

Validation of a Decision Aid to Assist Physicians in Reducing Unnecessary Antibiotic Drug Use for Acute Cystitis

Warren J. McIsaac, MD, MSc; Rahim Moineddin, PhD; Sue Ross, PhD

Background: In a previous study, use of a decision aid based on 4 clinical items would have reduced unnecessary antibiotic prescriptions for acute cystitis by 30% compared with usual physician care.

Methods: We assessed the decision aid in a different population of females seen in community-based practice. Between April 7, 2002, and March 20, 2003, 225 Canadian family physicians recorded clinical findings, urine dip test results, and treatment decisions for 331 females with suspected cystitis. The number of decision aid items present was determined for each patient, and the sensitivity and specificity of decision aid recommendations for empirical antibiotics were determined using the gold standard of a positive urine culture result ($\geq 10^2$ colony-forming units per milliliter). Total antibiotic prescriptions, unnecessary prescriptions (for negative culture results), and recommendations for urine cultures were determined and compared with physician management.

Results: Three of the original decision aid variables (dys-

uria, the presence of leukocytes [greater than a trace amount], and the presence of nitrites [any positive]) were associated with having a positive urine culture result ($P \leq .001$), but 1 variable (symptoms for 1 day) was not ($P = .96$). A simplified decision aid incorporating the 3 significant variables (empirical antibiotics without culture if ≥ 2 variables present; otherwise obtain a culture and wait for results) had a sensitivity of 80.3% (167/208) and a specificity of 53.7% (66/123). Following decision aid recommendations would have reduced antibiotic prescriptions by 23.5%, unnecessary prescriptions by 40.2%, and urine cultures by 59.0% compared with physician care ($P < .001$ for all).

Conclusion: A simple 3-item decision aid could significantly reduce unnecessary antibiotic drug prescriptions and urine culture testing in females with symptoms of acute cystitis.

Arch Intern Med. 2007;167(20):2201-2206

EXPERT RECOMMENDATIONS for the treatment of women with symptoms of acute cystitis advise empirical antibiotic drug treatment without obtaining a urine culture.¹⁻³ However, empirical treatment may result in up to 40% of women with urinary symptoms receiving antibiotics unnecessarily for nega-

See also page 2207

tive urine culture results.⁴ In a previous study,⁴ use of a clinical decision aid developed to assist in decisions about antibiotic drug therapy for cystitis would have reduced unnecessary prescriptions by 30% compared with usual care. Other algorithms and decision aids have also been proposed for the management of acute cystitis,^{3,5-9} but none have been prospectively evaluated for their effect on antibiotic use.

Standards for decision rules recommend validation in different patient populations before use in routine clinical care.^{10,11} Rules derived in one population may not perform as well in different populations owing to chance associations between predictors and outcomes in developing the rule or predictors that are idiosyncratic either to the original population or to physicians using the rule. A different prevalence of the target condition can also affect the performance of prediction rules.^{12,13}

 CME available online at www.archinternmed.com

The cystitis decision aid is a simple rule for use by primary care physicians when deciding whether to prescribe antibiotics or order a urine culture for adult women with symptoms suggestive of acute cystitis.⁴ Empirical antibiotic drug treatment is advised for women identified by the decision aid as having a high probability of

Author Affiliations: Ray D. Wolfe Department of Family Medicine, Mount Sinai Hospital (Dr McIsaac), and Department of Family and Community Medicine, University of Toronto School of Medicine (Drs McIsaac and Moineddin), Toronto, Ontario, Canada; and Departments of Family Medicine and Community Health Sciences, Foothills Medical Centre, and Department of Obstetrics and Gynaecology, University of Calgary School of Medicine, Calgary, Alberta, Canada (Dr Ross).

infection. For women with a low probability of infection, a urine culture is recommended before deciding about antibiotic treatment. The purpose of this study was to assess the validity of the cystitis decision aid in a population of adult women with symptoms of cystitis seen in community-based practice. In addition, the study sought to determine whether they would be willing to wait for urine culture results before being prescribed antibiotics.

