Background
The urinary tract comprises the kidneys, bladder and their collecting ducts (ureters and urethra) and an infection involving any of these structures constitutes a urinary tract infection (UTI). Whether acquired in the community or hospital setting, UTIs feature among the leading causes of patient morbidity. Each year, in the United States alone, UTIs account for over 8 million patient visits to physician practices and emergency departments and 100 000 hospital visits. Poor management of UTIs may have far-reaching consequences on the individual and public health at large because it can lead to severe complications such as sepsicaemia and increased antimicrobial resistance. Consequently, the value of establishing clear clinical management guidelines for UTI on the basis of sound research evidence cannot be overestimated.

Epidemiology and prevalence
The prevalence of UTIs in both males and females increases with advancing age, although women bear the greater burden of infections. Women are generally four to five times more likely than men to experience a UTI, with prevalence ranging from 3% in young girls under the age of 10 to a peak of 10% in post-menopausal women between the ages of 55 and 64. The female:male ratio decreases after the age of 50 and this coincides with increasing rates of male urethral instrumentation, urinary surgical procedures and prostate obstruction. At the opposite end of the age spectrum, neonatal UTIs occur with greater frequency in boys and is usually suggestive of congenital urinary abnormalities.

Classifications of UTIs
UTIs may be classified according to the site of infection or the presentation of symptoms, although in clinical situations, the classification is generally based on the latter. Lower urinary tract infections may involve the bladder (cystitis) and urethra (urethritis) and upper urinary tract infections usually involve the kidneys (pyelonephritis). These may further be classified as complicated or uncomplicated: when associated with underlying structural or functional urinary tract abnormalities and with risk factors for infection or therapeutic failure, UTIs are designated “complicated”; in contrast, an infection in individuals who are otherwise healthy is designated “uncomplicated”. The intent of classifying various clinical entities in this manner is to guide therapeutic decisions as well as pre- and post-therapeutic patient evaluations.

Etiology and pathophysiology
An intact urinary system is one that is typically sterile and resistant to microbial colonisation. This aseptic milieu is maintained by several physiological mechanisms such as the acidification of urine, regular emptying of the bladder and immunological and mucosal barriers. When these physiological mechanisms are challenged by host factors (e.g. urinary tract abnormalities, diabetes, immunosuppression, pregnancy, oestrogen deficiency) or contamination from external sources (e.g. catheterisation, urinary instrumentation), the ensuing proliferation of predominantly enteric bacteria in the mucosal lining of the urethra and bladder stimulates an inflammatory response. Further ascension of uropathogens into the kidneys via the ureters, may lead to pyelonephritis. It thus follows logically that the vast majority (95%) of bladder and kidney infections are due to ascending bacterial infections. In the remaining instances, micro-organisms are thought to reach the urinary tract by haematogenous or lymphatic spread.

The pathogenic causes of UTI are predominantly bacterial, although fungal and viral aetiologies are occasionally implicated. The chief implicating micro-organism in both community-acquired and nosocomal UTI is the Gram-negative colonic bacteria, Escherichia coli. In the community, E coli is implicated in 75% of cases, while the remaining pathogens comprise Gram-positive Staphylococcus saprophyticus and other Gram-negative Enterobacteriaceae. Approximately 50% of nosocomal UTI are...
attributable to *E. coli* while the remaining uropathogens are Gram-negative bacteria, including species of *Klebsiella*, *Proteus*, *Enterobacter* and *Serratia*.¹

It is postulated that anatomical and physiological differences in the male and female urogenital tract account for differences in susceptibility to UTI. The longer male perineum possibly confers protection against migrating colonic bacteria along the faecal-urethral route and the length of the male urethra (20 cm) may impede uropathogen ascension into the bladder. Furthermore, the sterilising effect exerted by prostatic secretions possibly protects males from uropathogen colonisation. In contrast, the shorter female urethra (3 cm) and the closer proximity of the urethral meatus to colonies of enteric bacteria in the perirectal, introitus vaginae and perianal region, may facilitate bacterial migration into the urethra and ascension into the bladder.¹

