMX and of obstetricians and gynecologists for nitrofurantoin may reflect the influence of physician "culture" in determining treatment preferences. The prescribing pattern observed for obstetricians and gynecologists to use nitrofurantoin more commonly for UTI during pregnancy is likely because of its profile as a class B drug. The habit of prescribing nitrofurantoin for UTI may, therefore, have been extended to include their nonpregnant patients.

The influence of local habit and culture, whether in the treatment of patients in a private office versus a hospital clinic or by physician specialty, is apparent. Measures to improve practices should include efforts to increase awareness of IDSA guidelines for the treatment of UTI. Education should target private offices. In addition, the development of local practice guidelines can help to assure physicians that these recommendations pertain to their community. Community antibiograms, although often not readily available, may help to alter location-specific practices in an effort to develop compliance with national guidelines.

Several study limitations warrant discussion. We identified cases of uncomplicated bacterial UTI by isolating observations in which the health care provider entered "cystitis" or "UTI" as a diagnosis on the survey. It is possible that, in some cases, the provider used these terms but, in actuality, treated a more complicated infection, such as recurrent UTI or pyelonephritis. In these circumstances, the diagnoses of pyelonephritis or recurrent UTI would have been excluded from our data analysis and TMP-SMX would not have been recommended as an empiric, first-line therapy. Other factors that were not elucidated but that may have affected the "complicatedness" of the infection included recent hospitalizations, recent antibiotic use, and abnormalities in urinary tract anatomy.

Finally, culture results may have been available to guide therapy decisions. In these cases, treatment would not have been empirical, but directed. However, these data were unavailable

Table 3. Logistic regression analysis of the effect of Infectious Diseases Society of America guidelines on the rate of antibacterial prescriptions.

Drug	OR (95% CI)	*P*
TMP-SMX	0.89 (0.60–1.30)	.530
Ciprofloxacin	1.75 (1.11–2.75)	.016
Nitrofurantoin	1.26 (0.72–2.19)	.414
Fluoroquinolones (except ciprofloxacin)	1.27 (0.75–2.16)	.370
Amoxicillin	0.53 (0.18–1.61)	.263

NOTE. *P* values ⩽.05 are statistically significant. TMP-SMX, trimethoprim-sulfamethoxazole.

to us. We attempted to minimize these possibilities by excluding patients who received diagnoses or had an underlying condition that would preclude a diagnosis of uncomplicated UTI, such as patients with long-term indwelling urinary catheters, as well as by repeating logistic regression analyses after excluding potential risk factors for complicated UTI, such as diabetes mellitus.

According to these data, ~7 million patient visits are made to health care facilities for cases of uncomplicated UTI in the United States every year. Given the volume of patients seen for this problem, physicians' choices regarding treatment are important and will have a major impact on yearly drug costs, as well as on the emergence of drug resistance. Our findings demonstrate a general lack of adherence to the IDSA guidelines for treatment of uncomplicated UTI [1], particularly among physicians in private offices, and raise concerns as to what factors motivate a physician to change his or her prescribing practices.

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