Management of urinary tract infections in female general practice patients

Eva Hummers-Pradier, Ann Marit Ohse, Matthias Koch, Wolfgang R Heizmann and Michael M Koch


**Background.** Though guidelines for the management of urinary tract infections (UTI) exist in several European countries, little is known about GPs’ adherence, and the appropriateness of their management with regard to antibiotic resistance.

**Objectives.** To describe German GPs’ management of female patients with symptoms of UTI, to assess the diagnostic accuracy of dipsticks in a German general practice setting, to develop diagnostic prediction rules for culture-confirmed UTI, and to compare the adequacy of empirical treatment strategies and GPs’ actual prescriptions.

**Methods.** In 36 (of 118 invited) teaching general practices, urine cultures and resistance testing were performed during 4 months on all symptomatic patients. GPs completed a questionnaire on each patients’ symptoms, risk factors and treatment. Adequacy of different treatment approaches was calculated based on culture results.

**Results.** 445 adult women (76% of all patients) were included, with a median age of 53 years. Complicating factors were present in 27%. Urine culture revealed UTI in 77%. GPs’ diagnostic accuracy, using both dipsticks and clinical impressions, was low. A positive nitrite test, dysuria and older age were the only predictive factors of culture-confirmed UTI, however the negative predictive value of dipsticks is low (35%). Empirical treatment of all symptomatic patients with either nitrofurantoin or fluoroquinolones would result in a higher rate of appropriate therapies than the individualized approach chosen by the GPs.

**Conclusion.** Most patients with urinary symptoms were not treated according to current guidelines, and GPs’ diagnostic and therapeutic accuracy was low. Empirical treatment of all symptomatic patients is probably the most effective policy, but implies unnecessary antibiotic prescriptions.

**Keywords.** Anti-bacterial agents/therapeutic use, family practice, female, physician’s practice patterns, sensitivity and specificity, urinary tract infection.

Empiric treatment with first choice antibiotics (trimethoprim, nitrofurantoin, in the US: cotrimoxazole) is usually recommended, either for all symptomatic women without additional risk factors, or after using dipsticks to identify patients with a high probability of UTI. However, recently, there has been some discussion on appropriate diagnosis and targeting of antibiotic prescriptions to contain rising resistance levels in urinary pathogens.

The aims of our study were:

- to describe German GPs’ management of female patients with symptoms of UTI;
- to assess the diagnostic accuracy of dipsticks in a German general practice setting;
- to develop diagnostic prediction rules for a microbiologically confirmed UTI;

**Introduction**

Urinary tract infections (UTIs) are common in women, and a frequent reason to prescribe antibiotics in general practice. Guidelines on management have been published in several European countries, and in the US. Recommendations for the decision to treat and first line antibiotics are summarized in Table 1.1–6

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7–9 The aims of our study were:
to estimate the appropriateness of different approaches: empiric therapy of all symptomatic patients or treatment decisions based on dipstick results; and to assess the appropriateness of GPs' therapy with regard to antibiotic resistance.

Methods

This survey is part of a larger study on urinary tract infection in Germany, and methods have already been described elsewhere.10 The local ethics review board had no objections to the study.

All 118 teaching general practices of the Department of General Practice, University of Göttingen, were invited for this study and 36 (31%) agreed to participate (8 female GPs, 14 working in group practices with 2–4 partners). During the study period of 4 months (November 2000–February 2001), active participation was encouraged by regular telephone monitoring of the practices.

To maximise generalizability and to reflect daily practice, we choose rather open inclusion criteria for a consecutive sample: all patients presenting to the participating practices in whom the GPs suspected UTI based on symptoms were to be recruited prospectively, including those with risk factors, comorbidity or recent antibiotic treatment. Only patients with an obvious other diagnosis explaining their symptoms (i.e. vaginitis) should be excluded. Patients were to be managed ‘as usual’ according to the GPs’ judgement. The use of dipsticks as well as prescription of empirical treatment was at GPs discretion. Each patient’s age, sex, current symptoms and risk or complicating factors as well as results of dipstick tests and diagnostic procedures (if performed) and treatment were documented on a short, structured form identified by a patient code number.

