ORIGINAL ARTICLE

Nitrofurantoin Compares Favorably to Recommended Agents as Empirical Treatment of Uncomplicated Urinary Tract Infections in a Decision and Cost Analysis

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OBJECTIVE: **To analyze the costs of nitrofurantoin use compared to those of other antibiotics recommended for treatment of uncomplicated urinary tract infection (UTI).**

PATIENTS AND METHODS: **We used a decision analysis model to perform cost-minimization and sensitivity analyses to determine the level of trimethoprim-sulfamethoxazole (TMP-SMX) and fluoroquinolone resistance that would favor the use of nitrofurantoin as a first-line empirical treatment of uncomplicated UTIs. The model used a program perspective to evaluate costs.**

RESULTS: **Nitrofurantoin was cost-minimizing when the prevalence of fluoroquinolone resistance exceeded 12% among uropathogens or the prevalence of TMP-SMX resistance exceeded 17%. On 2-way sensitivity analysis, variables that had a significant impact on our cost-minimization threshold included cost of antibiotics and probability of clinical cure with antibiotics.**

CONCLUSION: **From a payer perspective, nitrofurantoin appears to be a reasonable alternative to TMP-SMX and fluoroquinolones for empirical treatment of uncomplicated UTIs, especially given the current prevalence of antibiotic resistance among community uropathogens. On the basis of efficacy, cost, and low impact on promoting antimicrobial resistance, clinicians should consider nitrofurantoin as a reasonable alternative to TMP-SMX and fluoroquinolones for first-line therapy for uncomplicated UTIs.**

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AWP = average wholesale price; IDSA = Infectious Diseases Society of America; TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection

Uncomplicated urinary tract infections (UTIs) in women are a common problem in primary care. In 1995, 10.8% of women in the United States aged 18 years or older had a UTI, resulting in 11.3 million prescriptions written for the treatment of UTI and an annual social cost of $1.6 billion.[1]

For many years, trimethoprim-sulfamethoxazole (TMP-SMX) was the preferred antibiotic for the treatment of UTI, given its efficacy and low cost.[2] However, development of a high prevalence of TMP-SMX resistance among uropathogens[3-5] has discouraged use of this drug in many communities. An effective alternative for many clinicians has been the fluoroquinolone class of antibiotics, which achieve high concentrations in the urine and have excellent activity against most uropathogens.[2] Of note, the 2011 Infectious Diseases Society of America (IDSA) guidelines on the treatment of UTIs discourage use of fluoroquinolones for acute, uncomplicated UTI.[6] Experts are concerned about overuse of fluoroquinolones leading to increased prevalence of fluoroquinolone-resistant pathogens that has major implications for the treatment of more serious infections, such as community-acquired pneumonia, health care–associated pneumonia, and complicated UTIs.

Nitrofurantoin has been used for decades as an alternative treatment of uncomplicated UTIs. Additionally, nitrofurantoin has retained a high prevalence of sensitivity to most uropathogens and has a favorable side-effect profile.[7] A recently published randomized trial demonstrated that nitrofurantoin for 5 days is as effective as TMP-SMX for 3 days in treating acute UTI in women.[8] Moreover, nitrofurantoin, like TMP-SMX, is less expensive than fluoroquinolones in many communities.[9]

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Previous analyses have attempted to determine optimal therapy for uncomplicated UTIs on the basis of cost-minimization models and the prevalence of antimicrobial resistance among uropathogens. The first such investigation compared fluoroquinolones to TMP-SMX for empirical therapy and concluded that fluoroquinolones were cost-minimizing when the rate of TMP-SMX resistance exceeded 22% in the community.[10] A subsequent model of fluoroquinolones and TMP-SMX constructed by independent investigators showed similar conclusions.[11] No similar economic analyses have examined how nitrofurantoin compares to the IDSA-recommended empirical therapy for uncomplicated UTIs. Therefore, we performed a cost-minimization and sensitivity analysis comparing TMP-SMX, fluoroquinolones, and nitrofurantoin to determine

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the threshold level of antimicrobial resistance for which each of these antibiotics becomes cost-minimizing.