Other factors contributing to the high prevalence of UTIs in women include unprotected sexual intercourse, delayed post-coital urination, and the administration of antibiotics and diaphragm-containing spermicides. The latter risk factors change the natural flora surrounding the urethral meatus by reducing the resident lactobacillus population, and this, in turn, increases vaginal *E. coli* concentrations. The physiological and anatomical changes associated with pregnancy and the post-menopause render these female sub-populations more susceptible to developing UTIs.¹

**Clinical presentation**

Infections involving various sites of the urinary tract often share a triad of symptoms, namely dysuria and urinary urgency and frequency. This symptom overlap may hinder site-specific diagnoses.

Dysuria is the most common symptom of *urethritis* and, in males, this is characteristically accompanied by a urethral discharge that is either purulent (indicative of *Neisseria gonorrhoea*) or non-purulent (white mucoid, indicative of non-gonococcal infection). Symptoms consistent with *cystitis* are a sudden onset of burning on urination, urinary frequency and suprapubic pain. Signs of urine turbidity and haematuria are exhibited in about 30% of cases. It is common for males with *cystitis* to have concomitant prostatitis.² The classic symptom triad of dysuria, urinary frequency and urgency also characterises prostatitis and these are often accompanied by pain in the perineum or prostate (46%), scrotum and/or testes (39%), penis (6%), bladder (6%) or lower back (2%).³ In most cases, the clinical picture of *pyelonephritis* only differs from cystitis by the presence of constitutional symptoms such as fever, nausea and vomiting. Pyelonephritis may also manifest with flank pain. The aforementioned clinical presentation is less characteristic of pyelonephritis in children, as symptom exhibition in this age group is usually meagre. The insidious clinical presentation of pyelonephritis in children underlines the importance of diagnostic accuracy in the lower age groups. Finally, *asymptomatic bacteriuria*, a clinical entity that is most common in the elderly, is characterised by significant bacteria in the urine in the absence of typical UTI symptoms.¹

**Diagnosing**

**Diagnostic tools**

The diagnostic tools most often employed in clinical settings are the clinical examination (history-taking and physical examination) and urinalysis (e.g. urine dipstick tests, urine cultures). The clinical examination elicits the clinical symptoms of UTI and risk factors for complicated UTI (e.g. male gender, urinary catheter, immunosuppression).⁵ The urine dipstick test is an effective and inexpensive, qualitative screening tool for bacteriuria (evidenced by positive leukocyte esterase and/or nitrites). The more definitive urine culture (quantitative test) for significant bacteriuria (evidenced by >10⁵ colony-forming units/ml; lower thresholds are accepted for specific patient groups) is the gold standard microbiological test, however its use in clinical settings is constrained by cost and time.⁵

**Arriving at a differential diagnosis**

A growing body of evidence suggests that a clinical examination alone may be sufficient in diagnosing healthy, pre-menopausal women. A meta-analysis of various trial data demonstrated that specific clinical examination findings either increase or decrease the likelihood of lower UTI in otherwise healthy women. Dysuria (likelihood ratio (LR) = 1.5), frequency of urination (LR=1.8), haematuria (LR=2) and back pain (LR=1.7) are all independently predictive of UTI. On the other hand, factors that reduce the likelihood of a lower UTI diagnosis include vaginal irritation (LR=0.2), complaint of vaginal discharge (LR=0.3), absence of dysuria (LR=0.5) and vaginal discharge on examination (LR=0.7).⁶ Therefore, in women presenting with classic UTI symptoms and an absence of vaginal symptoms, the probability of a UTI is so high that empiric treatment is warranted without performing urinalysis. Contrasting those, presenting with non-specific complaints (e.g. dysuria and vaginal discharge) are candidates for urinalysis by way of dipstick testing. Urine culture and sensitivity testing is not routinely recommended in healthy, pre-menopausal women, unless the risks associated with incorrect diagnoses are potentially serious, as is often the case with children.

