Management of urinary tract infection in general practice: a cost-effectiveness analysis

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SUMMARY

Background. *Symptoms associated with urinary tract infection (UTI) are common in women in general practice and represent a significant burden for the National Health Service. There is considerable variation among general practitioners in the management of patients presenting with these symptoms.*

Aim. *To identify the most appropriate patient management strategy given current information for non-pregnant, adult women presenting in general practice with symptoms of uncomplicated UTI.*

Method. *A decision analytic model incorporating a variety of patient management strategies was constructed using available published information and expert opinion. This model was able to provide guidance on current best practice based upon cost-effectiveness (cost per symptom-free day).*

Results. *Empiric treatment was found to be the least costly strategy available. It saved two days of symptoms per episode of UTI at a cost of £14. The empiric-and-laboratory strategy involves an incremental cost-effectiveness ratio of £215 per symptom day averted per episode of UTI. The remaining patient management strategies are never optimal.*

Conclusion. *Empiric treatment of patients presenting with symptoms of UTI was found to be cost-effective under a range of assumptions for this patient group. However, recognition of the impact of this strategy upon antibiotic resistance may lead to the dipstick strategy being considered a superior strategy overall.*

Keywords: urinary tract infections; antibiotic resistance; general practice; decision analysis; cost-effectiveness analysis.

Introduction

SYMPTOMS associated with urinary tract infection (UTI) are common in general practice; dysuria and frequency have been reported in 27% and 34% of women.[1] These symptoms are a major cause of consultation in general practice and account for 1% of all general practitioner (GP) consultations[2] and 2% of all prescriptions.[3] Although the majority of cases in women are short-term and self-limiting, this condition does represent a considerable resource burden for the National Health Service (NHS).

Despite the publication of clinical guidelines,[4] there is considerable variation among GPs in the management of UTI symptoms in this specific group of patients.[5,6] Some prescribe on the basis of the symptoms alone (empiric therapy); others look at colour, opacity, and/or smell of the urine, a dipstick test or a full urine culture.[7] The accuracy of each of these procedures in diagnosing UTI varies as do the resources used, suggesting that some patients are not receiving the most appropriate treatment and that resources are not being employed efficiently.[8]

As a result of these clinical practice variations and the recent development of near-patient tests that can be used to confirm diagnosis, the NHS Health Technology Assessment programme has identified the 'use of dipsticks and diagnostic algorithms in the diagnosis of urinary tract infection' as a research priority and has recently called for proposals for primary research.

The aim of this study was to identify the most appropriate patient management strategy for non-pregnant, adult women presenting to general practice with the symptoms of uncomplicated UTI (frequency, dysuria, urgency, and nocturia) given the current levels of information available.

The decision analytic model constructed incorporates a variety of patient management strategies so that it can guide current best practice, based on cost-effectiveness.

Method

Management strategies

Early discussions with practitioners identified two main approaches for managing UTI in general practice. The first is empiric antibiotic treatment on presentation of symptoms and the second involves the use of diagnostic tests to exclude or confirm the presence of UTI prior to antibiotic treatment. Two test procedures were identified for consideration by the study: the dipstick test, a near-patient test generating immediate results; and the laboratory test, involving an overnight urine culture.

In consultation with practitioners, seven simple management strategies were generated from these two main approaches to the primary management of UTI. These seven strategies form the basis of the model (Table 1).

Model structure and assumptions

The initial decision node in the model represents the GP's choice of management strategy when consulted by a woman with the symptoms of UTI (Figure 1). Each patient management strategy is incorporated as a separate branch following from this decision node, representing the sequence of events that a treated patient may experience with the strategy, according to the assumptions of the model. A simplified version of the decision tree is constructed from Figure 1 by applying Trees 1 to 3 as appropriate.

A proportion of the women who present with symptoms of UTI in general practice will have other disorders. Each patient management strategy branch is modelled by splitting the symptomatic population according to the presence of UTI, using information from prevalence studies.[9] A lack of quantitative information of other possible causes of symptoms in this group led us to treat all non-UTI cases identically in the model. We make the

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Table 1. Strategies employed within the model of UTI management.