PATIENTS AND METHODS

To determine the threshold level of TMP-SMX and fluoroquinolone resistance among community uropathogens that would make nitrofurantoin cost-minimizing, we employed a decision tree model using the DATA software (version 4.0, TreeAge Software, Williamstown, MA). The model is based on previous models of uncomplicated UTI treatment caused by *Escherichia coli* in women older than 18 years.[10-12] All the models used a payer (program) perspective for the study. To obtain information on clinical outcomes and cost of uncomplicated UTIs, a systematic review of the literature was performed. We searched MEDLINE articles from 1996 through July 27, 2010, with the keywords *urinary*, *urine*, or *cystitis* and combined these words with *cost*, *cure*, *success*, *response*, or *efficacy*. Similar systematic searches were conducted using Embase and Cochrane Library databases. Three reviewers (J.A.M., C.W.J., L.G.M.) assessed the abstracts, and if an abstract suggested that the article contained data on clinical cure rates of uncomplicated UTIs based on antimicrobial susceptibility, the article was reviewed. Reference lists of retrieved articles were reviewed to find additional studies. For articles published in non-English languages, we reviewed only the abstracts.

The cost-minimization model of UTI treatment on scenarios was derived from the review of the literature and published models.[10-20] In the model, it was assumed that clinicians would choose to empirically treat uncomplicated UTIs with a 3-day course of generic TMP-SMX, a 3-day course of a generic fluoroquinolone (ciprofloxacin), or a 5-day course of generic nitrofurantoin macrocrystals. The 5-day course of nitrofurantoin was based on studies suggesting that a 3-day nitrofurantoin course may not be equivalent to that of TMP-SMX or fluoroquinolones.[8,13] It was also assumed that empirical treatment involved a clinic visit and urinalysis to confirm the presence of UTI and that urine cultures were not performed initially, as recommended by prior IDSA guidelines.[21]

In the model, infection would resolve with initial therapy or would fail to respond to initial therapy (Figure 1). In the latter case, the UTI would resolve after continuation with that treatment or the original antibiotic treatment would be changed. Potential complications of clinical nonresponse included persistence of cystitis symptoms, outpatient treatment of pyelonephritis, or hospitalization for pyelonephritis. Persistence of cystitis symptoms would result in a return visit to the physician, performance of a urine culture, and either an extended course of the same antibiotic or a change to a different antibiotic.

The decision analysis model for the comparison of TMP-SMX and fluoroquinolones is shown in Figure 1. Two similar models were constructed comparing nitrofurantoin with fluoroquinolones and TMP-SMX with nitrofurantoin. For simplicity, the Figure does not include the probability of vaginal yeast infection, which was calculated for each outcome on the basis of published probabilities.[7,22-25] Other potential antibiotic effects or complications (eg, Stevens-Johnson syndrome) were considered rare and not included in our model, given that a previous investigation of uncomplicated UTIs found that expensive but uncommon events had almost no effect on overall treatment costs.[26]

Finally, a model was constructed that compared all 3 treatments: nitrofurantoin, TMP-SMX, and fluoroquinolones. This model was used to evaluate the most cost-effective empirical therapy for uncomplicated UTI at varying levels of fluoroquinolone and TMP-SMX resistance. Because nitrofurantoin resistance has remained relatively stable in the United States and Europe, nitrofurantoin resistance was held constant at 1.2% for the model.[4,5,8]

On the basis of our model, 6 major scenarios arose: (1) treatment of a TMP-SMX–resistant infection with TMP-SMX; (2) treatment of a TMP-SMX–sensitive infection with TMP-SMX; (3) treatment of a nitrofurantoin-resistant infection with nitrofurantoin; (4) treatment of a nitrofurantoin-sensitive infection with nitrofurantoin; (5) treatment of a fluoroquinolone-resistant infection with ciprofloxacin; and (6) treatment of a fluoroquinolone-sensitive infection with ciprofloxacin. Ciprofloxacin was used in the model because it is widely considered by clinicians to be the fluoroquinolone of choice in the treatment of uncomplicated UTIs due to its efficacy, tolerability, and low cost.[27,28]