When one or more typical clinical features of lower UTI coexist with risk factors for pyelonephritis (e.g. flank pain, fever) or complicated UTI (e.g. male gender), then urine culture and antimicrobial susceptibility testing is justified. This, however, remains subject to the clinical judgement of the health care provider. Significant bacteriuria is determined by way of urine culture testing in males without urinary symptoms but with positive dipstick tests.⁵

**Implications for pharmacy practice**

The majority of patients presenting with UTI symptoms in a community pharmacy are likely to have cystitis.² It is prudent for the pharmacist to rule out other potential causes for symptoms, to exclude pyelonephritis and to identify underlying risk factors for complications. These objectives are generally achieved through a medical history-taking. The patient interview should encompass a general history (e.g. age of patient, history of illnesses, pregnancy) and a special history that pertains to the presenting complaint (e.g. duration of symptoms, accompanying symptoms, medications used for current complaint). The relevance of eliciting some of this information as it relates to decisions about referrals is summarised in Table I. Furthermore, the risk factors for complicated UTI that should trigger a referral by community pharmacists are listed in Table II.⁷

**Treatment options**

The therapeutic objectives in the clinical management of UTI are to eradicate the
Uropathogen, relieve the symptoms (if any) and to prevent recurrences of infections. To this end, a range of antimicrobial and non-antimicrobial therapeutic options are recommended on the basis of strong research evidence on drug efficacy (microbiological and clinical cure rates), antimicrobial resistance rates and safety of regimens for the duration of treatment. These are reviewed in some detail below for uncomplicated UTI and recurrent infections, while general principles of therapy will be described for complicated UTIs collectively.

**Uncomplicated UTI**

**Acute uncomplicated cystitis in pre-menopausal and non-pregnant women**

Untreated uncomplicated cystitis in young, non-pregnant women is rarely associated with long-term adverse effects or mortality, often resolving spontaneously after several months. However, since many women experience demonstrable discomfort from the symptoms of cystitis, attempts to reduce the duration of symptoms through antimicrobial administration are advocated. The role of over-the-counter (OTC) medication in symptom reduction remains debatable. Antimicrobial treatment is usually initiated empirically and routine requests for urine cultures and sensitivity testing are uncommon. A number of oral antimicrobial drugs have been investigated for selected clinical outcomes and these include trimethoprim (TMP) or TMP and sulphamethoxazole (SMX), selected fluoroquinolones, fosfomycin trometamol, pivmecillinam and nitrofurantoin. The patient findings of these antimicrobial and OTC product trials are summarised below.

**Over-the-counter (OTC) medication**

With the exception of urinary alkalinisers, there is a general lack of evidence to support the use of various OTC products for the amelioration of dysuria. Alkalinising agents are known to normalise the urinary pH. Their empirical use in treating the symptoms of UTIs is, however, weakly underpinned by a single uncontrolled study of 205 women presenting with symptoms of cystitis. The majority of women, in whom there was no clear clinical evidence of bacterial infection, experienced symptom relief after a 2-day course of sodium citrate. No research studies have demonstrated the effectiveness of analgesics in relieving dysuria, and similarly there is no evidence to suggest that increasing fluid (water) intake aids the "flushing" of bacteria from the urinary tract.

**Duration of antimicrobial therapy**

Research evidence is in overwhelming favour of a 3-day course for the treatment of uncomplicated cystitis. Therapeutic regimens exceeding three days are associated with a higher proportion of adverse effects as determined by a systematic review of randomised controlled trials (RCTs) comparing the efficacy of antibiotic regimens for 3 days with those of longer duration in the treatment of uncomplicated UTI in women. While no differences were observed in the clinical or bacteriological failure rates, fewer adverse effects were reported in the arm assigned to receive the shorter course of treatment (RR 0.83, 95%CI 0.79-0.91).

**TMP and TMP-SMX (co-trimoxazole)**

Co-trimoxazole is the most widely studied (30 studies) drug for uncomplicated cystitis in women and is regarded as the agent of choice for this condition when TMP resistance rates fall below 10–20%. In terms of microbiological cure rates and adverse effects, TMP compared favourably with co-trimoxazole, although at least one large-scale study (>10 000 participants) demonstrated that a 5–7 day course of TMP was superior to a 3-day regimen.

