Patient-Initiated Treatment of Uncomplicated Recurrent Urinary Tract Infections in Young Women

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Background: **Recurrent urinary tract infections (UTIs) are a common outpatient problem, resulting in frequent office visits and often requiring the use of prophylactic antimicrobial agents. Patient-initiated treatment of recurrent UTIs may decrease antimicrobial use and improve patient convenience.**

Objective: **To determine the safety and feasibility of patient-initiated treatment of recurrent UTIs.**

Design: **Uncontrolled, prospective clinical trial.**

Setting: **University-based primary health care clinic.**

Participants: **Women at least 18 years of age with a history of recurrent UTIs and no recent pregnancy, hypertension, diabetes, or renal disease.**

Intervention: **After self-diagnosing UTI on the basis of symptoms, participating women initiated therapy with ofloxacin or levofloxacin.**

Measurements: **Accuracy of self-diagnosis determined by evidence of a definite (culture-positive) or probable (sterile pyuria and no alternative diagnosis) UTI on pretherapy urinalysis and culture. Women with a self-diagnosis of UTI that was not microbiologically confirmed were evaluated for alternative diagnoses. Post-therapy interviews and urine cultures were used to assess clinical and microbiological cure rates, adverse events, and patient satisfaction.**

Results: **88 of 172 women self-diagnosed a total of 172 UTIs. Laboratory evaluation showed a uropathogen in 144 cases (84%), sterile pyuria in 19 cases (11%), and no pyuria or bacteriuria in 9 cases (5%). Clinical and microbiological cures occurred in 92% and 96%, respectively, of culture-confirmed episodes. No serious adverse events occurred.**

Conclusion: **Adherent women can accurately self-diagnose and self-treat recurrent UTIs.**

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Urinary tract infection (UTI) is an exceedingly common outpatient problem, accounting for more than 8 million office visits and $1 billion in health care costs per year. Approximately 50% to 70% of women will have a UTI sometime during their lifetimes, and 20% to 30% of women will have recurrent episodes (1–3). Thus, safe and effective management strategies that have the potential to improve patient convenience and decrease costs are of considerable interest to patients, providers, and health care organizations. The most well-studied and commonly accepted approach to managing recurrent UTIs uses low-dose antimicrobial prophylaxis given postcoitally, three times per week, or daily (4–6). This strategy has been shown to be safe and highly effective, even after 5 years of use. However, studies of the natural history of recurrent UTI demonstrate substantial variability in the number of recurrences experienced per woman (range, 0.3 to 7.6 episodes per year) (7). In addition, recurrences often cluster in time. Thus, continuous prophylaxis may result in unnecessary antimicrobial use in women who have infrequent recurrences or clustered recurrences. An alternative strategy, namely patient self-diagnosis and self-treatment of recurrent UTIs, may decrease antimicrobial use and improve patient convenience. However, this strategy has been evaluated in only two previous studies, both in relatively small groups of older women referred to specialty clinics for management of recurrent UTI (8, 9). To establish the safety and feasibility of this approach in a larger and more generalized sample, we assessed the accuracy of self-diagnosis and the cure rates seen with self-treatment of UTIs in 172 women who had a history of recurrent infection and were attending a university-based primary care clinic.

METHODS

Study Sample

We studied women at least 18 years of age who were attending a university-based primary care clinic and had had at least two UTIs in the previous 12 months. Women were recruited through advertisements in the campus newspaper and through referrals by primary health care providers. Potentially eligible women were

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screened by the study coordinator and were invited to participate if eligible. At enrollment, all participants were asymptomatic, were not pregnant, were regularly using contraception if sexually active, and were under the care of a primary provider. Women with a known allergy to fluoroquinolones; a full-term pregnancy in the past 12 months; or a history of diabetes, hypertension, or renal disease were excluded.

Study Procedures

Eligible women were briefly interviewed, instructed on how to obtain a clean-catch urine specimen, and given a urine collection kit containing a sterile urine cup and wipes for perineal cleaning to take home. Participants also received six 200-mg ofloxacin tablets to take twice daily for 3 days if UTI symptoms developed. Those who enrolled in the study after levofloxacin, the L-isomer of ofloxacin, became available were instead given three 250-mg levofloxacin tablets to take once daily for 3 days. The women were instructed to self-initiate antimicrobial therapy after collecting a clean-catch urine sample if they developed new symptoms suggestive of a UTI. They were asked to use symptoms experienced with previous UTIs as a guide for self-diagnosis during the study period.