METHODS

The cystitis decision aid was developed in clinics affiliated with the Department of Family and Community Medicine of the University of Toronto.⁴ The aid incorporates 4 criteria: the presence of burning or pain on urination, symptoms present for 1 day (vs >1 day), the presence of leukocytes (greater than a trace amount), and the presence of nitrites (any positive, including trace amounts). In the previous study,⁴ when 2 or more criteria were present, the probability of a positive culture result was greater than 70%. Empirical antibiotic drug treatment without culture was recommended owing to the high likelihood of infection, as suggested by other researchers.^{2,5} For females with fewer than 2 criteria, the probability of infection was less than 30%, and a urine culture was recommended before deciding about the need for antibiotics.⁴

In April 2002, a random sample of 2000 community-based members of the College of Family Physicians of Canada engaged in full-time clinical practice were contacted, and 418 (20.9%) agreed to participate. Physicians were asked to assess 2 females 16 years or older with new urinary symptoms when acute cystitis was suspected. No further inclusion criteria were specified to encourage physicians to include a broad range of cystitis cases seen in clinical practice. A checklist prompted physicians to exclude children younger than 16 years, men, pregnant women, nursing home residents, immunocompromised patients, and those taking antibiotics or with renal tract abnormalities, indwelling catheters, or the inability to understand English. Physicians recorded the patient's age, number of days with symptoms before the visit, history of previous cystitis episodes, current symptoms, physical findings, their diagnosis, and whether antibiotic agents were prescribed. The clinical items composing the decision aid were not specifically identified for physicians but were included as part of a larger clinical checklist. Urine dipsticks (Uristix 5; Bayer Inc, Toronto, Ontario, Canada) were provided to test for the presence of leukocytes and nitrites. A urine sample was requested and was sent for culture to the usual clinical laboratory that the physician used. Because a urine culture was obtained for all patients, physicians were asked if they would have normally ordered a urine culture in each instance. Urine cultures were paid for by the study, and physicians received a small honorarium.

After treatment recommendations were discussed, patients were asked to allow a copy of the culture report to be sent to the study center and to answer 2 questions. Consenting patients were asked to rate the severity of their symptoms (mild, moderate, severe, or no symptoms currently) and whether they would have been willing to wait for the urine culture report before their physician decided about the need for antibiotics (definitely not willing to wait, probably not, probably would, definitely would, or would prefer to wait for results). A colony count of 10^2 colony-forming units per milliliter or higher of a uropathogen was considered a positive culture result in these females with urinary symptoms.²

The primary outcome was the sensitivity of the decision aid, determined as the proportion of patients with a positive urine culture result recommended empirical antibiotics. Specificity

was calculated as the proportion of patients with a negative urine culture result not recommended empirical antibiotics. The positive predictive value of 2 or more criteria (start empirical antibiotics) was also determined. The sensitivities, specificities, and positive predictive values in the present study population were compared with estimates from the previous study⁴ to assess the reliability of the decision aid in different populations. Other outcomes assessed were the proportion of patients prescribed antibiotics by physicians compared with decision aid recommendations and the proportions of unnecessary antibiotic prescriptions and urine culture testing. For the present study, unnecessary antibiotic prescriptions were defined as prescribing an antibiotic empirically where the subsequent urine culture result was negative.

The sample size was calculated to estimate the primary outcome of the sensitivity of the decision aid with a precision of $\pm 10\%$. In the previous study,⁴ the sensitivity was estimated to be 81%. Using an estimated intraclass correlation coefficient for prescribing of 0.22,¹⁴ 158 positive urine culture results were needed, taking into account the clustering of patients by physician.¹⁵ A baseline prevalence of positive urine culture results of 50% was assumed,⁷ for a final sample size of 320 patients. Because more than half of the physicians provided data for only 1 patient, adjustments for clustering had no effect on the significance of any results. Only the unadjusted analysis is presented.

Clinical forms were matched to culture reports and double entered. Analysis was conducted using a statistical software program (Stata release 6.0; StataCorp, College Station, Texas). Frequencies or means were used to describe patient characteristics, symptoms, urine dipstick results, and willingness to wait for antibiotics. The χ^2 and Fisher exact tests were used to compare categorical variables. Exact binomial confidence intervals (CIs) were determined for estimates of main outcomes. The study was approved by the Research Ethics Board of Mount Sinai Hospital.