Costs

Costs used in this model were based on the systematic review of the literature and a survey of costs derived from national and local sources (Table 1). Antibiotic cost was defined as the median of all generic manufacturers' average wholesale price (median AWP) listed in the 2010 Red Book.[9] Costs of hospitalization were compiled from a national survey and incorporated the average cost of a day of hospitalization from the American Hospital Association.[39] Costs of physician visits were derived from the literature[31-33] and from physician payment schedules available from the Centers for Medicare and Medicaid Services.[34] For the cost of outpatient pyelonephritis treatment, it was assumed that high-dose fluoroquinolones were used as therapy. For outpatient treatment of a fluoroquinolone-resistant infection, the cost of therapy with intramuscular ceftriaxone or gentamicin was used.[29] Costs of urinalysis and urine culture were calculated as an average of costs obtained from 3 dif-

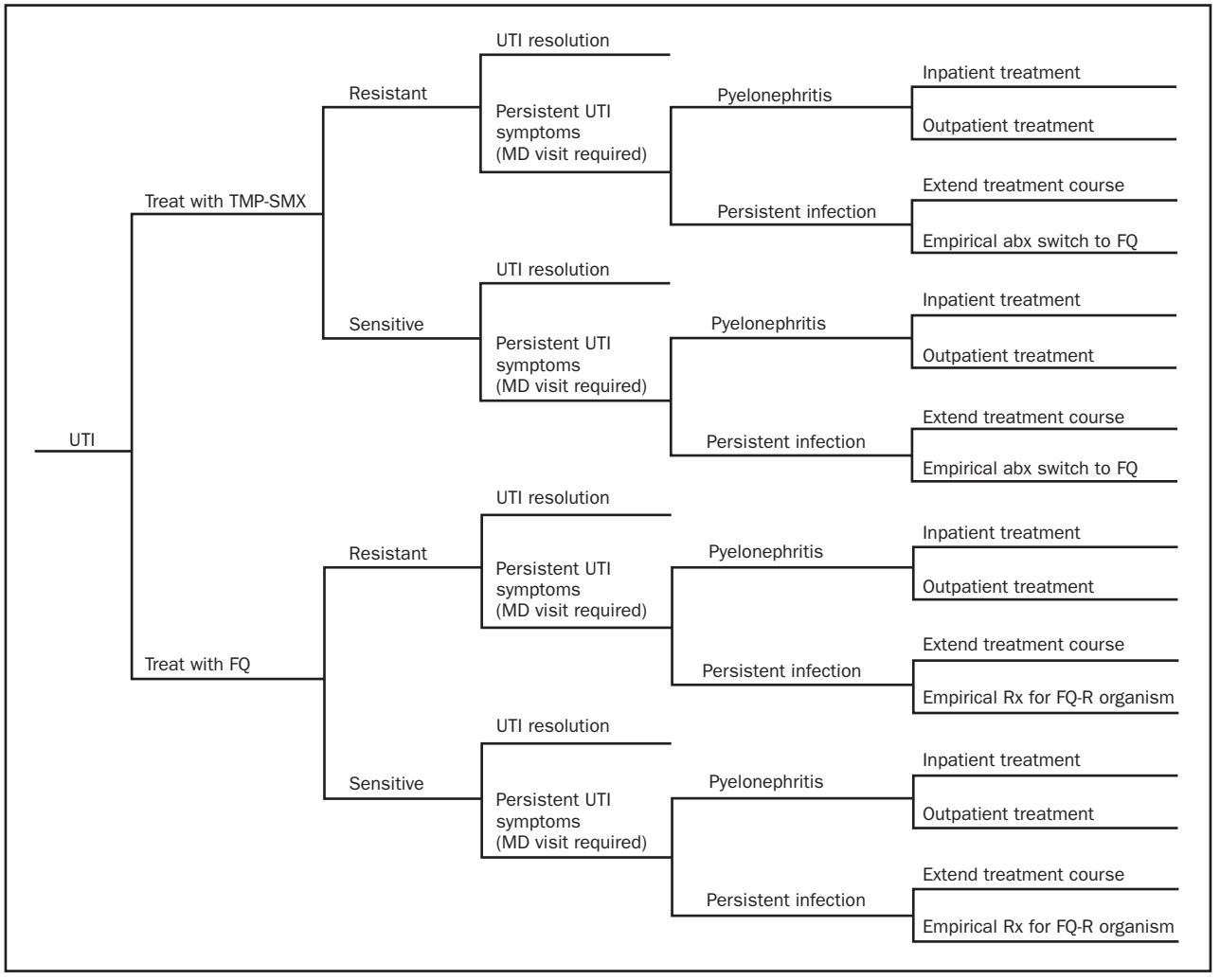

FIGURE 1. Decision tree diagram that shows intermediate and final outcomes for an uncomplicated *Escherichia coli* urinary tract infection (UTI) treated with either trimethoprim-sulfamethoxazole (TMP-SMX) or a fluoroquinolone (FQ). Similar trees were constructed comparing nitrofurantoin with FQ, TMP-SMX with nitrofurantoin, and a 3-way model comparing nitrofurantoin, TMP-SMX, and FQ. After each outcome on the right side of the tree, the probability of developing a vaginal yeast infection was considered (not shown; see text). abx = antibiotic; FQ-R = FQ resistant; MD = medical doctor; Rx = treatment.

ferent commercial laboratories (Diagnostic Laboratories, San Pedro, CA; Quest Diagnostics, Madison, NJ; American Bio-Clinical Laboratories, Los Angeles, CA). The cost of a course of self-treatment of vaginal yeast infection was calculated from a survey of prices for over-the-counter antifungal products available from 3 different national pharmacies (CVS, Walgreens, and Rite Aid).

Probabilities

Probabilities for clinical events were obtained from published estimates,[3-5,7,8,23-25,31,37,40-49] with use of the mean value as the point estimate in the model (Table 2). These estimates were derived from previous models and the systematic review of the literature.