Women were prospectively followed for up to 12 months. The only interactions with study staff occurred during telephone checks performed monthly to review study procedures and during follow-up visits after each UTI self-diagnosis and self-treatment event. Women who developed presumptive symptoms of a UTI collected and refrigerated a clean-catch urine sample and then self-initiated antimicrobial therapy. Participants were asked to deliver the refrigerated urine sample to the study nurse within 24 hours of collection. On days 10 and 30 after initiation of therapy, participants returned to the clinic for follow-up urinalysis and culture and a brief interview. They were also given a new urine collection kit and a refill of medication. Women who self-diagnosed a UTI but whose urine cultures were negative were evaluated for alternative diagnoses with urine testing for chlamydia by ligase chain reaction, a pelvic examination, vaginal wet mount, and repeated urinalysis and culture. If the work-up was nondiagnostic and UTI symptoms resolved after therapy, no further treatment was provided. If the symptoms persisted in the setting of a nondiagnostic work-up, the participant was referred to a primary care provider for further evaluation. Participants whose microbiologically confirmed UTIs did not resolve after 3 days of self-therapy were re-treated on the basis of results of a repeated urinalysis, results of previous microbiological tests, and the discretion of the study nurse, who consulted with study investigators as needed. Data on adverse events were collected by using an open-ended questionnaire after each self-treatment episode. Satisfaction with the study protocol and subjective reductions in symptom days and restricted-activity days were assessed by questionnaire after each self-diagnosis event. Written informed consent was obtained from all participants, and study procedures were approved by the University of Washington Human Subjects Review Committee.

Laboratory Methods

Pyuria was determined by using a hemocytometer counting chamber. Cultures were performed on clean-catch midstream urine specimens. Bacteria were isolated by using standard techniques, as described elsewhere (10). Significant bacteriuria was considered present when uropathogens (*Escherichia coli*, other aerobic gram-negative rods, enterococci, or *Staphylococcus saprophyticus*) were present in quantities of at least 10^2 colony-forming units (CFU)/mL. Group B streptococcus was considered a uropathogen if it was the predominant organism and was present in quantities of at least 10^5 CFU/mL. In vitro susceptibility testing was performed by using the Kirby–Bauer disc method (11). The urine ligase chain reaction for chlamydia was done as described elsewhere (12).

Statistical Analysis

The main outcomes of interest were the accuracy of self-diagnosis and the microbiological and clinical cure rates seen with self-treatment of each UTI event. Symptomatic episodes associated with bacteriuria ($\geq 10^2$ CFU/mL of a uropathogen on a pretreatment urine culture) were defined as definite UTIs, while symptomatic episodes without significant bacteriuria but with pyuria ($\geq$10 leukocytes per high-power field) and no other established diagnosis were defined as probable UTIs.

Definite (culture-positive) episodes of UTI were evaluated for clinical and microbiological cure rates after self-treatment. Clinical failure was defined as persistent symptoms requiring additional therapy. Microbiological

Table 1. **Baseline Characteristics of Study Women (*n* = 172)**

Characteristic	Data
Mean age (range), *y*	23 (18–51)
Unmarried, *n (%)*	147 (85)
Ethnicity, *n (%)*	
White	128 (74)
Black	3 (2)
Asian or Pacific Islander	29 (17)
Other	12 (7)
Education (highest year completed), *n (%)*	
High school graduate	4 (2)
Some college or technical school	116 (67)
College graduate	22 (13)
Graduate school	30 (17)
Number of sexual partners in the past month, *n (%)*	
0 (not sexually active)	9 (5)
1	155 (90)
2	8 (5)
Birth control methods, *n (%)**	
Oral contraceptives	100 (58)
Diaphragm, cervical cap, or foam and condom	16 (9)
Condom only	49 (28)
Other	16 (9)
History of sexually transmitted disease, *n (%)*	35 (20)
Number of lifetime urinary tract infections, *n (%)*†	
2–5	105 (61)
6–10	49 (28)
>10	19 (11)
History of kidney infection, *n (%)*	28 (16)
First urinary tract infection at ≤15 years of age, *n (%)*	31 (18)

* Birth control methods are not mutually exclusive.
† Overall, participants had a median of 4 lifetime urinary tract infections (range, 2 to >100).

failure was defined as isolation, at or before the 10-day follow-up visit, of at least 10^2 CFU of the original uropathogen per mL in symptomatic participants or at least 10^5 CFU of the original uropathogen per mL in asymptomatic participants. Women with both microbiological and clinical cure at 10-day follow-up who had less than 10^5 CFU of the original uropathogen per mL and were asymptomatic at day 30 were defined as having continued microbiological cure. Confidence intervals adjusted for multiple episodes per woman were calculated by using the method of Donner and Donald (13). Comparisons of cure rates between subgroups and of factors associated with accurate diagnosis were performed by using logistic regression analyses with generalized estimating equations to adjust for multiple observations per woman (14).

