Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women (Review)

Lutters M, Vogt-Ferrier NB



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[Intervention review]

Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Monika Lutters¹, Nicole B Vogt-Ferrier²

¹Apotheke, Kantonsspital Baden, Baden, Switzerland. ²Unité de Gérontopharmacologie Clinique, Hôpitaux Universitaires de Genève, Thônex, Switzerland

Contact address: Monika Lutters, Apotheke, Kantonsspital Baden, Baden, CH-5404, Switzerland. Monika.Lutters@ksb.ch. (Editorial group: Cochrane Renal Group.)

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ABSTRACT

Background

Urinary tract infections (UTI) are common in elderly patients. Authors of non systematic literature reviews often recommend longer treatment durations (7 to 14 days) for older women, but the evidence for such recommendations is unclear.

Objectives

To determine the optimal duration of antibiotic treatment for uncomplicated symptomatic lower UTI in elderly women.

Search strategy

We contacted known investigators and pharmaceutical companies, screened reference lists of identified articles, reviews and books, and searched MEDLINE, EMBASE, CINAHL, Healthstar, Popline, Gerolit, Bioethics Line, *The Cochrane Library*, Dissertation Abstracts International and Index to Scientific & Technical Proceedings without language restriction.

Date of most recent search: 7 May 2008.

Selection criteria

All randomised controlled trials (RCTs) comparing different treatment durations of oral antibiotics for uncomplicated symptomatic lower UTIs in elderly women were included. Whenever possible we obtained outcome data for older women included in studies with a broader age range. We excluded patients with fever, flank pain or complicating factors; studies with treatment durations longer than 14 days and prevention studies.

Data collection and analysis

The two authors independently assessed study quality and extracted data. Statistical analyses were performed using the random effects model and results expressed as risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes with 95% confidence intervals (CI).

Main results

Fifteen studies (1644 elderly women) were included. Three studies compared single dose with short-course treatment (3 to 6 days), six compared single dose with long-course treatment (7 to 14 days) and six compared short- with long-course treatment. Methodological quality of all studies was low except for a more recent geriatric study. There was a significant difference for persistent UTI between single dose and short-course treatment (RR 2.01, 95% CI 1.05 to 3.84) and single versus long-course treatment (RR 1.93, 1.01 to 3.70 95% CI), in the short-term (< 2 weeks post-treatment) but not at long-term follow-up or on clinical outcomes. Patients preferred single dose treatment (RR 0.73, 95% CI 0.60 to 0.88) to long-course treatments, but this was based on one study comparing different antibiotics. Short versus longer treatments showed no significant difference in efficacy. Rate of adverse drug reactions increased significantly with longer treatment durations in only one study.

Authors' conclusions

Short-course treatment (3 to 6 days) could be sufficient for treating uncomplicated UTIs in elderly women, although more studies on specific commonly prescribed antibiotics are needed.

PLAIN LANGUAGE SUMMARY

Antibiotic duration for treating uncomplicated symptomatic lower urinary tract infection in elderly women

As people age (especially women), they become more prone to infections in the bladder (UTI - urinary tract infections). Older people are more likely to have adverse reactions to drugs. Up to the present time older women with uncomplicated UTI were treated longer than younger patients - without any scientific evidence and with an increased risk of adverse drug reactions. We defined three groups of treatment durations: single-dose, short (3 to 6 days) and longer courses (7 to 14 days).

We identified 15 studies (1644 elderly women) comparing single dose, short-course (3 to 6 days) and long course (7 to 14 days) antibiotic treatment for uncomplicated symptomatic UTI in elderly women. Our review suggests that single dose treatments are less effective than short or long courses, but better accepted by the patients. On the other hand longer courses may have more side effects. On the basis of the evidence available at present, an antibiotic treatment of 3 to 6 days could be sufficient for treating uncomplicated UTIs in elderly women, although more studies on specific, commonly prescribed antibiotics are needed.