RESULTS

A total of 225 of 418 physicians (53.8%) completed the study between April 7, 2002, and March 20, 2003, and assessed 422 females. Although every province in Canada was represented, 244 of 422 patients (57.8%) were from Ontario. Culture results were available for 357 patients (84.6%). The number of females with complete information for all 4 clinical items in the decision aid and culture results was 331 (78.4%).

The mean age of patients was 45.2 years (range, 16-99 years), and most had experienced 2 or more urinary tract infections previously (**Table 1**). Most patients presented to their family physician within the first 3 days of the onset of symptoms (211/331, 63.8%). At least 1 of the symptoms of frequency, urgency, and burning or painful urination was reported by almost all the patients (320/327, 97.9%). The prevalence of positive urine culture results was 62.8%.

ASSESSMENT OF CYSTITIS DECISION AID VALIDITY

The number of decision aid criteria⁴ (symptoms for 1 day, dysuria, leukocytes greater than trace, and any nitrites) present was determined for each patient. **Table 2** indicates a graded relationship between the number of criteria present and the proportion of positive urine cul-

Table 1. Characteristics of Patients Presenting to Community-Based Family Physicians With Symptoms of Cystitis and Association With a Positive Urine Culture Result

Characteristic	Patients, No./Total No. (%)		P Value
	Proportion of Sample ^a	Positive Urine Culture Result if Finding Present	
Urine culture	331/331 (100)	208 (62.8)	
Age, y			
16-49	204/331 (61.6)	126 (61.8)	.61
≥50	127/331 (38.4)	82 (64.6)	
≥2 Previous UTIs	207/321 (64.5)	125 (60.4)	.15
Duration of symptoms, d			
1	92/331 (27.8)	58 (63.0)	.96
≥2	239/331 (72.2)	150 (62.8)	
Symptoms			
Frequent urination	304/330 (92.1)	194 (63.8)	.16
Urgency	273/328 (83.2)	182 (66.7)	.001
Burning/painful voiding	262/331 (79.2)	176 (67.2)	.001
Voiding small amounts	244/327 (74.6)	165 (67.6)	.002
Suprapubic pain/pressure	216/327 (66.1)	134 (62.0)	.86
Flank pain/discomfort	83/327 (25.4)	43 (51.8)	.02
Vaginal discharge	35/324 (10.8)	19 (54.3)	.30
Reports fever (temperature >37.6°C)	13/324 (4.0)	8 (61.5)	.93
Signs			
Suprapubic tenderness	143/316 (45.3)	89 (62.2)	.97
CVA tenderness	37/314 (11.8)	18 (48.7)	.06
Vaginal discharge on examination ^b	10/89 (11.2)	5 (50.0)	.74
Urine dip test			
Presence of leukocytes (greater than trace)	243/331 (73.4)	175 (72.0)	<.001
Presence of nitrites (any)	88/331 (26.6)	75 (85.2)	<.001

Abbreviations: CVA, costovertebral angle; UTI, urinary tract infection.

^aMissing data resulted in denominators for some items being less than 331.

^bIn 231 of 320 encounters (72.2%), physicians reported that a vaginal examination was not warranted.

ture results. For women with no criteria or 1 criterion, corresponding to a decision aid recommendation to wait for culture results before deciding about antibiotic drug use, the proportion of positive urine culture results was 37.0% (34/92) and the negative predictive value was 63.0% (58/92). For patients with 2 or more criteria (decision aid recommendation for empirical antibiotic treatment), the rate of positive urine culture results (positive predictive value) was 72.8% (174/239) ($P < .001$).