The reference standard for this study was a conventional urine culture. In addition to their usual proceeding and for the purpose of this study, GPs were required to order a culture for all patients (regardless of dipstick results) before beginning treatment, but to wait for the culture results only if this would have been their usual policy. According to current recommendations, GPs were to sample freshly voided urine only, but midstream sampling was not required.1,4,11 Urine samples were stored in sterile containers supplied by the laboratory and kept refrigerated until processing the same day at the laboratory. A urine culture was performed and antibiotic susceptibility tested in case of bacterial growth, using internationally recommended standard procedures.12,13 All cultures and susceptibility tests were performed by three trained microbiology technicians in the same specialised laboratory (Medical Partnership Wagner Stibbe Kast Bispink & Partners). Technicians were informed of any particular question or information the GPs had noted on the order form (usually nothing). However, they had no access to the documentation form, dipstick results, or other clinical information. Susceptibility testing was performed in samples with more than 10^2 CFU/ml and less than 3 pathogens, though international literature now suggests that 10^2 CFU/ml are consistent with UTI.14,15 Therefore, we did not restrict our analysis to traditionally defined ‘high count UTI’ (≥10^5 CFU/ml), but also included cultures yielding low count bacteriuria (≥10^2 CFU/ml) or mixed growth in our definition of UTI. Culture results were labelled with the patients’ code numbers and communicated to the department of general practice. Participating GPs were informed of culture results assigned to patients’ names.

Documentation forms were collected by the laboratory’s transport service together with the urine samples for the GPs’ convenience. They were then sent to the department of general practice without any further processing and without disclosing patients’ identity. There, all data were entered into SAS, Version 8;16 patients’ documentation and laboratory results were linked with the patient code number. Descriptive statistics, 2 × 2 contingency tables and logistic regression models [odds ratios (OR), 95% confidence intervals (CI)] were calculated in SAS. Age (younger than 50, 50–74,
older than 74), dysuria, urgency/frequency, flank pain, fever, relapse (within 2 weeks of last episode) or recurrent UTI (more than 2 weeks since last episode), presence of any additional risk factors, as well as leucocytes and nitrite on dipsticks were used as independent variables to compare GPs’ diagnostic decision with a prediction of culture-confirmed UTI.

In order to assess the adequacy of different treatment approaches, dummy variables were used. The treatment prescribed by the study GPs was assessed using a dummy variable indicating resistance to the antibiotic chosen. Generally, not treating culture-confirmed UTI with antibiotics was considered inadequate, as well as treatment with an antibiotic to which the pathogen was resistant (cultures with intermediate susceptibility to fluoroquinolones were considered susceptible). Antibiotic treatment for patients with sterile urine was also considered inadequate. Not treating patients with sterile urine and treating patients with UTI with an antibiotic to which the pathogen is susceptible is considered adequate. If information was missing, i.e. either dipsticks or susceptibility testing had not been performed or the antibiotic prescribed had not been specified by the GP, adequacy was defined as ‘unknown’. Treatment duration was not considered when assessing adequacy, as no precise recommendations are available for elderly patients.

**Results**

Of the 118 invited GPs, 36 (31%) participated in the study (8 women, 14 working in group practices with 2–4 partners). 585 patients of both sexes were recruited within 4 months. Only the subgroup of adult women (76%, \(n = 445\)) is considered here. Results of male patients have been analysed and published separately, as well as a detailed analysis of factors predicting antibiotic resistance. Symptoms were documented on the study sheet in 89% of the women; median duration of symptoms was 3 days. Patients’ characteristics, symptoms and risk factors are presented in Table 2.