Sensitivity analyses

One-way sensitivity analyses were performed for the following comparisons: mean cost of empirical treatment with nitrofurantoin and fluoroquinolones vs fluoroquinolone resistance, mean cost of empirical treatment with TMP-SMX and nitrofurantoin vs TMP-SMX resistance, and mean cost of empirical treatment with TMP-SMX and fluoroquinolones vs TMP-SMX resistance. In addition, a 2-way sensitivity analysis was performed to determine how changing the values of each cost and probability in the model would affect the cost-minimization threshold. For costs, a range incorporating 50% to 200% of the point estimate was used (Table 1). For probabilities, the range of probabilities for clinical events found in the literature survey was used

TABLE 1. **Cost of Interventions to Treat Uncomplicated UTIs Caused by *Escherichia coli* That Were Used in 2-way Sensitivity Analyses**

Description	Mean cost per unit time or per item (US $)	Range tested (US $)	Variables with >5% change in cost-minimization threshold at extremes of range tested			References
			NTF vs FQ	TMP-SMX vs NTF	TMP-SMX vs FQ	
Ciprofloxacin, 250 mg twice daily (AWP)	4.44/day	2-10	X		X	29
Ciprofloxacin, 500 mg twice daily (AWP)	5.38/day	2-11				29
TMP-SMX, 1 DS tablet twice daily (AWP)	0.87/day	0.5-2		X		29
Nitrofurantoin, 100 mg twice daily (AWP)	1.95/day	1-4	X	X		29
Self-treatment of yeast infection	16.14	8-32				See text
Hospitalization for pyelonephritis	1782.28/day	850-3600				30
Outpatient treatment of infection unresponsive to fluoroquinolones or pyelonephritis caused by fluoroquinolone-resistant *Escherichia coli*	29.77/day	15-60	X		X	29
Initial physician visit for UTI	97.77	67-152				31-34
Follow-up physician visit	97.77	65-132				31-34
Initial urinalysis	20.78	10-42				See text
Follow-up urinalysis	20.78	10-42				See text
Urine culture	46.42	23-93				See text
	Duration (days)	Range (days)				
Hospitalization for pyelonephritis	3	1-5				35, 36
Outpatient treatment of infection unresponsive to fluoroquinolones	5	3-10	X			21
Outpatient treatment of pyelonephritis	7	5-14				37, 38

AWP = average wholesale price; DS = double strength; FQ = fluoroquinolone; NTF = nitrofurantoin macrocrystals; TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection.