BACKGROUND

Urinary tract infections (UTIs) are very common in older people. It is the most frequent bacterial infection recorded in older people, followed by pneumonia and skin/soft tissue infections (Emori 1991; Michel 1991; Smith 1994). Bacteriuria is present in less than 5% of women and less than 0.1% of men in the young to middle-age age range (Kaye 1980), compared with at least 20% of women and 10% of men over the age of 65 (Sobel 1990). The prevalence of bacteriuria depends on where a person is living and is very high in institutionalised women with functional disability (25% to 50%) (Abrutyn 1991; Nicolle 1993).

The causes of the increased susceptibility to UTI in older people are multiple: decline in cell-mediated immunity, altered bladder defences due to obstructive uropathy, neurogenic bladder dysfunction, increased bacterial receptivity of uroepithelial cells (Reid 1984), increased risk of contamination due to faecal and urinary incontinence as well as urethral instrumentation and catheterization, and decrease in prostatic and vaginal antibacterial factors associated with changes in zinc levels, urinary and vaginal pH, and hormones, especially lack of estrogens (Sant 1987).

The bacteriological features of UTI also differ between elderly and young patients. Escherichia coli and Staphylococcus saprophyticus are the most common causative organisms of UTI in young adults, accounting for 80% to 90% of all cases (Winickoff 1981). E. coli is also the most common pathogen in elderly women, varying from 90% in outpatients to 45% in hospitalised patients. In contrast with younger people, Proteus, Klebsiella, Enterobacter, Serratia, Pseudomonas spp., and other gram-negative bacteria as well as enterococci are also frequently encountered (Kunin 1987). S. saprophyticus is very rarely isolated in older people. In addition, elderly patients often show a different response to treatment (Harding 1991; Nolan 1988). The most important factors that affect pharmacokinetic and pharmacodynamic drug response in elderly patients are a decline in renal function, reduced body weight, decreased response to homeostatic changes, presence of multiple underlying disease, and polypharmacy, which lead to an increased risk of drug interactions and toxicity (Borrego 1997). All these differences suggest that older patients with UTI need a different treatment approach than younger patients.

UTIs are classified as either asymptomatic or symptomatic UTIs. Symptomatic UTI include uncomplicated lower (cystitis) and up-

per UTI (pyelonephritis) and complicated infections of the lower or upper urinary tract (Stamm 1992; Wood 1996). UTIs in men are considered as complicated infections.

In young women with uncomplicated lower UTI, many studies have shown that short-term treatments with antibiotics (1 to 3 days) are as effective as the traditional longer treatments (7 to 14 days), are less expensive, associated with fewer side effects and result in better compliance. However, the results from several studies and two systematic reviews have shown that single-dose treatment is less effective than longer treatments (Norrby 1990; Warren 1999). Most authors, including the Infectious Diseases Society of America, recommend a 3-day treatment for lower, uncomplicated UTI in young women (Norrby 1990; Warren 1999). In elderly women, the situation is less clear. Excessively long antimicrobial therapy may have negative implications with respect to community levels of antimicrobial resistance (Goessens 2007; Tam 2007).

We performed a critical quality assessment of the many published review articles on UTIs in older people (Lutters 2000). The overall methodological quality was low (mean score 2.0 1.1 on a scale of 9). In particular, none of the identified reviews specified the methods of identifying, selecting and validating the included information. The resulting treatment recommendations varied enormously, especially for the treatment duration for uncomplicated lower UTI in elderly women, which differed from 3 to 10 days (Wood 1996). Many authors did not recommend short treatment (1 to 3 days) in elderly women because it is said to be less effective than in younger women (Baldassarre 1991; Humbert 1992; Nicolle 1992; Nygaard 1996; Stamm 1993). However, this recommendation was based either on previous review articles or on results from three studies which did not specifically assess efficacy in elderly women. Indeed, two of these studies compared women over and under 40 years old (Pfau 1984; Saginur 1992). The participants mean age was 26 in one study and 36 years in the other (Pfau 1984; Saginur 1992). The third study included only women with urinary catheters, i.e. complicated UTI (Harding 1991).

Since this survey, the Infectious Diseases Society of America published guidelines on the treatment of UTI based on an extensive review of the literature using meta-analytical techniques (Warren 1999). However their findings applied primarily to younger women and did not include clinical outcomes like improvement of urinary symptoms.