The sensitivity of a recommendation for empirical antibiotics with 2 or more criteria in relation to a positive urine culture result was 83.7% (95% CI, 77.9%-88.4%; 174/208). There was no difference in sensitivity compared with the previous study (81.3%, 87/107; $P = .60$).⁴ The specificity of a recommendation to not prescribe antibiotics for patients with no criteria or 1 criterion was 47.2% (95% CI, 38.1%-56.4%; 58/123) with a negative culture result. This estimate was lower than the specificity estimate from the previous study (64.5%, 60/93; $P = .01$).⁴

One of the predictor variables (symptoms for 1 day) was not associated with a positive urine culture result (Table 1). In the present study, 63.0% of patients with 1 day of symptoms had a positive urine culture result compared with 62.8% of patients with symptoms for more than 1 day ($P = .96$). In the previous study,⁴ 28 of 36 patients (77.8%) with 1 day of symptoms had a positive urine culture result compared with 79 of 164

patients (48.2%) with more than 1 day of symptoms ($P = .001$). Because this predictor variable was not reliably related to the outcome of a positive urine culture result, a 3-item version of the decision aid without this criterion was evaluated.

REVISED 3-ITEM CYSTITIS DECISION AID

The remaining 3 variables (burning or discomfort with urination, the presence of leukocytes [greater than a trace amount], and the presence of any nitrites) all demonstrated significant associations with a positive urine culture result (Table 1). Similar to the original 4-item decision aid, there was a graded relationship between the number of decision aid criteria and the outcome of a positive urine culture result ($P < .001$). The rate of positive urine culture results was 23.1% (6/26) with 0 criteria, 43.2% (35/81) with 1 criterion, 68.8% (110/160) with 2 criteria, and 89.1% (57/64) with 3 criteria.

To assess the reliability of this revised 3-item decision aid, the population in the previous study was used and the number of items present was determined for each patient.⁴ The sensitivity and proportion of positive culture results for a recommendation for empirical antibiotics for patients with 2 or more items and the specificity of a recommendation to wait for culture results with 1 or fewer items were determined in each population and compared (Table 3).

There was no difference in the sensitivity of a 3-item decision aid recommendation for empirical antibiotics to women with 2 or more criteria in the present study population (80.3%) compared with women in the previous study⁴ (78.8%; $P = .75$). Similarly, the positive predictive value of treating when 2 or more criteria were present was not different in the 2 populations of patients (74.6% vs 74.4%, respectively; $P = .98$). The specificity of the 3-item decision aid was also somewhat lower in the present study (53.7%) than in the original study (68.9%; $P = .02$).

COMPARISON WITH USUAL PHYSICIAN CARE

Compared with observed physician care in the present study, following the 3-item decision aid recommendations would have reduced overall antibiotic prescriptions by 23.5% and unnecessary prescriptions by 40.2% (**Table 4**). Urine culture testing would have been reduced by 59.0%. However, more patients not willing to wait for antibiotics or with severe symptoms would have received empirical antibiotics with usual physician care than with decision aid recommendations ($P < .001$).

There were 140 of 319 patients (43.9%) who reported that they definitely would not have been willing to wait for urine culture results before being prescribed antibiotics. These patients were more likely to report se-

vere symptoms (51/140, 36.4%) than other women (24/179, 13.4%; $P < .001$). Overall, the decision aid would have recommended that 36 of 319 patients (11.3%) who would not have been willing to wait for culture results do so. However, only 9 of 36 patients (25.0%) had a positive urine culture result.

COMPARISON WITH DECISIONS BASED ON SYMPTOMS ALONE

Because it has been suggested that the presence of 2 symptoms can be used to diagnose cystitis and guide empirical treatment,⁵ we assessed the effect of this approach on antibiotic drug use. Using the symptoms of dysuria, frequency, and urgency (empirical treatment if ≥ 2 symptoms) would result in 294 of 327 patients (89.9%) being prescribed antibiotics, and 100 of 327 (30.6%) would receive an unnecessary antibiotic prescription because the subsequent urine culture result would be negative. These estimates were similar to those for observed physician care in the present study ($P = .56$ for total antibiotic prescriptions) (Table 3). The specificity of a symptom-only approach was low (23/123, 18.7%).

Table 2. Rate of Positive Urine Culture Results by Number of Decision Aid Criteria in 331 Patients With Suspected Acute Cystitis

No. of Criteria ^a	Urine Culture Results, No. (%)		Total
	Negative	Positive	
0	16 (76.2)	5 (23.8)	21
1	42 (59.2)	29 (40.9)	71
2	38 (31.9)	81 (68.1)	119
3	25 (24.0)	79 (76.0)	104
4	2 (12.5)	14 (87.5)	16
Total	123 (37.2)	208 (62.8)	331

^aSymptoms present for only 1 day, burning or discomfort with urination, urine dip test positive for leukocytes (greater than trace), and urine dip test positive for nitrites (any).