Strategy name	Strategy description
No treatment	GPs provide general advice on relieving symptoms and inform patients that symptoms will resolve within seven days.
Empiric treatment	All individuals presenting with symptoms of UTI receive a three-day course of general antibiotics.
Empiric treatment plus laboratory test	The laboratory test is used to supplement empiric treatment. While all patients provide a urine sample for testing during the initial consultation, the results only affect the management of those patients with persistent symptoms. For these patients antibiotic sensitivity will be available at the second visit to the GP for those who tested positive, which will enable the GP to prescribe a course of specific antibiotics. This gives the patients with UTI who test positive a second chance for antibiotics to clear the infection. Antibiotics will not be altered on the basis of the sensitivity results until the second consultation.
Dipstick and treatment	The dipstick test is employed within the initial consultation to provide an indication of presence of disease and to restrict the use of antibiotics to those considered most likely to have UTI, as denoted by the result of the dipstick test.
Dipstick and treatment plus laboratory test	The laboratory test is used to supplement the dipstick test. While all patients with a positive dipstick result provide a urine sample for further testing during the initial consultation, the results only affect those patients with persistent symptoms. For these patients antibiotic sensitivity will be available at the second visit to the GP for those who tested positive, which will enable the GP to prescribe a course of specific antibiotics. This gives the patients with UTI who test positive a second chance for antibiotics to clear the infection. Antibiotics will not be altered on the basis of the sensitivity results until the second consultation.
Laboratory test and wait for preliminary results	All patients provide a urine sample at the initial consultation and treatment is determined by the positive/negative result of this test. Hence treatment is delayed until this result is available.
Laboratory test and wait for sensitivities	All patients provide a urine sample at the initial consultation and treatment is determined by the sensitivity result of this test. Hence treatment is delayed until the results of the sensitivity analysis are available. As a result, specific antibiotics are given to every confirmed case of UTI as a first treatment, leaving no secondary course of treatment for those with persistent symptoms.

assumption that those with non-UTI will not benefit from any of the strategies considered, and the only possible health outcome for these patients is that symptoms will persist, as illustrated in Figure 1. However, as these patients are not immediately identifiable, resources are still used in the management of their symptoms and these are included within the analysis of each strategy.

Uncomplicated UTI tends to be a self-limiting condition. Fifty per cent of cases resolve naturally after three days;[9] the remainder resolving after an average of a week (base case). Where no treatment is given to patients with UTI, either as a deliberate strategy or as the result of an incorrect test result, symptoms are assumed to either disappear after three days or to persist for seven days (Tree 1). The period of symptoms can be reduced through the use of antibiotics, which may resolve symptoms after two days from the start of the course.[9] We assume that the use of antibiotics has no impact upon the probability of natural resolution. Therefore, where antibiotics are given symptoms may resolve, either naturally or as a result of the antibiotics, or may persist (Tree 2).

When used, test results dictate the subsequent management of the patient. Antibiotics (and possibly a confirmatory laboratory culture) follow a positive result and no further treatment follows a negative one. When laboratory tests are undertaken an initial positive or negative result can confirm the presence or absence of UTI and further analysis of positive results provides details of bacterial sensitivities that can direct prescribing. Where available, this information is employed to manage patients whose symptoms persist (Tree 3).

Patients given antibiotics are assumed to comply fully with the course of treatment. Ten per cent are expected to experience side-effects because of the antibiotics,[10] which prolong the period of symptoms by an extra two days.[11] We assume that there is no worsening of symptoms or progression to pyelonephritis owing to withholding or delaying antibiotic treatment within this patient population.

This model deals with the primary management of uncomplicated UTI in women. As such, subsequent investigations in those whose symptoms persist following the completion of the management strategy are considered to be outside the scope of the model. Therefore, while patients are assumed to return to the GP where symptoms persist, and the resources associated with these visits are included within the model, any further investigations are excluded from the model.

Analysis

Costs. As the environmental setting is identical for each option, the model ignores fixed costs and concentrates upon the differences in variable costs between strategies that depend upon the resources used. At each stage, the model records test usage, drugs prescribed, and the number of attendances at the GP's surgery for both the UTI and non-UTI branches of the model. Each possible pathway in the model is then costed by applying unit costs (Table 2) to the expected resource volumes associated with the pathway.

The analysis takes a NHS perspective, concentrating upon the costs that fall directly upon the NHS and excluding any costs that fall upon private individuals or other public services. As such, the costs of over-the-counter treatments for side-effects are excluded from the analysis as we assume that these are purchased privately by patients.