We performed this systematic review to determine the optimal treatment duration of uncomplicated symptomatic lower UTIs in elderly women. Men and patients with upper or complicated UTI were excluded from this review because they usually require longer and more aggressive treatment (Baldassarre 1991; Childs 1996; Nicolle 1994; Wood 1996) Patients with asymptomatic UTI were also be excluded, because there is consensus in the medical literature that elderly patients without symptoms should not be treated (Humbert 1992).

First published in 2002, our objective is to update this review as new studies appear.

OBJECTIVES

To determine the benefits (clinical and bacteriological efficacy) and harms (adverse drug reactions) of different durations of antibiotic treatment for uncomplicated symptomatic lower UTIs in elderly women.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) comparing different treatment durations of oral antibiotics for uncomplicated lower UTIs in elderly women.

Types of participants

Elderly women (over 60 years old or as defined by the study), with acute uncomplicated lower UTI, (i.e. symptoms of dysuria, urgency, frequency or suprapubic pain) and a significant positive urine culture ($\geq 10^3$ colony forming units (cfu)/mL) and pyuria (≥ 5 leukocytes/mm³) (Naber 1990; Rubin 1992; Stamm 1992). Studies including other persons (e.g. men, younger persons, patients with asymptomatic bacteriuria) were included if those patients made up $\leq 20\%$ of all participants or if separate data for elderly women were available. If a study included such a mixed population without giving details on subgroups, we contacted the authors of the study to ask for separate data for the group of elderly women with acute uncomplicated lower UTI.

Patients with pyelonephritis (symptoms of fever or flank pain) and those with complicating factors such as indwelling or intermittent urinary catheters, > 100 mL post-void residual urine, obstructive uropathy, vesicoureteral reflux and other urological abnormalities, azotaemia due to intrinsic kidney disease or kidney transplantation, were excluded.

Types of interventions

Treatment group

Any oral antibiotic treatment used for the treatment of UTI.

Control group

Any oral antibiotic treatment with a different treatment duration. We preferred studies comparing the same antibiotic with the same dosage (except when a single dose is used), but a different treatment

duration. We included only antibiotic treatments used at a dose recommended in an official pharmacopoeia for the treatment of lower uncomplicated UTI.

We also included studies comparing a different antibiotic with a different treatment duration, because they provided more information, especially on clinical outcomes. However, these studies are confounded by the different antibiotics used (see discussion). To anticipate large variations in durations, we defined the following categories of duration and made comparisons between these:

- 1. Single dose
- 2. Short-course (3 to 6 days)
- 3. Long-course (7 to 14 days)
- 4. 3 to 14 days (combination of group 2 and 3)

Longer as well as prophylactic treatments were excluded.

Types of outcome measures

Studies which measured at least one of the following outcomes (as defined in the study report):

- clinical treatment failure: persistence of urinary symptoms (i.e. dysuria, frequency, urgency and suprapubic pain), as study defined
- mental and functional status (e.g. confusion, weakness, falls)
- incidence of new symptoms of cystitis (after initial clinical cure)
- development of pyelonephritis, urosepsis or other renal complications
- long-term mortality, all cause and related to UTI
- total rate of adverse drug reactions (as study defined)
- discontinuations of treatment due to adverse drug reactions
- quality of life
- convenience for the patient (e.g. compliance, satisfaction with the treatment)
- persistent UTI (significant positive urine culture at followup: ≥ 10³ cfu/mL)
- recurrence of bacterial infection after initial eradication of bacteria (i.e. relapse with the same organism or reinfection with a different one)

We anticipated that studies would report outcomes at different time points. If possible, outcomes were to be recalculated for common time points from the raw data. As this was not possible, outcomes were pooled for short-term effects (i.e. during, immediately after or up to two weeks post-treatment) and long-term effects (> two weeks post-treatment).

Search methods for identification of studies

Initial search

We searched the following databases: MEDLINE, EMBASE, CINAHL, Healthstar, Popline, Gerolit, Bioethics Line, *The Cochrane Library*, the trial register of the Cochrane Renal Group, Dissertation Abstracts International (1991-95), Index to Scientific & Technical Proceedings (1978-85).

In MEDLINE, the first two sections of the optimal MEDLINE search strategy (Dickersin 1994) were applied to identify RCTs, and combined with the terms used in Appendix 1 - *Electronic Databases*

EMBASE was searched by a professional librarian.