**Fluoroquinolones**

Comparative trials featuring three-day regimens of fluoroquinolones (ciprofloxacin, fleroxacin, norfloxacin and ofloxacin) and co-trimoxazole have demonstrated equivalence in terms of efficacy and safety. These selected fluoroquinolones are thus recommended as alternative first-line agents when resistance to TMP exceeds 10%. One trial showed comparable efficacy between three-day regimens of levofloxacin (250 mg od) and ofloxacin (200 mg twice daily), although more side effects were experienced in individuals assigned to the latter regimen.

In another study, a 3-day course of ciprofloxacin sustained release (500 mg once daily) was as effective and safe as conventional ciprofloxacin (250 mg twice daily) for three days. Resistance to fluoroquinolones is on the incline in certain countries and...
EAU recommends that alternative regimens (Table III) be selected when rates of resistance are known to exceed 10%.

**β-lactams**

There is an absence of large enough comparative trials assessing the relative efficacy and safety of the aforementioned agents and β-lactams (second or third generation oral cephalosporins and aminopenicillin plus a β-lactamase inhibitor (BLI)), although β-lactams as a class of antibiotics are generally less effective than fluoroquinolones and TMP or co-trimoxazole. In one adequately sized study comparing 7 days of pivmecillinam with that of a 3-day course, the efficacy for both regimens was equivalent, although the rate of recurrence associated with the shorter regimen was noted.

Pivmecillinam shows low resistance rates for *E coli* and other *Enterobacteriaceae*, and no cross-resistance to other antimicrobials used to treat UTI.

**Fosfomycin**

A meta-analysis comparing a single dose of fosfomycin trometamol with other drugs (ranging from single dose to 7 day regimens) on 2048 UTI patients in 13 trials, identified short-term bacteriological eradication in an equal proportion of patients on fosfomycin (85.6%) and other treatments (86.7%). Furthermore, in a recent large trial (n = 547) equal microbiological cure rates (83%) were attained for patients on a single dose regimen of fosfomycin and a 5-day course of TMP. Since the inception of single-dose regimens in various countries, resistance rates have remained low and without cross-resistance to other antimicrobials used for the treatment of UTI.

**Nitrofurantoin**

A short course (3 days) of nitrofurantoin is regarded as an inferior choice to a 5–7 day regimen in the management of uncomplicated cystitis caused by bacteria. Nitrofurantoin has a limited spectrum of activity against the micro-organisms implicated in cystitis and has notable inactivity against *P mirabilis* and *Klebsiellae* spp. Of great concern among the elderly is the side effect profile, which includes acute and chronic pulmonary syndrome. Despite long-standing clinical use of the drug, resistance remains low.

The European Association of Urology (EAU) has developed therapeutic recommendations for uncomplicated cystitis, which are based on the aforementioned research evidence and expert opinions. These recommendations are summarised in Table III and graded with respect to strength (A to C). “A” denotes recommendations based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial, “B” denotes recommendations based on well-conducted clinical studies, but without randomised clinical studies and a “C” denotes recommendations made despite the absence of directly applicable clinical studies of good quality.

**Acute uncomplicated pyelonephritis in pre-menopausal and non-pregnant women**

Untreated or inadequately treated pyelonephritis may lead to severe complications, including septicaemia. Recommendations for the treatment of uncomplicated pyelonephritis in young women are based on the conclusions drawn from an analysis of 10 prospective RCTs. These recommendations are enumerated below.