Role of the Funding Source

The study protocol was initiated and written by the authors. Ortho-McNeil Pharmaceutical funded the study in part and provided the 3-day packets of ofloxacin and levofloxacin but had no role in the design, conduct, analyses, or reporting of the study.

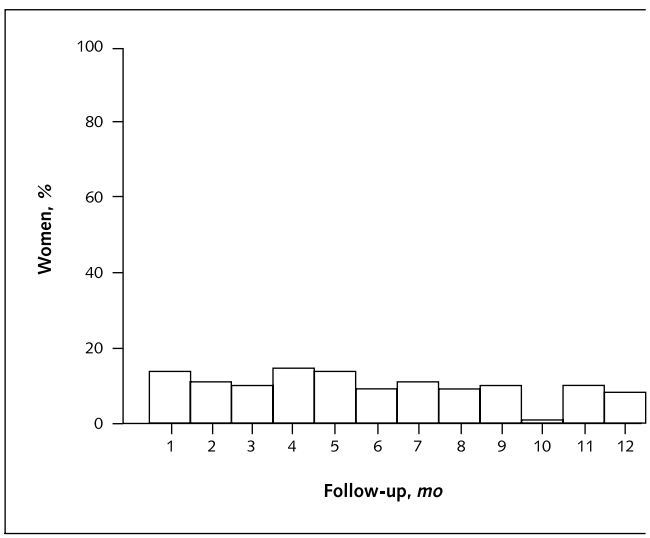
RESULTS

One hundred seventy-two women were enrolled and prospectively followed for 2 to 12 months each, with a mean follow-up period of 242 days (approximately 8 months) per woman and total follow-up of 114 person-years. The demographic characteristics and genitourinary history of the study sample are shown in **Table 1**. The mean age was 23 years, and most women were never married, were white, and were sexually active. Eighteen percent of women had their first UTI before 16 years of age, and 11% had had more than 10 UTIs in their lifetimes. Approximately 20% of women reported a history of one or more sexually transmitted diseases, including trichomoniasis, herpes simplex, genital warts, chlamydial cervicitis, or pelvic inflammatory disease. None reported a history of syphilis or gonorrhea.

Accuracy of Patient Self-Diagnosis

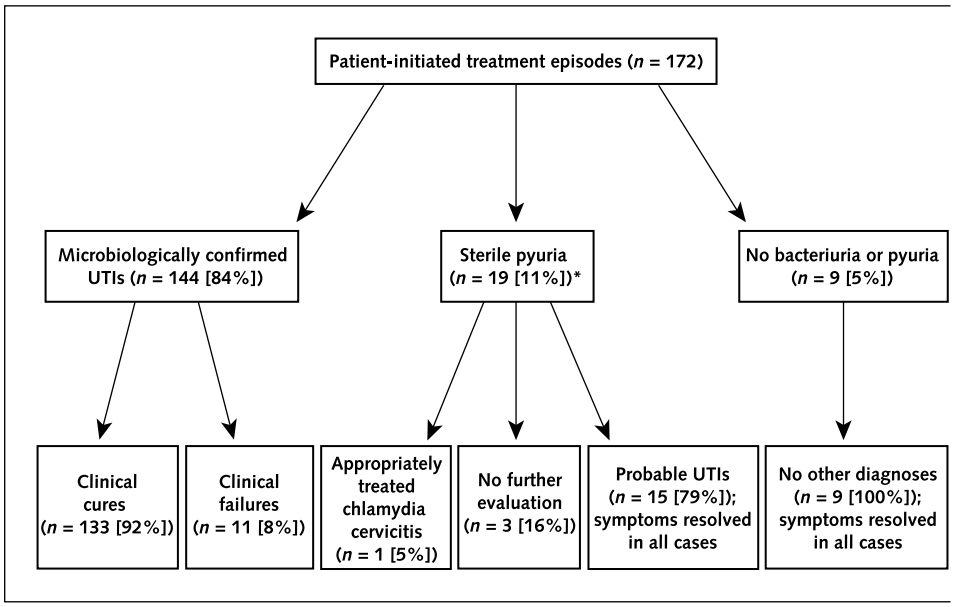
During the study period, 88 of the 172 women (51%) self-diagnosed at least one episode of UTI. These 88 women experienced a total of 172 symptomatic events, with a mean of two episodes per woman. Most