For the other databases a similar, often simplified search strategy was used.

The reference lists of identified articles, reviews, books and book chapters on the treatment of infections in older people were searched. Available abstracts of conferences in the fields of infectious diseases, geriatric medicine and pharmacology were screened. Unpublished data were sought from known authors working in this field as well as from pharmaceutical companies marketing antibiotics that are used in UTIs.

Review updates

For updates, electronic searches in CENTRAL, the Cochrane Renal Group's specialised register and MEDLINE were performed. No language restriction was applied. Articles written in languages other than those familiar to the authors have been translated and evaluated by native speakers.

Date of most recent search: May 2008

Data collection and analysis

Study selection and data extraction were independently performed by both authors, using specifically designed forms (available on request from the authors). Authors were not blinded to authors or text source, because a RCT has shown that blinding did not significantly decrease bias when conducting meta-analyses of RCTs (Berlin 1997). Discrepancies were resolved by discussion, or, if no consensus could be reached, by seeking advice from a third party. Where important data have not been reported, triallists were contacted to get the necessary information.

The following data were extracted for each included study:

- study design
- method of randomizations
- blinding
- number of participants
- exclusions after randomizations
- loss-to-follow-up
- setting (community, long-stay institution, hospital)
- description of the study population
- detailed description of the treatments used (substance, galenical form, dosage, duration)
- · description and results of all measured outcomes

The level of allocation concealment was assessed using the criteria described in the Cochrane Handbook (Mulrow 1994). Studies were graded A if the assigned treatment was adequately concealed

prior to allocation, B if there was inadequate information to judge concealment, and C if the assigned treatment was clearly not concealed prior to allocation. All data were analysed together, and then a subgroup analysis was performed to determine if the inclusion of lower quality studies (levels B and C) affects the overall result. To further test the robustness of the results, we planned to perform several other subgroup analyses (if enough studies were available):

- blinded versus non blinded studies
- studies with a high versus a low drop-out rate
- studies including only elderly persons versus studies with a mixed population.

Statistical assessment

Risk ratio (RR) and 95% confidence intervals (CI) were used for dicotomous outcomes and mean difference (MD) for continuous outcomes. Heterogeneity was tested using the I² statistic (Higgins 2003). I² values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity. The RR from each study were combined using a random effects model. If enough studies were identified, variables which are likely to influence the outcome of the studies were assessed in subgroup analyses. Such variables include:

- studies comparing the same antibiotic
- different antibiotic classes (e.g. beta-lactams, quinolones) or molecules
- place of residence (community, long-stay institution, hospital)
- patients' age (over 75 years old).

We planned to use the funnel plot approach to assess the likelihood of publication bias.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Our initial literature search identified more than 7000 references (see Appendix 2 - *Results of Initial Search*). After triage of titles and abstracts, we retained 69 articles (of 56 authors) that could be included in our review. However, most of these articles did not report precise age data of included patients, and a subgroup analysis of elderly patients was often missing. We contacted the authors of all these studies, but we got either no answer, the raw data were no longer available or they only included younger patients. We finally included only those studies which were done in elderly populations or which reported separate outcome data for elderly patients.

In most of the cases, the two authors took the same decision of selection or non-selection of identified references (94%). Although

they screened only a part of all identified references two times independently, none of the finally selected studies would have been missed (see Appendix 3 - Inter-individual variability of study selection).

We included 15 studies in our review. Only seven of these studies (Andersen 1986; Gellermann 1988; Flanagan 1991; Lacey 1981; van Merode 2005; Vogel 2004) compared the same antibiotic in different treatment durations. We did a separate analysis for those seven studies. The 15 included studies were published between 1981 and 2005. Eleven were discovered by a MEDLINE search, one in EMBASE and one in the Cochrane Renal Group's specialised register. The remaining two studies were found by screening the bibliographies of identified studies and reviews and by contacting pharmaceutical companies (see Appendix 4 -Sources of included studies). We did not find duplicate publications. The majority of the 15 studies were conducted in European countries. Ten studies took place in an outpatient setting, two in hospitals, one in both settings, and two studies did not describe the setting. Two studies included men (Ferraro 1990; Lacey 1981) and Lacey 1981 also included asymptomatic and complicated UTIs. In nine studies (Andersen 1986; Gellermann 1988; Guibert 1996; Guibert 1997; Jardin 1990; Matsumoto 1994; Piipo 1990; Stein 1992; van Merode 2005) we considered only the outcome results of the subgroup of elderly women. Elderly patients were defined differently throughout the studies (i.e. over 50, 58, 60, 63 or 65 years), so seven studies (or analysed subgroups) also included patients under 60 years. All these studies compared different antibiotics.