(Table 2). To minimize authors' bias, if the literature was scarce (only 1 source) describing the probability of an event, a range incorporating values from at least 50% to 200% of the point estimate was used (Table 2).

RESULTS

For the comparison of nitrofurantoin and fluoroquinolones, the sensitivity analysis demonstrated that, when the percentage of fluoroquinolone-resistant *E coli* exceeds 12%, empirical treatment with nitrofurantoin becomes cost-minimizing; below that level, fluoroquinolones are cost minimizing compared to nitrofurantoin (Figure 2). At the 12% fluoroquinolone resistance breakpoint, the mean total cost of empirical treatment of UTI with fluoroquinolones and nitrofurantoin was $159. When comparing nitrofurantoin and TMP-SMX, nitrofurantoin was cost-minimizing when the percentage of TMP-SMX–resistant *E coli* exceeded 17%. When TMP-SMX resistance was below 17%, TMP-SMX was cost-minimizing compared to nitrofurantoin. When comparing fluoroquinolones and TMP-SMX, fluoroquinolones were cost-minimizing when the percentage of TMP-SMX–resistant *E coli* exceeded 10%.

For the model comparing all 3 treatments, nitrofurantoin was cost-minimizing when the percentage of TMP-SMX resistance exceeded 17% and fluoroquinolone resistance

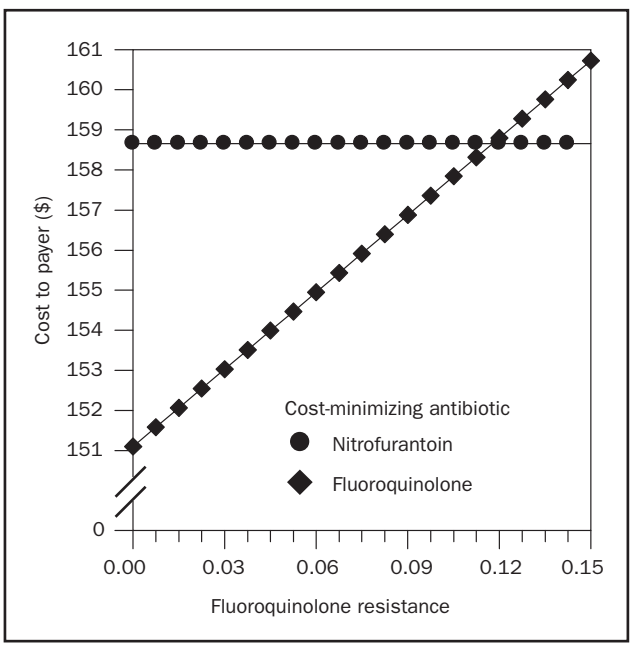

FIGURE 2. Comparison of the mean cost of treatment of uncomplicated *Escherichia coli* urinary tract infection with nitrofurantoin and a fluoroquinolone vs the community prevalence of fluoroquinolone-resistant *E coli*. The threshold for fluoroquinolone resistance above which nitrofurantoin becomes less expensive was 12% with an estimated cost of $159 to the payer.

TABLE 2. **Probability Values for Nodes Tested With Respect to Treatment of Uncomplicated UTIs Caused by *Escherichia coli***