Table 3. Reproducibility of a 3-Item Cystitis Decision Aid in 2 Cohorts of Patients With Symptoms Suggesting Acute Cystitis

	Positive Urine Culture Results, No./Total No. (% [95% CI])	
	Present Study	Previous Study ^d
No. of criteria ^a		
0 or 1	41/107 (38.3 [29.1-48.2])	25/96 (26.0 [17.6-36.0])
≥ 2	167/224 (74.6 [68.3-80.1])	93/125 (74.4 [65.8-81.8])
Sensitivity ^b	167/208 (80.3 [74.2-85.5])	93/118 (78.8 [70.3-85.6])
Negative urine culture results		
Specificity ^b	66/123 (53.7 [44.4-62.7])	71/103 (68.9 [59.1-77.7])

Abbreviation: CI, confidence interval.

^aBurning or pain on urination, the presence of leukocytes greater than trace, and the presence of any nitrites.

^bSensitivity and specificity of the decision to prescribe antibiotic agents empirically if 2 or more criteria are present.

Table 4. Comparison of Observed Physician Management and Cystitis Decision Aid Recommendations Regarding Antibiotic Use, Urine Culture Testing, and Proportion of Patients Not Willing to Wait for Culture Results Receiving Empirical Antibiotics

	Patients, No./Total No. (%)		
	Observed Care by Family Physicians	3-Item Cystitis Decision Aid	Relative Difference, %
Antibiotics prescribed	292/330 (88.5) ^a	224/331 (67.7) ^b	-23.5
Unnecessary antibiotics ^c	95/330 (28.8)	57/331 (17.2) ^b	-40.2
Urine cultures	259/329 (78.7)	107/331 (32.3) ^b	-59.0
Not willing to wait for culture results and recommended empirical antibiotics	136/140 (97.1)	104/140 (74.3) ^b	-23.5
Severe symptoms and recommended empirical antibiotics	73/75 (97.3)	57/75 (76.0) ^b	-21.9

^aComplete physician prescribing information for 330 of 331 patients.

^b $P < .001$.

^cAntibiotic prescription to patients with negative urine culture results.

This study found that the use of a cystitis decision aid in the management of suspected acute cystitis in females could significantly reduce overall antibiotic drug use, unnecessary antibiotic prescriptions, and urine culture testing compared with usual physician care. These results were similar in 2 populations of females from different primary care settings, suggesting that the decision aid is sufficiently reliable for use in routine clinical care.

The volume of antibiotic agents prescribed and urine culture testing associated with the management of acute cystitis in the community is substantial. Half of all females experience at least 1 episode of acute cystitis in their lifetime.¹ In the United States, there are approximately 4 million outpatient visits annually by females for uncomplicated urinary tract infections.¹⁶ An antibiotic agent is prescribed in 67% of visits, and a urinalysis is ordered in 81%,¹⁶ with wide variations in physician management.^{17,18} As many as 40% of antibiotics prescribed may be unnecessary because the subsequent urine culture result is negative.⁴ The cystitis decision aid is a simple clinical approach that could reduce practice variation as well as unnecessary antibiotic prescriptions and urine culture testing. In this community-based study of females with typical symptoms of acute cystitis, following decision aid recommendations would have reduced unnecessary antibiotic prescriptions by 40.2% and urine culture testing by 59.0% compared with observed physician care.

In a previous study,⁴ a 4-item decision aid was proposed. However, 1 of the predictor variables, symptoms present for 1 day, was not related to a positive culture result in the present study. Standards for clinical decision rules include demonstration of the reproducibility of predictor variables in the rule.^{10,11} As a result, the original decision aid could not be considered sufficiently reliable for clinical use. Omitting this variable resulted in a simplified and more reliable decision aid. The sensitivity and positive predictive value of the revised 3-item decision aid as well as the reduction in total antibiotic drug prescriptions, unnecessary antibiotic use, and urine culture results compared with usual physician care were similar in 2 different populations of females. Thus, this study suggests that the effect of the 3-item cystitis decision aid on antibiotic use and urine culture testing is reproducible in different clinical settings.