The presence of resistant organisms in the urine was handled differently throughout the studies. Flanagan 1991 did not use one specific antibiotic/treatment group but chose the treatment from four antibiotics according to the sensitivity of urinary pathogens. Piipo 1990 and Vogel 2004 stated that all initially isolated bacteria were sensitive to the study antibiotic. Two studies (Lacey 1981; Raz 1996) excluded all patients with resistant organisms. Guibert 1993 and Stein 1992 excluded these patients only for the evaluation of the bacteriological efficacy, but included them for all other outcomes. van Merode 2005 included also resistant uropathogens and gave detailed outcome information of patients with trimethoprim-resistant isolates. The remaining seven studies did not mention how they handled resistant pathogens. However they did not formally exclude resistant uropathogens from the study.

All 15 studies used various antibiotic treatment regimens (e.g. sulfamethizole, trimethoprim, fosfomycin trometamol, cephalexin, and various fluoroquinolones). Six studies compared single dose treatment with short-term (3 to 6 days) treatment (Andersen 1986; Gellermann 1988; Guibert 1996; Jardin 1990; Lacey 1981; Matsumoto 1994), three compared single dose to longer treatment durations (7 to 14 days) (Ferraro 1990; Flanagan 1991; Guibert 1993) and five studies assessed short-term versus long-term treatment (Guibert 1997; Piipo 1990; Raz 1996; Stein 1992; Vogel 2004). In the last update we identified one study comparing a 3day with a 5-day treatment (van Merode 2005). We included this

study in a separate comparison group.

With respect to the seven studies comparing the same antibiotic, three studies compared single dose with short-term treatment (Andersen 1986; Gellermann 1988; Lacey 1981), one study compared single dose versus long-term treatment (Flanagan 1991), two compared 3-day with 7-day treatment (Piipo 1990; Vogel 2004), and one study 3 days versus 5 days of treatment (van Merode 2005).

Risk of bias in included studies

Allocation concealment

In only five studies (Guibert 1996; Guibert 1997; Piipo 1990; Stein 1992; Vogel 2004) the assigned treatment was adequately concealed prior to allocation (numbered boxes, by telephone, numbered sealed envelopes). In eight studies (Andersen 1986; Ferraro 1990; Gellermann 1988; Guibert 1993; Jardin 1990; Lacey 1981; Matsumoto 1994; Raz 1996; van Merode 2005) the allocation concealment was not clear or not described, and Flanagan 1991 used an open random list.

Randomisation method

The method of randomisation was described in 6/15 studies (random tables or computer generator) (Flanagan 1991; Gellermann 1988; Guibert 1993; Stein 1992; van Merode 2005; Vogel 2004).

Blinding

In nine studies, neither patients nor outcome assessors were blinded to treatment (Ferraro 1990; Guibert 1993; Guibert 1996; Guibert 1997; Jardin 1990; Matsumoto 1994; Raz 1996; Flanagan 1991; Gellermann 1988). Of the remaining six studies, four were double-blind (Andersen 1986; Piipo 1990; Stein 1992; Vogel 2004) and two were single-blind (Lacey 1981; van Merode 2005). Only two studies provided an intention-to-treat analysis of the results (Gellermann 1988; Vogel 2004). Eleven studies described why patients had been excluded after randomisation (Flanagan 1991; Guibert 1993; Guibert 1996; Guibert 1997; Jardin 1990; Lacey 1981; Piipo 1990; Raz 1996; Stein 1992; van Merode 2005; Vogel 2004;).