Description	Probability	Range of probabilities tested	Variables with >5% change in cost-minimization threshold at extremes of range tested			References
			NTF vs FQ	TMP-SMX vs NTF	TMP-SMX vs FQ	
TMP-SMX resistance	0.15	0-0.4				3-5, 40, 41
Fluoroquinolone resistance	0.025	0-0.4			X	3-5
Nitrofurantoin resistance	0.012	0-0.05				3-5
Clinical cure of TMP-SMX–resistant infection treated with TMP-SMX	0.55	0.4-0.7		X	X	8, 40, 41
Clinical cure of TMP-SMX–sensitive infection treated with TMP-SMX	0.91	0.8-1.0		X	X	8, 40, 41
Clinical cure of fluoroquinolone-resistant infection treated with fluoroquinolone	0.78	0.4-0.8	X			24,25
Clinical cure of fluoroquinolone-sensitive infection treated with fluoroquinolone	0.94	0.9-1.0	X		X	24, 25, 37, 48
Clinical cure of nitrofurantoin-resistant infection treated with nitrofurantoin	0.67	0.4-0.8				8,23
Clinical cure of nitrofurantoin-sensitive infection treated with nitrofurantoin	0.89	0.8-1.0	X	X		7, 8, 23, 47
Hospitalization for pyelonephritis	0.2	0-0.5	X		X	43, 44
Pyelonephritis if initial empirical therapy unsuccessful	0.04	0-0.08	X		X	2, 43, 44
Vaginal yeast infection after ≤3 d of therapy	0.05	0-0.2		X		25, 31, 44
Vaginal yeast infection after >3 d of therapy	0.07	0-0.2		X		7, 23, 24
Medical visit for vaginal yeast infection	0.25	0-0.5				49
Change of therapy due to lack of clinical response to TMP-SMX (vs extending TMP-SMX treatment)	0.75	0-1			X	43, 44
Change of therapy due to lack of clinical response to fluoroquinolone (vs extending fluoroquinolone treatment)	0.25	0-1	X			43, 44
Change of therapy due to lack of clinical response to nitrofurantoin (vs extending nitrofurantoin treatment)	0.75	0-1				43, 44

FQ = fluoroquinolone; NTF = nitrofurantoin; TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection.

exceeded 12%. With lower percentages of TMP-SMX and fluoroquinolone resistance, TMP-SMX or a fluoroquinolone was cost-minimizing depending on prevalence of resistance to these 2 agents (Figure 3).

In 2-way sensitivity analyses of all comparison models, the cost of antibiotics had a significant effect on the cost-minimization thresholds. In particular, the resistance threshold of fluoroquinolones that makes nitrofurantoin cost-minimizing was sensitive to the cost of nitrofurantoin (Figure 4). Cost of outpatient therapy for a UTI that was not responsive to a fluoroquinolone had a moderate effect on the threshold (Table 1). At the extreme values of the range for cost of outpatient therapy after fluoroquinolone failure, the 12% breakpoint for fluoroquinolone resistance varied from 6% to 18%. The costs of most other interventions, including physician visits, urinalyses, and treatment of yeast infections, had a negligible effect on the cost-minimization thresholds (Table 1). Two-way sensitivity analyses with greater than 5% (absolute) difference in the threshold at extreme values of the range are noted in Table 1 and Table 2.

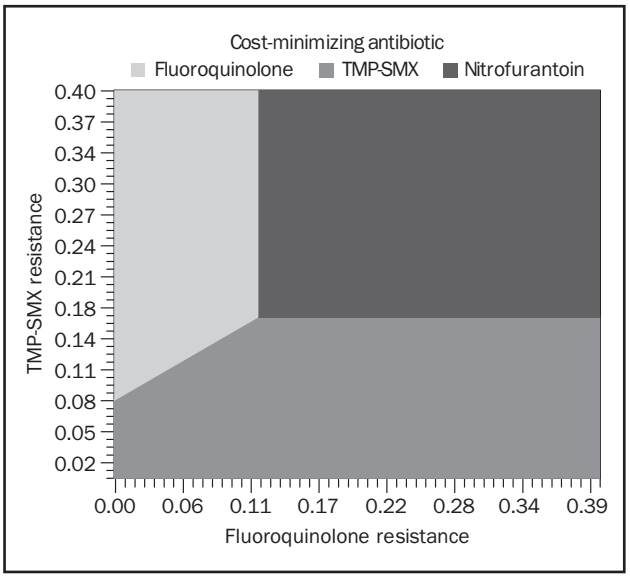

Figure 3. Three-way strategy analysis demonstrating the threshold level of fluoroquinolone and trimethoprim-sulfamethoxazole (TMP-SMX) resistance among *Escherichia coli* above which empirical treatment of urinary tract infection with nitrofurantoin is cost-minimizing. This Figure assumes a constant prevalence of nitrofurantoin resistance at 1.2% (see text for details).