Health outcomes. The number of symptom days suffered by patients is calculated for each possible pathway in the model with reference to the average times taken for symptoms to resolve, the average length of time for laboratory results to be available, and the additional days of symptoms caused by side-effects to antibi-

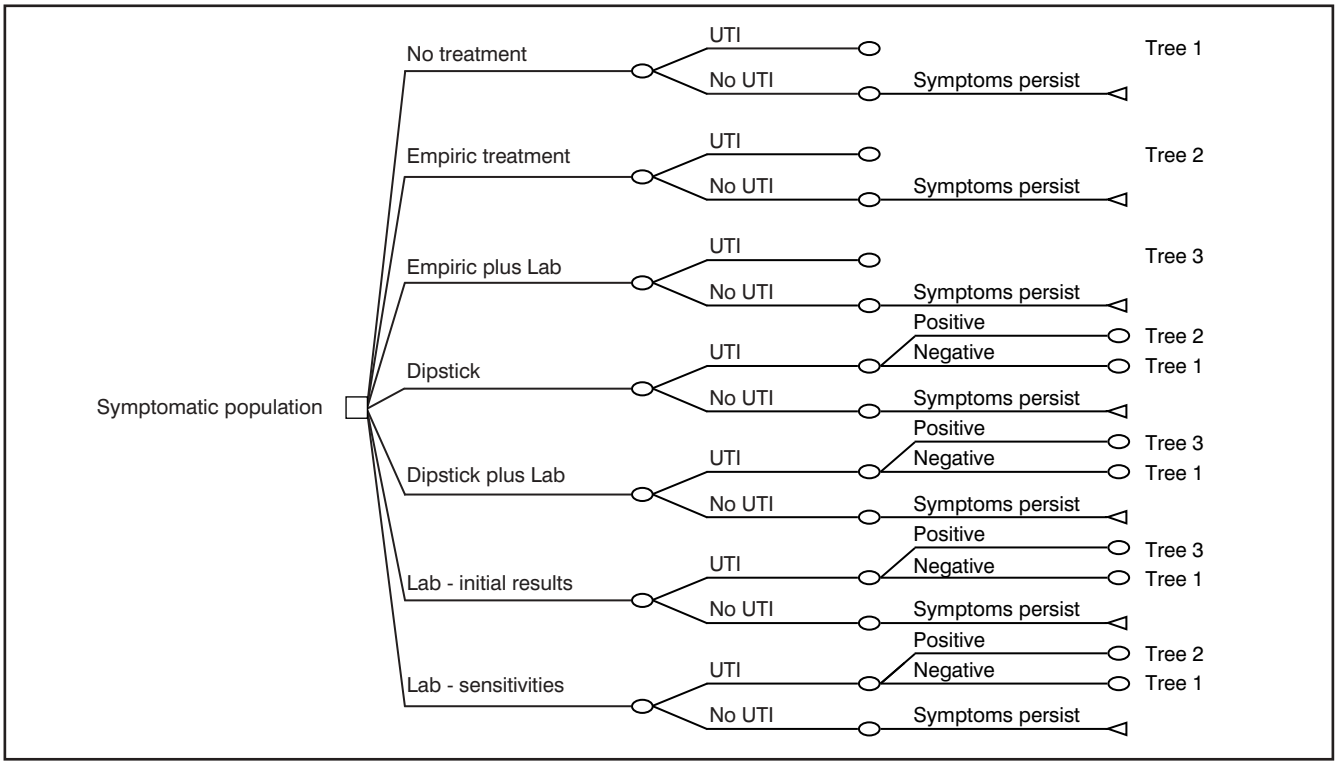

Figure 1. The patient management decision.

otics (Table 2). The health benefit is calculated as the difference between the number of symptom days experienced for non-responsive UTI (seven days within the base case) and the number of symptom days associated with the particular pathway — the number of symptom days that are averted.

Cost-effectiveness. The cost and health outcomes associated with each possible pathway through the tree are used in conjunction with the pathway probabilities for this patient group (Table 2) to determine the expected costs and expected health outcomes associated with each patient management strategy per episode of UTI. The cost-effectiveness of each strategy is then determined by identifying the additional costs incurred for the additional health outcomes secured owing to that patient management strategy, compared with the next less effective strategy.[12,13] It is the ratio of these additional costs and health outcomes that forms the incremental cost-effectiveness ratio (ICER) for each successively more effective strategy.[14] These ratios can then be examined to determine whether a strategy is considered good value for money, with reference to the ICERs of other programmes funded by the health service or to an externally determined cut-off value.[14]

Sensitivity analysis

All of the model parameters are subject to uncertainty. The robustness of the model results is therefore investigated through one-way sensitivity analysis, where the value of each parameter is varied over a plausible range of values (Table 2). This analysis illustrates how the results of the model respond to changes in the parameters individually. Strategies that are never optimal can be identified and the impact of uncertainty upon cost-effectiveness can be measured for other strategies.