---

**Table III: Recommended oral antimicrobial regimens for treatment of acute uncomplicated bacterial cystitis and pyelonephritis in adult pre-menopausal non-pregnant women according to grade of recommendation**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosage (duration)</th>
<th>GOR</th>
<th>Dosage (duration)</th>
<th>GOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cystitis</strong></td>
<td></td>
<td></td>
<td><strong>Pyelonephritis</strong></td>
<td></td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>1000 mg bid (3 days)</td>
<td>A</td>
<td>200 mg bid (10 days)</td>
<td>B</td>
</tr>
<tr>
<td>Ciprofloxacin*</td>
<td>250 mg bid (3 days)</td>
<td>A</td>
<td>500 mg bid (7 days)</td>
<td>A</td>
</tr>
<tr>
<td>Cipro XR</td>
<td>500 mg od (3 days)</td>
<td>A</td>
<td>1000 mg od (7 10 days)</td>
<td>A</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>-</td>
<td>A</td>
<td>400 mg od (10 days)</td>
<td>A</td>
</tr>
<tr>
<td>Fosfomycin trometamol</td>
<td>3000 mg SD (1 day)</td>
<td>A</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Levofloxacin*</td>
<td>250 mg od (3 days)</td>
<td>A</td>
<td>250 mg od (10 days)</td>
<td>A</td>
</tr>
<tr>
<td>Lomefloxacin</td>
<td>-</td>
<td>-</td>
<td>400 mg od (10 days)</td>
<td>B</td>
</tr>
<tr>
<td>Nitrofurantoin*</td>
<td>50 100 mg tid (5 7 days)</td>
<td>B</td>
<td>100 mg SR (5 7 days)</td>
<td>B</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>400 mg bid (3 days)</td>
<td>A</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ofloxacin*</td>
<td>200 mg bid (3 days)</td>
<td>A</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pivmecillinam</td>
<td>200 mg bid (7 days)</td>
<td>B</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TMP*</td>
<td>200 mg bid (5 7 days)</td>
<td>A</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TMP-SMX*</td>
<td>160/800 mg bid (3 days)</td>
<td>A</td>
<td>160 mg/800 mg bid (14 days)</td>
<td>B</td>
</tr>
</tbody>
</table>

*These substances are only recommended for empirical therapy when the resistance rate of *E coli* is < 20%.

GOR = Grade of recommendation; C = cystitis; P = pyelonephritis; bid = twice daily; Cipro XR = ciprofloxacin sustained release; od = once daily; SD = single dose; tid = thrice daily; TMP = trimethoprim; TMP-SMX = trimethoprim and sulphamethoxazole

Adapted from reference 5

1. TMP-SMX is preferred over ampicillin.
2. A 14-day regimen with TMP-SMX appears to be adequate for the majority of women.
3. One week of therapy with ciprofloxacin (500 mg twice daily) showed superior efficacy (higher rates of bacterial eradication) and safety (lower rates of adverse effects) when compared with a two week regimen with TMP-SMX (960 mg twice daily).
4. Other fluoroquinolones proved to be comparable to ciprofloxacin 500mg twice daily, viz, ciprofloxacin extended release formulation (1000 mg once daily), gatifloxacin (400 mg once daily), levofloxacin (250 mg twice daily), and lomefloxacin (400 mg once daily).
5. No sufficiently powered comparative studies have been conducted on β-lactam antibiotics versus fluoroquinolones or TMP-SMX, although some evidence suggests that a 10-day therapy with cefpodoxime proxetil 200 mg twice daily was comparable in clinical efficacy to ciprofloxacin 500 mg twice daily.
6. Fluoroquinolones (orally for 7 days) are recommended as first-line agents in re-
gions where resistance is still low (<10%).

7. Aminopenicillin plus a B-lactamase inhibitor or 3rd generation cephalosporins are suitable alternatives to fluoroquinolones when resistance rates rise beyond 10% or where contraindications (e.g. pregnancy, lactation and adolescence) preclude its use.

Table III summarises oral antimicrobial treatment options for acute uncomplicated bacterial pyelonephritis in adult pre-menopausal non-pregnant women according to grade of recommendations as defined earlier.\(^5\)

**Other**

**Urethritis**
The EAU has issued guidelines for the therapeutic management of urethritis that comply with the recommendations of the Centre for Disease Control and Prevention. Dual antimicrobial therapy is recommended due to extensive evidence of co-existing gonorrhoea and chlamydial infections. The following antimicrobial regimens have demonstrated efficacy in the treatment of gonorrhoea: cefixime, 400 mg orally as a single dose; ceftriaxone, 125 mg intramuscularly (with local anaesthetic) as a single dose; ciprofloxacin, 500 mg orally as a single dose; ofloxacin, 400 mg orally as single dose, and levofloxacin, 250 mg orally as a single dose. To ensure antimicrobial coverage of both micro-organisms, an additional regimen is known to be effective against *Chlamydia trachomatis* should be selected from the following two options: azithromycin 1g orally as single dose or doxycycline 100mg orally twice daily for 7 days.\(^5\)