GPs’ diagnostic procedures, diagnoses and prescriptions are presented in Table 3. Median antibiotic treatment duration was 5 days, irrespective of patients’ age and presence of complicating factors. 70% of young patients with uncomplicated UTI were treated for longer than 3 days. On the other hand, 25% of patients of any age with additional risk factors (complicated UTI) received antibiotics for 3 days or less. One fifth (19.3%) of the patients were not prescribed antibiotics though their GPs had diagnosed UTI. These patients were less likely to have dipsticks positive for nitrite (OR 0.38, 95% CI 0.19–0.76) and leucocytes (OR 0.48; 95% CI 0.25–0.91) than those who had been prescribed antibiotics. Patients who had flank pain, but in whom GPs had diagnosed UTI rather than pyelonephritis were less likely to receive antibiotics than other patients with UTI (OR 2.94; 95% CI 1.45–6.25). Treated and untreated patients with GP-diagnosed UTI did not differ with regard to other symptoms, age, recurrent UTI or risk factors.
Urine culture results were available for 430 patients (97%); results are shown in Table 4. Bacterial species were identified in the 282 patients with $10^3$ cfu/ml or more and no more than two pathogens: 67.7% were infected with *Escherichia coli*, 10.3% with enterococci, 9.6% with *Proteus* spp., 7.4% with *Streptococcus agalactiae*, several others were found in 1–4 urine samples, respectively.

**Prediction rule for UTI**

GPs apparently diagnosed UTI based on both their clinical assessment and dipstick tests, which had been performed in 91.6% of all patients. Detailed documentation of a stepwise approach was not available for feasibility reasons. Table 5 illustrates the diagnostic value of dipsticks with regard to culture results.

Table 6 compares predictors for GPs’ diagnosis of ‘infection’ (either UTI or pyelonephritis) and culture-confirmed bacteriuria. Fever (OR 6.44, 95% CI 1.15–36.03) and flank pain (OR 22.06, 95% CI 7.13–68.32) were the only significant predictors for a diagnosis of pyelonephritis; however, one in 5 patients with either fever or flank pain was diagnosed as not having pyelonephritis (data not shown). Using culture-confirmed UTI ($\geq 10^2$ CFU/ml) as a gold standard, GPs’ diagnosis had a sensitivity of 70.8% and a specificity of 38.8%, the positive predictive value (PPV) was 79.7%, the negative predictive value (NPV) 28.2%.

**Adequacy of different treatment approaches**

Figure 1 illustrates the appropriateness of treatment decisions for all patients in this study in a flow chart. 60.2% of the 332 patients with culture-confirmed UTI received antibiotics, and 42.9% of those with sterile urine ($n = 98$). 39.8% of all women with UTI received no treatment. In 24% of the women with UTI who were prescribed antibiotics, pathogens were resistant to the treatment and this occurred significantly more often in patients with complicating factors (52.1 versus 22.5%; OR 3.74; 95% CI 1.84–7.62).

### Table 4

**Results of urine cultures (available for n = 430 patients)**

<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile urine</td>
<td>98</td>
</tr>
<tr>
<td>UTI $&gt; 10^2$ cfu/ml, single growth</td>
<td>230</td>
</tr>
<tr>
<td>UTI $&gt; 10^2$ cfu/ml, 2 pathogens</td>
<td>35</td>
</tr>
<tr>
<td>UTI $&gt; 10^2$ cfu/ml, 3 pathogens</td>
<td>17</td>
</tr>
<tr>
<td>Low count UTI $10^2$ cfu/ml</td>
<td>50</td>
</tr>
</tbody>
</table>

Resistance levels in all cultures with more than $10^2$ cfu/ml and less than 3 pathogens ($n = 298^a$)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>% resistant pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>36.9</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>28.5</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>38.6</td>
</tr>
<tr>
<td>Cefixime</td>
<td>16.1</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>21.5</td>
</tr>
<tr>
<td>Ofloxacin$^b$</td>
<td>6.7</td>
</tr>
<tr>
<td>Ciprofloxacin$^b$</td>
<td>6.4</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>31.5</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>33.6</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>13.1</td>
</tr>
</tbody>
</table>

$^a$ Refers to 265 patients; in 33 patients two pathogens were tested for susceptibility.