Baseline characteristics

Baseline characteristics of the different treatment groups were described and compared in 11 studies (Andersen 1986; Flanagan 1991; Gellermann 1988; Guibert 1993; Guibert 1996; Guibert 1997; Jardin 1990; Lacey 1981; Raz 1996; Stein 1992; Vogel 2004). In 8/15 studies there was no statistically significant difference between the groups (Ferraro 1990; Gellermann 1988; Guibert 1993; Guibert 1996; Guibert 1997; Lacey 1981; Matsumoto 1994; Piipo 1990).

Sample size/power calculation

Eight studies described a sample size and power calculation (Guibert 1993; Guibert 1996; Guibert 1997; Jardin 1990; Raz 1996; Stein 1992; van Merode 2005; Vogel 2004). The total number of patients enrolled in these studies ranged from 60 to 595 patients. Sample size for elderly patients (used for the meta-analysis) ranged from 23 to 482 subjects assessed for outcome analysis, most included < 100 elderly women.

The quality of the seven studies comparing the same antibiotic was not better than the overall quality of studies (2/7 studies were graded A for allocation concealment, 5/7 single- or double-blinded), but overall the most recently published study (Vogel 2004) showed greater attention to study design quality. See Appendix 5 - *Quality of included studies*.

Effects of interventions

The clinical failure rate (persistence of urinary symptoms), our main outcome parameter, was reported in only 7/15 studies. In contrast, the bacteriological eradication rate was always reported. In three studies, the bacterial eradication rate was not given for the subgroup of elderly patients (in case of studies with mixed populations). Adverse drug reactions were evaluated in most studies, but these data were often missing for the subgroup of elderly patients. Other outcome parameters such as quality of life or the development of complications (e.g. pyelonephritis, urosepsis) were not reported at all. Due to the variety of included studies (i.e. comparison of various treatment durations) and the resulting classification into five comparison groups, the data of only one study were available for many outcome parameters.

Guibert tested in two studies the acceptability of single dose versus 3 days (Guibert 1996) and 10 days of treatment (Guibert 1993). Patients were asked if they were "very satisfied," "satisfied", "little satisfied" or "not satisfied" with the treatment.

Single dose versus short-course treatment

Persistent UTI (i.e. significant positive urine culture at follow-up)

The rate of persistent UTI at short-term follow-up (\leq two weeks post-treatment) was significantly higher for single dose therapy compared to short-course treatment (Analysis 1.1: RR 2.01, 95% CI 1.05 to 3.84; I² = 36%). At long-term follow-up (> two weeks), the rate of bacteriological persistence was similar in both groups (Analysis 1.2: RR 1.18, 95% CI 0.59 to 2.32; I² = 0%). There was no significant heterogeneity.

Clinical failure

One study (Matsumoto 1994) reported short-term clinical failure and found no difference between single dose and short-course treatment (Analysis 1.3: RR 1.69, 95% CI 0.08 to 37.26).

Reinfection rate

Lacey 1981 reported no significant differences in either shortterm (Analysis 1.7: RR 0.67, 95% CI 0.28 to 1.62) and long-term (Analysis 1.8: RR 2.81, 95% CI 0.81 to 9.79) reinfection rates.

Treatment acceptability/dissatisfaction

Guibert 1996 reported less patients were dissatisfied with single dose compared to short-course treatment, however this was not significant (Analysis 1.9: RR 0.30, 95% CI 0.09 to 1.05).

Single dose versus long-course treatment

Persistent UTI

There was a significant decrease in persistent UTI for long-course treatment compared to single dose therapy at short-term followup (≤ 2 weeks post-treatment) (Analysis 2.1: RR 1.93, 95% CI 1.01 to 3.70; I² = 31%) but not at long-term follow-up (> 2 weeks) (Analysis 2.2: RR 1.28, 95% CI 0.89 to 1.84; I² = 0%). There was no significant heterogeneity between the studies.

Clinical failure

One study (Guibert 1993) reported short-term clinical failure and found no difference between single dose and long-course treatment (Analysis 2.3: RR 1.94, 95% CI 0.68 to 5.57).