**UTI in pregnancy**

There is some debate as to whether UTI in pregnancy should be classified as complicated or uncomplicated. Pregnant women are particularly susceptible to asymptomatic bacteriuria and cystitis and if left untreated, both of these clinical conditions could potentially develop into pyelonephritis, premature delivery and foetal mortality.\(^7\) As such, it is prudent to screen all pregnant women for asymptomatic bacteriuria and to initiate antibiotic therapy promptly. Comparative studies evaluating short-term and longer courses of therapy yielded inconclusive evidence, however, due to the high risks of adverse effects associated with long-term therapy, experts recommend the shortest duration proven to be effective in non-pregnant women. Conventional therapy should be followed, except where contraindications exist in the first trimester (e.g. quinolones, tetracycline and TMP) and last trimester (e.g. sulphonamides).\(^5\)

**UTI in post-menopausal women**

In post-menopausal women, susceptibility to UTI increases due to a deficiency of oestrogen. In the absence of underlying tumours, obstructive problems, detrusor failure or genital infection, the conventional therapeutic schedule for uncomplicated UTI in pre-menopausal women should be followed.\(^5\)

**Acute uncomplicated UTIs in young men**
The incidence of uncomplicated UTI in males between the ages of 15 and 50 years is very low and as such, there is no data from controlled treatment studies. Experts recommend the use of standard regimens for uncomplicated cystitis and pyelonephritis in adult pre-menopausal women. Since prostatic involvement is commonly associated with pyelonephritis in males, empiric therapy should include agents that penetrate tissue and prostatic fluid, such as the fluoroquinolones.\(^5\)

**Asymptomatic bacteriuria**

This clinical entity is equally common among the healthy and those with anatomical or physiological problems of the urogenital tract. Screening and treatment is only advocated for selected groups such as pregnant women (referred to earlier) and patients undergoing traumatic urological interventions. In the case of the latter, antimicrobial therapy should be initiated before the procedure.\(^5\)

**Complicated UTI**
The empirical treatment of a UTI is based on the knowledge of the spectrum of possible uropathogens and antibiotic resistance patterns, and additionally, in the case of complicated UTI, an assessment of the underlying clinical condition. Resistance due to the high likelihood of relapse or reinfection is, however, a concern when using empirical therapy and this should be replaced with more specific therapy after the micro-organisms are identified through urine culture. Numerous therapeutic trials have been published on the use of specific antimicrobial therapy for complicated UTI, however, the lack of clearly defined variables in these studies has undermined their value in clinical decision-making. Limited evidence has shown that there is no superior agent among drugs that have shown microbial susceptibility. The most effective duration of therapy is 7–14 days, although a 21-day course of antimicrobials may be required for certain clinical presentations. An important policy in the management of complicated UTI is the routine follow-up or post-therapy urine cultures at 5–9 days after completion of therapy and again 4–6 weeks later.\(^5\)

**Prevention**

A UTI is defined as recurrent when it occurs on more than three occasions annually or more than twice over a 6-month period. Both drug and non-drug regimens have been investigated to varying degrees, although no direct comparative studies have been conducted as yet. The most widely studied and highly recommended prophylactic agents are antibiotics, while relatively sparse evidence underlies recommendations for using non-antibiotic alternatives such as methenamine hippurate, hormonal therapy, and cranberry products.