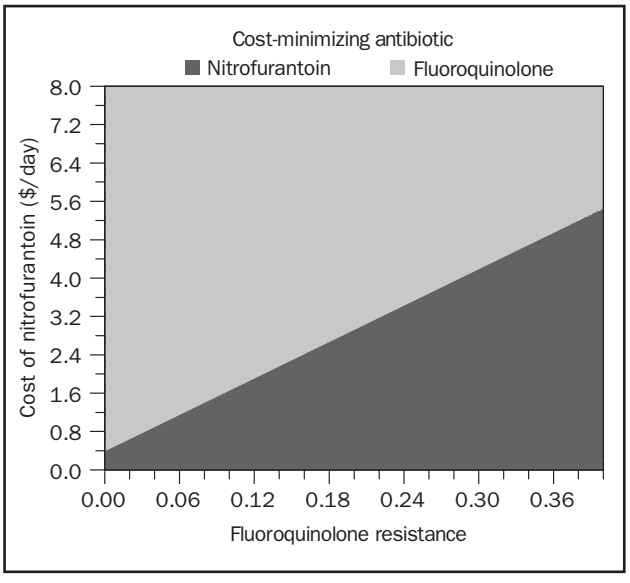

FIGURE 4. Two-way sensitivity analysis showing the effect of varying the cost of nitrofurantoin on the threshold of fluoroquinolone-resistant *Escherichia coli* needed to make nitrofurantoin cost-minimizing.

DISCUSSION

Using a cost-minimization model of empirical treatment of uncomplicated UTIs, we have performed, to our knowledge, the first decision analysis to explore the role of nitrofurantoin in empirical therapy for uncomplicated UTIs. In comparison with fluoroquinolones, nitrofurantoin was found to be cost-minimizing when the prevalence of fluoroquinolone-resistant *E coli* in the community reached 12%. In comparison with TMP-SMX, nitrofurantoin was cost-minimizing when *E coli* resistance to TMP-SMX was 17%. The 3-way model that considered nitrofurantoin, fluoroquinolones, and TMP-SMX demonstrated that, within ranges of uropathogen resistance found in many communities, nitrofurantoin can be cost-minimizing. Our data support the 2011 IDSA recommendations that nitrofurantoin be considered as first-line empirical therapy for uncomplicated UTIs.[6]

To date, nitrofurantoin has been a less commonly used treatment of uncomplicated UTIs. Older monohydrate formulations of nitrofurantoin required dosing 4 times per day and were more cumbersome than twice-daily ciprofloxacin or TMP-SMX. In addition, data from the literature suggested that a 3-day course of nitrofurantoin was not as effective as a 3-day course of TMP-SMX or fluoroquinolones.[8,13] Until recently, nitrofurantoin was considered an inferior agent for the treatment of uncomplicated UTIs.[50] Currently available macrocrystal formulations of nitrofurantoin allow for twice-daily dosing. Furthermore, a recent clinical trial published after 1999 IDSA guidelines data suggests that nitrofurantoin for 5 days is as effective as TMP-SMX for 3 days in treating acute UTIs in women.[8] Supported by these newer data, the 2011 IDSA guidelines have elevated nitrofurantoin from an alternative agent to first-line therapy for uncomplicated UTIs.[6]

In contrast, the new IDSA guidelines demote fluoroquinolones from first-line therapy to an alternative agent for uncomplicated UTIs.[6] A major impetus for limiting the use of fluoroquinolones has been to delay the progression of resistance to these drugs. Fluoroquinolones are among the most commonly used antibiotics, and the development of widespread resistance to these agents may have grave implications for the treatment of more serious infections, such as pneumonia and complicated UTIs. By providing an effective alternative for the treatment of uncomplicated UTIs, nitrofurantoin may contribute to a reduction in overall fluoroquinolone use and thus help to reduce selection pressure for increased resistance to fluoroquinolones.[51-53]

Despite availability and use of nitrofurantoin for more than 5 decades, the prevalence of nitrofurantoin resistance among common uropathogens remains low. In the United States and worldwide, the prevalence of nitrofurantoin resistance among uropathogens is 1% to 2%.[4,5,8,54] For TMP-SMX, the prevalence of resistance among uropathogens is greater than 15% in every area of the United States and as high as 42% in the West South Central region.[4] For fluoroquinolones in the United States, the prevalence of resis-

tance among uropathogenic *E coli* in some regions has been reported as high as 20%.[4] The prevalence of fluoroquinolone resistance in other regions of the world is similarly high.[54-57] Of note, these measures of resistance prevalence may overestimate resistance found in uncomplicated UTIs because surveillance of resistance of cystitis is rarely performed.[50] However, the last nationwide survey of antibiotic resistance among uropathogens causing outpatient UTIs was conducted in 2005,[58] and the prevalence of resistance may be higher. Our model suggests that nitrofurantoin use for uncomplicated UTIs may be cost-minimizing compared with TMP-SMX in many areas of the United States and cost-competitive compared with generic ciprofloxacin.