Figure 1. **Proportion of women who initiated treatment for symptoms of urinary tract infections during each month of follow-up.**



Most patient-initiated treatment episodes occurred during the first 6 months of follow-up.

Figure 2. **Diagnostic accuracy and outcomes of 172 patient-initiated treatment episodes of recurrent urinary tract infection (*UTI*).**



* Sterile pyuria was defined as ≥10 leukocytes per high-power field.

symptomatic events occurred in the first 6 months after study enrollment (**Figure 1**). Pretherapy urinalysis and culture performed to confirm these presumed UTI episodes showed a uropathogen in 144 cases (84% [95% CI, 77% to 90%]), sterile pyuria in 19 cases (11% [CI, 6% to 16%]), and no pyuria or bacteriuria in 9 cases (5% [CI, 1% to 10%]) (**Figure 2**). Twenty-five of the 28 culture-negative symptomatic episodes were further evaluated for alternative diagnoses; 3 episodes of sterile pyuria were not evaluated because of protocol error. A positive chlamydia ligase chain reaction was identified in one woman with acute dysuric symptoms and sterile pyuria; she was treated with a 7-day course of doxycycline. None of the remaining 24 evaluable culture-negative episodes had alternative diagnoses confirmed; all responded clinically to self-treatment, and none required further therapy (**Figure 2**). The microbiologically confirmed episodes were considered definite UTIs, and the 15 sterile pyuria episodes without an alternative diagnosis were considered probable UTIs. Therefore, overall, 159 (94% [CI, 90% to 99%]) of the 169 evaluable episodes for which self-diagnosis was initiated seemed to be UTI episodes requiring antimicrobial therapy.

Participants with microbiologically confirmed UTIs did not differ significantly from those with culture-negative symptomatic episodes. Lifetime history of UTI, recent history of UTI, number of new sex partners, history of sexually transmitted diseases, and adherence to study procedures (collecting urine before starting the antimicrobial therapy and delivery time of urine to the laboratory) were similar in the two groups ($P > 0.2$ for each variable). Comparison of culture-positive and culture-negative episodes showed a statistically significant difference in the prevalence of pyuria. Almost all of the 139 evaluated culture-positive episodes (99%) but only 19 of 28 culture-negative episodes (68%) were associated with pyuria (odds ratio, 31.9 [CI, 6.5 to 156.7]; $P < 0.001$).

During the study period, 64 women reported mild genitourinary symptoms that they did not consider indicative of a UTI. These symptoms were reported on 106 routine follow-up interviews and included mild dysuria, urgency, burning, frequency, and "a general UTI feeling." These episodes did not prompt participants to initiate self-therapy or seek the aid of a health care provider, and all resolved spontaneously.

Self-Treatment Outcomes

Clinical cure was observed in 133 of 144 (92% [CI, 89% to 95%]) confirmed UTI episodes (**Figure 2**). Of

the 11 clinical failures that required retreatment, 5 of 10 episodes evaluated with repeated urinalysis were associated with persistent pyuria and 3 of 8 episodes evaluated with repeated urine culture were associated with persistence of at least 10^2 CFU of the original uropathogen per mL. Of interest, in all women with probable UTIs ($n = 15$) or with no pyuria or bacteriuria ($n = 9$), symptoms resolved without further therapy (**Figure 2**). Microbiological cure at day 10 was seen in 126 of 131 (96% [CI, 93% to 99%]) episodes. Continued microbiological cure was demonstrated in 81 (98% [CI, 94% to 100%]) of the 83 episodes evaluated at the 30-day follow-up visit.

Nineteen women reported deviations from the self-treatment protocol, including loss of the study drug ($n = 9$), use of the study drug for a UTI without collecting a pretherapy urine sample ($n = 6$), improper completion of the antimicrobial regimen ($n = 2$), and use of study medications for a nonstudy indication ($n = 2$). Twelve of these 19 women had 16 culture-confirmed self-treatment episodes during the study period. All of these episodes (100%) resulted in clinical and microbiological cure, compared with 91% and 96%, respectively, of the culture-confirmed episodes in women who did not report self-treatment protocol deviations ($P > 0.2$ for comparison of clinical and microbiological cure rates, respectively).