The sensitivity of the decision aid was less than that of usual physician care when measured by empirical prescriptions at the time of the office visit. However, patients not initially prescribed antibiotics are recommended to undergo urine culture testing. As a result, all infections are treated and identified. One problem may be that some women are advised to wait for culture results before receiving antibiotics. In this study, three-quarters of patients reporting that they definitely would not be willing to wait for culture results would have received empirical antibiotic treatment under decision aid recommendations. Only 11% of all patients with symptoms of cystitis would be advised to wait and not be willing to do so. However, the rate of positive culture re-

sults in these females was only 25%. Although physicians prescribed antibiotics to 89% of patients, they also waited for culture results in 11% of cases. Thus, decision aid recommendations to wait for culture results are consistent with current clinical practices and are likely acceptable to most women.

Other decision aids and treatment algorithms have been proposed for the management of acute cystitis.^{3,5-9} Only 2 have been assessed in independent populations.^{3,7} Neither was assessed for its effect on unnecessary antibiotic prescriptions or acceptability to women. Relying on symptoms alone to guide empirical prescribing decisions has also been suggested.⁵ This latter approach was associated with a high rate of unnecessary antibiotic use in the present study. In the context of increasing uropathogen antibiotic resistance¹⁹ and lack of clinical agreement about how to manage acute cystitis,^{17,18} practical and validated strategies that can help physicians use antibiotics judiciously could be clinically useful.

In this study, only 54% of physicians recruited completed the study. However, it is unlikely that the cases of cystitis seen by physicians in the study were significantly different from those seen by other physicians in the community. The symptoms reported by patients in the study suggest that these were typical cases of cystitis. Another issue could be defining prescriptions given to patients with negative urine culture results as unnecessary. However, there is no consensus that prescribing antibiotics to patients with symptoms of cystitis but negative urine culture results is appropriate. We also used only 1 brand of urine test strips in developing and validating the decision aid. Use of a different urine test strip could affect the performance of the decision aid. Although the decision aid performed similarly in 2 populations regarding sensitivity and effect on antibiotic use, its specificity was lower in the present study. As a result, further studies in other populations with acute cystitis may be prudent. Finally, this study did not demonstrate that the decision aid reduced antibiotic use but rather that antibiotic use could be reduced if its recommendations were followed. Although some have suggested that this argument is largely academic because physicians fail to follow any guideline,²⁰ use of an actively disseminated treatment algorithm reduced antibiotic drug use in suspected cystitis in a nursing home population.²¹

Guidelines for the treatment of acute cystitis in females recommend empirical antibiotic treatment without urine culture testing when patients have typical cystitis symptoms.¹⁻³ This may, however, result in high levels of unnecessary antibiotic use.⁴ This study confirmed that a 3-item cystitis decision aid is a practical and reliable method to assist physicians in reducing unnecessary antibiotic prescriptions and urine culture testing in acute cystitis.

Accepted for Publication: June 14, 2007.

Correspondence: Warren J. McIsaac, MD, MSc, Granovsky-Gluskin Family Medicine Centre, 60 Murray St, Fourth Floor, Toronto, ON M5T 3L9, Canada (wmcisaac@mtsina.on.ca).

Author Contributions: Dr McIsaac had full access to all of the data in the study and takes responsibility for the

integrity of the data and the accuracy of the data analysis. *Study concept and design*: McIsaac and Ross. *Acquisition of data*: McIsaac and Moineddin. *Analysis and interpretation of data*: McIsaac, Moineddin, and Ross. *Drafting of the manuscript*: McIsaac, Moineddin, and Ross. *Critical revision of the manuscript for important intellectual content*: McIsaac, Moineddin, and Ross. *Statistical analysis*: Moineddin. *Obtained funding*: McIsaac and Ross. *Administrative, technical, and material support*: McIsaac and Ross. *Study supervision*: McIsaac.