$^b$ 17% of all pathogens had intermediate susceptibility to ofloxacin and ciprofloxacin. As fluoroquinolones are likely to be clinically effective for UTI in these patients, they were considered susceptible.

### Table 5

**Dipstick test results and diagnostic value with regard to any UTI $\geq 10^2$ CFU/ml, including mixed growth**

<table>
<thead>
<tr>
<th></th>
<th>Totals</th>
<th>Nitrite positive</th>
<th>Nitrite negative</th>
<th>Leucocytes positive</th>
<th>Leucocytes negative</th>
<th>Both positive</th>
<th>At least one positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>308</td>
<td>121</td>
<td>187</td>
<td>221</td>
<td>87</td>
<td>107</td>
<td>235</td>
</tr>
<tr>
<td>Sterile urine</td>
<td>86</td>
<td>10</td>
<td>76</td>
<td>46</td>
<td>40</td>
<td>10</td>
<td>46</td>
</tr>
<tr>
<td>Totals $^a$</td>
<td>394</td>
<td>131</td>
<td>263</td>
<td>267</td>
<td>127</td>
<td>117</td>
<td>281</td>
</tr>
</tbody>
</table>

Sensitivity (%) | 39.3 | 71.8 | 34.7 | 76.3
Specificity (%) | 88.4 | 46.5 | 88.4 | 46.5
PPV (%) | 92.4 | 82.8 | 91.5 | 83.6
NPV (%) | 28.9 | 31.5 | 27.4 | 35.4
Pos. likelihood ratio | 3.39 | 1.34 | 2.99 | 1.43
Post-test probability (%) | 92.4 | 82.7 | 91.5 | 83.6

$^a$ Dipstick and cultures had been performed in all patients. Urine culture was not available for 15 patients; dipsticks had not been performed in 36 patients.

$^b$ Positive predictive value.

$^c$ Negative predictive value.
A simulation of different therapeutic strategies is presented in Table 7; and the adequacy of empiric treatment with several antibiotics of either all patients with suspected UTI or patients with a positive nitrite test is compared with the treatment prescribed by the GPs in our study.

**Discussion**

Our cross-sectional study combines results of systematic urine cultures with an observational survey of GPs’ management of urinary tract infections.

Table 6  **Comparison of factors predicting GPs diagnosis and culture results (multivariate logistic regression; significant predictors in bold type)**

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>UTI or pyelonephritis diagnosed by GP OR (95% CI)</th>
<th>Culture-confirmed UTI ≥10^5 cfu/ml OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrite on dipstick</td>
<td>2.77 (1.39–5.55)</td>
<td>3.41 (1.87–6.21)</td>
</tr>
<tr>
<td>Leucocytes on dipstick</td>
<td>3.53 (2.08–6.00)</td>
<td>1.57 (0.97–2.54)</td>
</tr>
<tr>
<td>Complicating factors</td>
<td>1.04 (0.56–1.93)</td>
<td>1.16 (0.67–1.99)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>7.59 (4.29–13.42)</td>
<td>1.97 (1.22–3.17)</td>
</tr>
<tr>
<td>Flank pain</td>
<td>6.39 (2.90–14.09)</td>
<td>0.44 (0.23–0.79)</td>
</tr>
<tr>
<td>Urgency/frequency</td>
<td>2.28 (1.34–3.87)</td>
<td>0.87 (0.55–1.38)</td>
</tr>
<tr>
<td>Suprapubic pain</td>
<td>1.67 (0.74–3.74)</td>
<td>0.85 (0.46–1.70)</td>
</tr>
<tr>
<td>Fever</td>
<td>18.12 (1.72–190.85)</td>
<td>2.37 (0.58–9.68)</td>
</tr>
<tr>
<td>Relapse</td>
<td>1.66 (0.71–3.89)</td>
<td>0.61 (0.30–1.25)</td>
</tr>
<tr>
<td>Reinfection</td>
<td>2.30 (1.16–4.56)</td>
<td>1.51 (0.86–2.67)</td>
</tr>
<tr>
<td>Older age (&lt;50, 50–74, &gt;74)</td>
<td>1.36 (0.95–1.96)</td>
<td>1.48 (1.08–2.02)</td>
</tr>
</tbody>
</table>