No serious adverse events were related to the study medication or to the treatment protocol. Eleven of the 172 women (6% [CI, 5% to 11%]) required antimicrobial prophylaxis. Eighteen of the 88 women who initiated self-therapy (20% [CI, 13% to 30%]) reported minor side effects that did not require discontinuing use of the study drug. One woman discontinued study participation because of palpitations. Pyelonephritis occurred in one woman who waited 9 days before self-treating UTI symptoms because she was away from her study medication; she was successfully treated as an outpatient with a 14-day course of oral ofloxacin.

Satisfaction with the Management Protocol

Overall, patient satisfaction with the study procedures was high (**Table 2**). Most women indicated that they felt comfortable with the process of self-diagnosis and self-treatment and would feel comfortable using this method for management of subsequent UTIs. Women also felt that they were able to start therapy earlier, had a shorter duration of symptoms, and were able to resume normal activity sooner than with previous episodes of UTI that had been managed traditionally (that is, by consulting a health care provider before starting therapy).

Table 2. **Patient Satisfaction with Self-Diagnosis and Self-Treatment of Recurrent Urinary Tract Infections**

Question	Episodes for Which Women Answered Affirmatively, *n (%)**
Did you feel comfortable with the process of self-diagnosis and self-treatment for this urinary tract infection?	148 (94)
Do you feel that self-diagnosis and self-therapy allowed you to start medication earlier than if you had seen a health care provider before starting therapy?	158 (100)
Do you feel that this approach shortened the length of time of your symptoms?	151 (96)
Do you feel that this approach allowed you to resume normal activity sooner than with previous urinary tract infections?	153 (97)
Would you feel comfortable using this process to manage your recurrent urinary tract infections in the future?	157 (99)
Would you recommend this approach to a friend with a similar problem?	156 (99)

* 84 women at follow-up visits for treatment of 158 urinary tract infections.

Discussion

Despite advances in our understanding of the pathogenesis and epidemiology of UTIs, these infections remain a significant cause of morbidity and health care utilization, particularly among otherwise healthy adult women who have recurrent infections. Foxman and Frerichs (15) demonstrated that each episode of UTI results in an average of 6 symptomatic days and 2 restricted-activity days, as well as time lost from work. Repeated infections therefore produce considerable morbidity and costs.

Our study provides strong evidence to support the safety and feasibility of a management strategy that can simplify the care of women with recurrent UTIs. This strategy depends on the ability of women who have had previous UTIs to accurately self-diagnose a recurrent episode. Approximately 94% of 172 suspected UTIs met criteria for definite or probable UTI. These findings are similar to those of a smaller study conducted in a highly selected sample of women with recurrent UTIs who were attending a special UTI referral clinic. In that study, 92% of 35 suspected UTI episodes were microbiologically confirmed (8). In a recent study of 34 older

women with recurrent UTI who were attending a urology clinic, 86% of suspected UTI episodes were culture-confirmed by using a dipslide method (9). It should be noted that the results seen in our patients, who were mostly university students, may not be generalizable to all young women with recurrent UTIs. However, in previous UTI studies, cause, risk factors, and response to therapy were very similar in both university women and women in a health maintenance organization (16). Therefore, our results would probably be similar in other groups of young, sexually active, adherent women in a primary care setting.

We chose to study this group of women because they have a high incidence of recurrent UTIs and because the close proximity of the students to the primary care center made it possible to obtain and process pretherapy urine specimens in a timely fashion. In practice, a urine culture would not be necessary because patients eligible for this management strategy would usually be treated empirically. We do not advocate use of patient-initiated therapy in women who would not be considered candidates for empirical therapy because of a high risk for sexually transmitted diseases, other comorbid conditions, or pregnancy.