Our investigation has limitations. One limitation was the sensitivity of the model to several variables for which testing extreme values of the range caused a greater than 5% change in the cost-minimization threshold. This was especially evident for antibiotic cost. In the comparison of nitrofurantoin and fluoroquinolones, a small change in the cost of either drug was associated with substantial changes in the cost-minimization threshold. Comparing TMP-SMX with fluoroquinolones, fluoroquinolones were cost-minimizing when TMP-SMX resistance was 10%. Our breakpoint of TMP-SMX resistance is lower than previously published breakpoints (19%-21%) because generic fluoroquinolones that are less costly have become available since the publication of those analyses.[10,11]

Other variables that had a significant effect on the cost-minimization threshold included the probability of clinical cure with antibiotics. This finding is likely a result of our very conservative approach and the wide ranges in probability that were used for these clinical events. For example, the point estimate for the probability of clinical cure of an infection with a nitrofurantoin-resistant organism treated with nitrofurantoin was 67%. The range used for the sensitivity analysis was between 40% and 80%. However, this range is probably overly broad. The cure rate of uncomplicated UTIs with placebo is reported to be more than 50%.[59] Therefore, cure rates of nitrofurantoin treatment of nitrofurantoin-resistant uropathogens are unlikely to be as low as 40%.

Another limitation of our study is the paucity of data on clinical cure rates of uncomplicated UTIs when the causative organism is resistant to the antibiotic selected for treatment. We found only 2 studies that reported clinical cure rates of uncomplicated UTIs due to nitrofurantoin-resistant organisms treated with nitrofurantoin. In these studies, a total of only 14 patients were infected with such organisms.[8,23] There was a similar lack of data for fluoroquinolones[24,25] but relatively more data for TMP-SMX.[8,40,41] More research is needed to better determine the probability of curing UTIs when the causative organism is resistant to the antibiotic used, especially given how increasingly common this scenario is in primary care. A final limitation is that our model does not contain data on the wide range of adverse events that can occur with each agent. However, precise rates of these rare events in the population being treated are not available, and previous UTI models found that, in sensitivity analyses, rare and expensive events have almost no effect on study results.[26]

Our investigation has several strengths. First, the decision analysis is the first to compare nitrofurantoin against IDSA recommended antibiotics for uncomplicated UTI treatment. Second, the model is based on previously published decision analysis models developed independently by 2 different investigative groups. In addition, the model is the first to address cost-minimization of empirical treatment of uncomplicated UTIs since generic fluoroquinolones have become available. Finally, the 3-way comparison of nitrofurantoin, TMP-SMX, and fluoroquinolones evaluates the cost-effectiveness of the most popular antibiotics used in the treatment of uncomplicated UTIs at current rates of antibiotic resistance among uropathogens. The 3-way model may help policy makers, hospital administrators, and antimicrobial stewardship committees customize their recommendations for first-line therapy for uncomplicated UTIs based on local resistance patterns.

CONCLUSION

Nitrofurantoin is an important treatment option for uncomplicated UTIs in the current era of increasing fluoroquinolone and TMP-SMX resistance among uropathogens. Nitrofurantoin is likely cost-minimizing compared with TMP-SMX in most areas of the United States and cost-competitive compared with generic ciprofloxacin. Our findings complement recent data that demonstrate that the efficacy and tolerability of nitrofurantoin are comparable with the efficacy and tolerability of TMP-SMX for treating uncomplicated UTIs. On the basis of the efficacy, cost, and relatively low effect of nitrofurantoin on promoting further antimicrobial resistance, clinicians, local guidelines, and payers should support its use as a first-line option for empirical treatment of uncomplicated UTIs.

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