Financial Disclosure: None reported.

Funding/Support: This study was funded by grant MOP-53290 from the Canadian Institutes for Health Research.

Role of the Sponsor: The funding agency did not have any role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

Additional Contributions: Janet Raboud, PhD, provided helpful comments and suggestions and Joanne Permaul, BSc (Hons), provided logistical support for the study and supervision of data entry.

REFERENCES

1. Fihn SD. Acute uncomplicated urinary tract infection in women. *N Engl J Med*. 2003;349(3):259-266.
2. Warren JW, Abrutyn E, Hebel R, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clin Infect Dis*. 1999;29(4):745-758.
3. Saint S, Scholes D, Fihn SD, Farrell RG, Stamm WE. The effectiveness of a clinical practice guideline for the management of presumed uncomplicated urinary tract infection in women. *Am J Med*. 1999;106(6):636-641.
4. McIsaac WJ, Low DE, Biringer A, Pimlott N, Evans M, Glazier R. The impact of empirical management of acute cystitis on unnecessary antibiotic use. *Arch Intern Med*. 2002;162(5):600-605.
5. Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. The rational clinical examination: does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002;287(20):2701-2710.
6. Rothberg MB, Wong JB. All dysuria is local: a cost-effectiveness model for de-signing site-specific management algorithms. *J Gen Intern Med*. 2004;19(5, pt 1):433-443.
7. Wigton RS, Hoellerich VL, Ornato JP, Leu V, Mazzotta LA, Cheng IHC. Use of clinical findings in the diagnosis of urinary tract infection in women. *Arch Intern Med*. 1985;145(12):2222-2227.
8. Dobbs FF, Fleming DM. A simple scoring system for evaluating symptoms, history and urine dipstick testing in the diagnosis of urinary tract infection. *J R Coll Gen Pract*. 1987;37(296):100-104.
9. Komaroff AL, Pass TM, McCue JD, Cohen AB, Hendricks TM, Friedland G. Management strategies for urinary and vaginal infections. *Arch Intern Med*. 1978;138(7):1069-1073.
10. McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS. Users' guides to the medical literature, XXII: how to use articles about clinical decision rules. *JAMA*. 2000;284(1):79-84.
11. Laupacis A, Sekar N, Stiell IG. Clinical prediction rules: a review and suggested modifications of methodological standards. *JAMA*. 1997;277(6):488-494.
12. Poses RM, Cebul RD, Collins M, Fager SS. The importance of disease prevalence in transporting clinical prediction rules: the case of streptococcal pharyngitis. *Ann Intern Med*. 1986;105(4):586-591.
13. Morise AP, Diamond GA, Detrano R, Bobbio M, Gunel E. The effect of disease-prevalence adjustments on the accuracy of a logistic prediction model. *Med Decis Making*. 1996;16(2):133-142.
14. McIsaac WJ, To T. Antibiotics for lower respiratory tract infections: still too frequently prescribed? *Can Fam Physician*. 2004;50:569-575.
15. Diggle PJ, Liang K-Y, Zeger S. *Analysis of Longitudinal Data*. Oxford, England: Clarendon Press; 1994.
16. Huang ES, Stafford RS. National patterns in the treatment of urinary tract infections in women by ambulatory care physicians. *Arch Intern Med*. 2002;162(1):41-47.
17. Wigton RS, Longenecker JC, Bryan TJ, Parenti C, Flach SD, Tape TG. Variation by specialty in the treatment of urinary tract infection in women. *J Gen Intern Med*. 1999;14(8):491-494.
18. Olesen F, Oestergaard I. Patients with urinary tract infection: proposed management strategies of general practitioners, microbiologists and urologists. *Br J Gen Pract*. 1995;45(400):611-613.
19. Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. *JAMA*. 1999;281(8):736-738.
20. Linder JA, Chan JC, Bates DW. Evaluation and treatment of pharyngitis in primary care practice: the difference between guidelines is largely academic. *Arch Intern Med*. 2006;166(13):1374-1379.
21. Loeb M, Brazil K, Lohfeld L, et al. Effect of a multi-faceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomized controlled trial. *BMJ*. 2005;331(7518):669-674.