GPs participating in our survey were not routinely involved in research, they practice in both rural and urban settings. Though there may be selection bias concerning GPs, their patients are not likely to differ from patients in non-participating practices. Typical for general practice studies in countries without practice lists, we do not know the precise catchment rate of our study, but had to rely on participating GPs to include all their eligible patients. We attempted to ensure active participation though regular telephone monitoring. The number of included patients (of both sexes) corresponds to the practice prevalence reported in other German studies on UTI. All urine cultures and susceptibility tests were performed in a single laboratory, but dipsticks were assessed by the individual GPs (or their practice staff), who reported their reading. Though GPs’ reading of urinary dipsticks is known to vary, our approach reflects practice reality better than ‘standardised’ reading in a study centre (which was not done for feasibility reasons).

![Figure 1](https://example.com/figure1.png)

**Figure 1**  Adequacy of all patients’ management with regard to the presence of culture-confirmed UTI and susceptibility to the individual antibiotic prescribed in each case.
Inadequately treated patients had a favourable clinical outcome. Additionally to the apparent difficulty in targeting antibiotic prescriptions, treatment duration was shorter than recommended\(^1,2,4,14\) in one quarter of patients with additional risk factors, and longer than necessary in most young women with uncomplicated UTI.\(^{26}\)

In our comparison of different treatment approaches to the patients in this study, empirical treatment with either nitrofurantoin or fluoroquinolones proved superior, and empirical treatment with trimethoprim was equivalent to the individualized approach preferred by the study GPs. Treatment of all symptomatic patients has been shown to be the most cost-effective option,\(^{27}\) but costs of rising resistance levels were not considered.\(^{28}\) However, this would result in inadequate treatment for one quarter to one third of all patients, including unnecessary antibiotic exposure of patients who did not have UTI (22% in our study). This should be a reason for concern in presence of high resistance levels for all common antibiotics.\(^{29,30,31}\) In our study, pathogens proved resistant to the antibiotic the patient had received in almost a quarter of all cases. GPs seemed to be aware of resistance problems and choose to prescribe fluoroquinolones in one third of cases. Though still highly effective at the time of our study, the high prevalence of intermediate susceptibility indicates a dropping susceptibility level: in Germany, the level of resistance against ciprofloxacin in \(E.\) coli increased from 7.7% in 1998 to 14.5% in 2001\(^{32}\) and similar tendencies have been observed in other countries.\(^7,33\)

One possibility to reduce unnecessary antibiotic use is to treat only patients with a positive nitrite test. This would have reduced the number of inadequately treated patients in our study (as dipsticks were performed for only 90% of the patients, however, adequacy could not be judged in many cases). Due to the low negative predictive value of dipsticks, cultures should then be considered for symptomatic patients with a negative nitrite test.

Ordering cultures for all patients and delaying antibiotic treatment until results are available could limit overtreatment.\(^8\) However this would increase direct costs, and often cultures would have no impact on management. In many patients without additional risk factors, UTI seems to be a self-limiting condition: A trial in Belgium has shown that half of the patients were free of symptoms after 3 days of placebo.\(^{35}\) Symptomatic treatment of uncomplicated UTI may be an option which merits further research.

**Acknowledgements**

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Declaration

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Ethical approval: the local ethics review board had no objections to the study.

Conflicts of interest: none.

References