Results

Base case scenario

Empiric treatment is the least costly strategy, providing 2.15 symptom-free days per episode of UTI at a cost of £13.90. The next least costly strategy involves empiric treatment and laboratory culture, which provides 2.19 symptom-free days per episode of UTI (a reduction of 0.04 symptom days) at a cost of £22.50 (an increase of £8.60). Thus, the empiric treatment and laboratory culture strategy involves an additional cost of £215 per additional symptom day averted (ICER). The remaining patient management strategies all generate fewer symptom-free days at a higher cost than empiric treatment, and are therefore not considered.

Sensitivity analysis

Sensitivity analysis reveals that empiric treatment remains the least costly strategy when the parameters are individually varied over the ranges specified (Table 2). The no-treatment strategy and the strategies employing laboratory tests as the initial element of patient management were constantly more costly and less effective than the empiric strategy, and are therefore not considered. The results show that, while the simple dipstick strategy and that complemented by the laboratory culture are often more costly and less effective than the empiric strategy, the cost-effectiveness is affected by the sensitivity of the dipstick and both the duration and probability of side-effects owing to antibiotics. When the values for these parameters are high both the dipstick and dipstick-plus-laboratory strategies become potentially cost-effective. In these cases, the ICER associated with the dipstick strategy varies between £2 and £45 per incremental symptom day averted, while the ICER for the dipstick-plus-laboratory strategy varies between £117 and £163 per incremental symptom day averted. The ICER associated with the empiric-plus-laboratory strategy varies between £39 and £492 per

Table 2. Parameters of the model.

Parameter	Base value and source	Range
Pathway probabilities		
Prevalence of symptoms in target group	5%[9]	5%–20%
Probability of UTI given symptoms	50%[6]	43%–90%
Sensitivity of dipstick	89%[a]	88%–99.5%
Specificity of dipstick	68%[a]	53.3%–82.5%
Sensitivity of laboratory culture	100%[a]	90%–100%
Specificity of laboratory culture	100%[24]	90%–100%
Probability symptoms resolve naturally given UTI	50%[9]	20%–65%
Probability antibiotics resolve symptoms given UTI	90%[9]	81%–95%
Probability specific antibiotics resolve symptoms given UTI	90%[6]	81%–95%
Probability of side-effects owing to antibiotic treatment	10%[10]	5%–30%
Resource cost		
Dipstick	£0.20[6]	£0.05–£0.50
Antibiotics: three-day course, general (Trimethoprim 200mg bd)	£0.21[25]	£0.05–£0.50
Specific antibiotics: three-day course[b]	£2.82[25]	£1.00–£4.50
Laboratory culture and sensitivity	£5.42[a]	£2.50–£8.50
Laboratory culture	£2.60[a]	£1.00–£4.00
Attendance at GP's surgery	£9.00[26]	£4.00–£13.00
Procedure/event times		
Symptom days for non-responsive UTI	7 days[a]	5–15 days
Period before antibiotics resolve symptoms	2 days[9]	1–3 days
Period before infection resolves naturally	3 days[9]	1–4 days
Period before basic laboratory results known	2 days[a]	1–3 days
Period before laboratory sensitivity results known	3 days[a]	1–4 days
Duration of side-effects	2 days[11]	2–4 days

[a]Expert opinion; [b]the unit cost of specific antibiotics is a simple average of the costs of the following individual drugs that could be prescribed: Amoxycillin 250 mg three times daily (£0.33); Cephalexin 500 mg four times daily (£2.54); Co-amoxiclav 375 mg three times daily (£4.20); Cephradine 500 mg four times daily (£4.20).

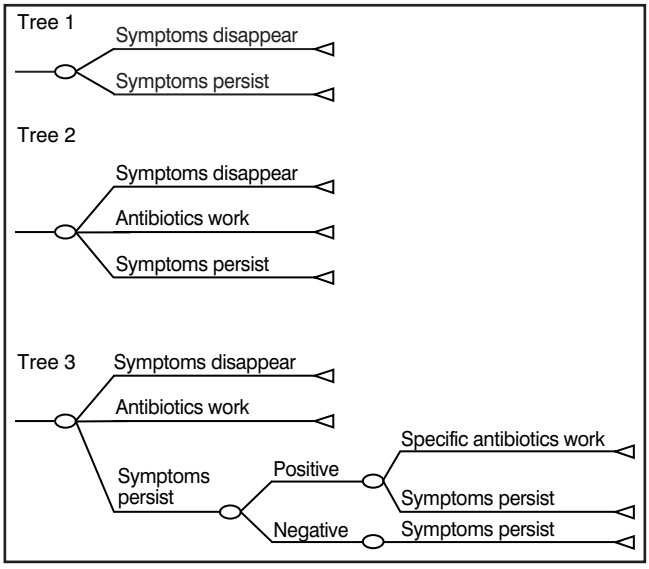

Figure 2.

incremental symptom day averted, and when the average length of a UTI is reduced this strategy becomes less effective than the empiric strategy and is not considered.