It is important to note that few significant adverse events were specifically related to the management protocol. One case of pyelonephritis occurred and was managed successfully on an outpatient basis with oral therapy. Given that the average rate of pyelonephritis among women with recurrent UTI is 0.1 episode per patient-year, this occurrence was perhaps not unexpected (7). One patient who self-diagnosed a UTI was found instead to have sterile pyuria and a chlamydial infection. While it is possible that the acute symptomatic event was in fact a UTI and that the chlamydial infection was long-standing, the absence of a positive urine culture, the presence of pyuria, and a urine ligase chain reaction assay positive for chlamydia make it likely that acute *Chlamydia trachomatis* infection caused the symptomatic episode (17). Since sexual activity is a risk factor for both recurrent UTIs and sexually transmitted diseases, patients with recurrent UTIs are also at risk for sexually transmitted diseases. Therefore, before a self-diagnosis and self-treatment management protocol are implemented, counseling about use of barrier contraception with new sexual partners and chlamydia screening in high-prevalence populations would be warranted.

Twenty-five women evaluated in the current study (and 3 others who were not evaluated) had UTI symptoms and negative urine cultures. Studies for alternative diagnoses that might mimic UTI (18) were done, but a treatable infection other than UTI was diagnosed in only 1 of 25 self-treatment episodes. Of interest, 19 women had symptomatic episodes associated with pyuria but not bacteriuria. Recognized causes of the "sterile pyuria–dysuria" syndrome include *C. trachomatis*, *Neisseria gonorrhoeae*, and *Ureaplasma urealyticum* (18, 19).

As noted, one case in the present study was caused by *C. trachomatis*. We did not test for *N. gonorrhoeae* or *U. urealyticum*, but extensive previous studies have shown that *N. gonorrhoeae* infection is very rare (<1 case per 1000 women) in this patient population (18). *Ureaplasma urealyticum* could have caused some of these cases, since they responded to ofloxacin. Some of these episodes may also have been bacterial UTIs with fastidious bacteria and false-negative cultures. Finally, other infectious agents may account for some of the remaining cases that were associated with pyuria and responded to antimicrobial therapy. Further studies to identify novel pathogens in this group would be of interest.

Clinical and microbiological cure rates were high after self-treatment with ofloxacin or levofloxacin, consistent with those seen in previous studies of provider-initiated 3-day fluoroquinolone therapy (20, 21). An equivalence study comparing cure rates seen with patient-initiated therapy and rates seen with provider-initiated therapy would be ideal, although the latter approach has been extensively studied and recently reviewed (22). Cure rates seen in practice may be lower than those we observed, given that women with very frequent recurrences dropped out of the current study to initiate prophylaxis and that we studied a highly motivated and adherent group of women. It is reassuring to note that cure rates in women who reported a protocol deviation did not differ significantly from those in women who adhered to self-treatment procedures. This strategy is not recommended for women with very frequent recurrences or in settings where adherence is a concern.

Only 6% of the women studied ultimately required antimicrobial prophylaxis for management of recurrent infections. This greatly reduced the overall antibiotic usage that would have occurred if prophylaxis had been routinely prescribed to all study women. Of importance,

84 of the 172 women did not have a recurrent infection during the study and thus did not require any antibiotic. These data emphasize the unpredictable nature of recurrent UTIs in women. Finally, the women used the study drugs responsibly, only infrequently using them for other purposes or for nontreatable infectious episodes. Patient initiation of antibiotics has generally been cautioned against as a potential contributor to the development of antibiotic resistance. However, it is important to emphasize that although our approach used patient-initiated therapy, access to antimicrobial agents was still controlled by the practitioner, and both the patient group and the indications for therapy were highly specific. At the initiation of self-therapy, patients were instructed about the indications for antimicrobial use and were cautioned against using the drugs for other purposes or for other persons.

Almost all of the participants preferred this method of management to the traditional practice of seeing a health care provider for diagnosis and treatment. Although symptom duration was not formally quantified, most patients reported feeling that the duration was reduced and that they were able to resume normal activity sooner than with previous, traditionally managed UTIs. In addition, studies have shown that patients are more likely to be satisfied with their health care when their physicians or other health care professionals have spent time discussing one or more health education topics with them (23). Therefore, the time spent educating and counseling patients in preparation for self-diagnosis and therapy of recurrent UTIs may lead to improved patient–provider communication and relationships.

In conclusion, a strategy in which a health care professional provided a prescription for self-diagnosis and self-treatment of UTIs in young women with a recent history of uncomplicated UTIs seemed safe and feasible, reducing the need for repeated office visits and for antimicrobial prophylaxis. We emphasize that this approach should be used only in adherent women with uncomplicated UTIs, not for UTIs associated with complicating conditions or for cases in which the diagnosis is in doubt.

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