**Antibiotics**

A Cochrane review of 19 RCTs (n = 1120) investigating the efficacy of antibiotic prophylaxis over a 6-month period (against either placebo or non-antibiotic) showed, within this time frame, an overall lower risk of recurrence either microbiologically (RR 0.21, 95% CI 0.13-0.34) or clinically (RR 0.15, 95% CI 0.08-0.28) in the antibiotic-assigned groups. This protective effect did not extend beyond the period of prophylaxis, as evidenced by the lack of significantly lower risks of experiencing one recurrent infection after 6 months while on antibiotics (RR 0.82, 95% CI 0.44-1.53). The recommended regimens informed by individual trials are summarised in Table IV.\(^5\)

**Oestrogens**

The underlying cause of recurrent UTI in women over the age of 50 is post-menopausal oestrogen deficiency. In a meta-analysis of RCTs to establish the effect of oestrogen (oral and vaginal) on recurrent infections, oral oestrogens did not reduce recurrences of UTI compared to a placebo (4 studies, 2798 women: RR 1.08, 95% CI 0.88-1.33). Vaginal oestro-
gen proved to protect against recurrent infection in two trials that investigated different methods of application; a lower risk of recurrence, favouring oestrogen use, was reported in both studies (RR 0.25, 95% CI 0.13-0.5 and RR 0.64, 95%CI 0.47-0.86).  

**Methenamine hippurate**

Thirteen RCTs (n = 2032) were reviewed systematically for trends in respect of the efficacy of methenamine against a control/no drug. An analysis of the pooled results using a random effects model showed disparities in efficacy based on renal function. Within the subgroup of participants with renal abnormalities, the rate of UTI recurrence between the active and control group lacked statistical significance; the relative risk of developing symptomatic UTI and bacteriuria while receiving methenamine was 1.54 (95% CI 0.38-6.2) and 1.29 (95% CI 0.54-3.07) respectively. On the other hand, methenamine lowered the risk of UTI in patients without undergoing kidney problems with relative risk values of 0.24 (95% CI 0.07-0.89) for a diagnosis by clinical examination and 1.29 (95% CI 0.37-0.85) for positive bacteriuria.  

**Cranberry juice and cranberry products**

Ten studies (n = 1049) investigating cranberry products (juice or tablets versus placebo, juice or water) were included in a Cochrane review to establish their effectiveness as prophylactic agents. The output from a random effects model showed that cranberry products significantly reduced the incidence of UTIs at 12 months (RR 0.65, 95% CI 0.46 to 0.90) compared with placebo/control, although the protective effect was confined to women with recurrent UTI. All the studies sustained a high drop out rate and this, coupled with a high incidence of reported side effects, indicates that cranberry products may not be acceptable over a long period of time. Further comparative studies are required to determine the most suitable dose and dosing form for cranberry.  

**Conclusion**

There is certainly no shortage of therapeutic options available to the medical practitioner when treating the gamut of UTIs. However, in light of increasing worldwide rates of antimicrobial resistance, a call for more judicious prescribing practices according to evidence-based management guidelines is necessary and urgent one. Pharmacists play an integral role in policing inappropriate medication prescribing and it is therefore incumbent on them to become familiar with up-to-date evidence-based treatment protocols. Additionally, pharmacists should continue to institute routine safeguards against the myriad of reasons for patient non-compliance to antimicrobial therapy.  

### Table IV: Grade A recommendations for antimicrobial prophylaxis of recurrent uncomplicated UTI in women  

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard regimen</td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>50 mg od</td>
</tr>
<tr>
<td>Nitrofurantoin macrystals</td>
<td>100 mg od</td>
</tr>
<tr>
<td>TMP + SMX</td>
<td>40/200 mg od or 3 times weekly</td>
</tr>
<tr>
<td>TMP</td>
<td>100 mg od</td>
</tr>
<tr>
<td>Fosfomycin trometamol</td>
<td>3 g every 10 days</td>
</tr>
</tbody>
</table>

**“Breakthrough” infections**

| Ciprofloxacin | 125 mg od    |
| Norfloxacin | 200-400 mg od |
| Pefloxacin | 800 mg once weekly |

**During pregnancy**

| Cephalexin | 125 mg od |
| Cefacol | 250 mg od |
| od = once daily; TMP = trimethoprim; SMX = sulphamethoxazole |

Taken at bedtime for a duration of 6 months.

**References:**