Discussion

This model was developed to investigate some of the strategies currently used to manage non-pregnant women presenting in general practice with symptoms of uncomplicated UTI. Pregnant women, men, children, and women presenting with symptoms suggesting upper urinary tract infection (fever, chills, nausea, and loin pain) were excluded from the study owing to their increased risk of underlying structural abnormalities and other complications.

The model identifies that three strategies are inferior to the others: no treatment; laboratory and wait for preliminary results; and laboratory and wait for sensitivity results. The no-treatment strategy is inferior because without antibiotics symptoms persist in a high proportion of patients (75%) who revisit the GP, incurring a high cost (relative to antibiotics). The laboratory strategies are inferior owing to both the additional symptom days suffered during the wait before results are known and any treatment commences and the additional cost of the test.

In addition, the results of the model suggest that empiric treatment is cost-effective and robust to uncertainty within the model parameters. Even when other patient management strategies are viable the extent of the associated ICERs suggests that empiric treatment will be the preferred strategy. If, as suggested in a recent model of UTI,[15] a symptom day is associated with a disutility of 0.2894 then the empiric-plus-laboratory strategy would equate to an incremental cost of over £270 000 per quality adjusted life year (QALY) per episode of UTI. This level is far in excess of what is generally considered cost-effective.

Lack of published information and the preliminary nature of the study mean that the management strategies used within the analysis were deliberately kept simple. The model can be refined and the strategies developed as additional information becomes available. The lack of published information for some of the parameters has not proved to be a limitation for the study, as sensitivity analysis has shown the results to be robust to variation within the parameters. The model focuses upon the benefits of the various patient management strategies for those who have UTI by assuming no benefit for those whose symptoms are caused by something other than UTI. In fact antibiotics may impact upon non-UTI, with some disorders improved by antibiotics (chlamydial infection and acute urethral syndrome[16]) while others are

worsened (vaginitis) or unaffected (genital herpes and urethritis). Given a lack of information concerning the possible causes of non-UTI the overall impact of antibiotics is unclear for this patient group. However, if, as suggested by a recent article,[16] a large proportion of the non-UTI cases had acute urethral syndrome then the model underestimates the effectiveness of empiric treatment by excluding the benefits to these patients. Inclusion of these benefits would make empiric treatment more cost-effective.

The model ignores the complications that can occur, including pyelonephritis, when treatment is delayed or incorrectly withheld. However, inclusion of these rare but important effects would only favour immediate empiric therapy and reinforce the results of the study. The assumption is made that patients fully comply with treatment given as part of the management strategy, which does not seem unreasonable given the short duration of the course of antibiotics. Sensitivity analysis has shown that the results are robust to variations in the probability that antibiotics resolve symptoms, suggesting that changes in the assumptions concerning patient compliance with treatment will have little impact on the results.

One limitation of the model is that it does not incorporate the long-term impact of empiric therapy upon antibiotic resistance, either for individual patients or for society more generally. There are important concerns about the potential future global implications associated with the overuse of antibiotics,[17,18] but there are practical difficulties associated with including the impact within health care evaluations.[19] Very little information is currently available concerning how bacteria become resistant and at what speed, and how the use of particular antibiotics affects this process.[20-22] It is therefore difficult to assess the future cost and health impacts associated with current use of a particular antibiotic.

Several approaches have been suggested to tackle the problem of antibiotic resistance;[18,21-23] these involve reducing patients' demands for antibiotics and the pressure upon doctors to prescribe. One useful weapon in the fight to combat antibiotic resistance is the increased use of near-patient tests for rapid diagnosis.[18,21-23] Therefore, while the patient management strategy incorporating dipstick testing prior to prescribing antibiotics is not optimal within this model, it may well be considered a superior strategy overall if antibiotic resistance was included. The analysis undertaken here suggests that employing the dipstick strategy for this patient group within a typical primary care group of 100 000 individuals would involve an additional cost of £714 per year (£0.34 per episode) compared with empiric treatment, and result in 150 extra symptom days or 0.12 fewer QALYs. This may be considered a price worth paying to achieve 820 fewer antibiotic prescriptions per primary care group per year, of which 705 (86%) are unnecessarily given to those without UTI. Without further research into the impact of antibiotics upon resistance the debate concerning whether the additional cost (in terms of resources and health) of dipsticks is worthwhile will continue and recommendations for managing patients with symptoms of UTI will necessarily involve qualitative consideration of this important issue.

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