Adverse reactions

There were no significant differences in the rate of adverse drug reactions (Analysis 2.5: RR 0.80, 95% CI 0.45 to 1.41; $I^2 = 0\%$) or discontinuation due to adverse reactions (Analysis 2.6: RR 0.33, 95% CI 0.01 to 7.87) between single dose and long-course treatment.

Treatment acceptability/dissatisfaction

Guibert 1993 reported significantly more patients were satisfied with single dose compared to long-course treatment (Analysis 2.7: RR 0.73, 95% CI 0.60 to 0.88).

Short-course versus long-course treatment

Raz 1996 compared two different antibiotics (ofloxacin for 3 days with cephalexin given for 7 days), Vogel 2004 compared 3 days versus 7 days ciprofloxacin in a large population of elderly women and Piipo 1990 compared 3 days versus 7 days norfloxacin in a small subgroup of elderly women. Stein 1992 compared 3 days temafloxacin versus 7 days ciprofloxacin including a subgroup analysis of patients over 65 years.

Persistent UTI

There was no significant difference in the number of persistent UTIs for those on short-course compared to long-course treatment

within the first two weeks (Analysis 3.1.1: RR 0.85, 95% CI 0.29 to 2.47). There was no difference between the two groups at long-term follow-up (Analysis 3.2.1: RR 0.85, 95% CI 0.54 to 1.32). Including only studies comparing the same antibiotic (Piipo 1990; Vogel 2004), there was no significant difference at short (Analysis 3.1.2; RR 1.00, 95% CI 0.39 to 2.19) and long-term (Analysis 3.2.2; RR 1.18, 95% CI 0.50 to 2.81) follow-up.

Clinical failure

There was no difference between short-course and long-course treatment for short-term clinical failure (Analysis 3.3.1: RR 0.98, 95% CI 0.62 to 1.54). One study (Raz 1996) reported no difference between short-course or long-course treatment for long-term clinical failure (Analysis 3.4: RR 0.75, 95% CI 0.49 to 1.13). Excluding Raz 1996 did not change these results (Analysis 3.3.2: RR 0.96, 95% CI 0.27 to 3.47).

Adverse reactions

There were no significant differences in the rate of adverse drug reactions (Analysis 3.5: RR 0.87, 95% CI 0.26 to 2.93) or discontinuation due to adverse reactions (Analysis 3.6: RR 0.11, 95% CI 0.01 to 1.97) between short-course and long-course treatment. Vogel 2004 reported statistically significant decreases in the mean number of adverse events/patient at day 5 (Analysis 3.10: MD - 0.70, 95% CI -1.09 to -0.31) and day 9 (Analysis 3.11: MD - 0.90, 95% CI -1.33 to -0.47) for short-course treatment.

Reinfection rate

Raz 1996 reported no significant differences in the short-term reinfection rate (Analysis 3.7: RR 4.37, 95% CI 0.98 to 19.49). Two studies reported long-term reinfection rates (Raz 1996; Vogel 2004) and this showed no significant difference between short-course and long-course treatments (Analysis 3.8: RR 1.30, 95% CI 0.42 to 4.01; $I^2 = 72\%$).

Treatment acceptability/dissatisfaction

Guibert 1997 reported more patients were satisfied with shortcourse treatment compared to long-course treatment, however this was not significant (Analysis 3.9: RR 0.35, 95% CI 0.07 to 1.72).

Single dose versus short- or long-course treatment (3 to 14 days)

We combined the short-course and long-course treatment groups and compared to single dose treatment.

Persistent UTI

The rate of persistent UTI was not significantly different for single dose therapy compared to short-course or long-course treatment at either short-term follow-up (≤ 2 weeks post-treatment) (Analysis 4.1.1: RR 1.51, 95% CI 0.92 to 2.49; I² = 28%) or long-term

follow-up (> 2 weeks) (Analysis 4.2.1: RR 1.14, 95% CI 0.80 to 1.63; I² = 0%).

Clinical failure

There was no statistical difference between single dose and shortor long-course treatment for short-term clinical failure (Analysis 4.3: RR 1.91, 95% CI 0.70 to 5.19; $I^2 = 0\%$).

Adverse reactions

There were no significant differences in the rate of adverse drug reactions (Analysis 4.5: RR 0.80, 95% CI 0.45 to 1.41; $I^2 = 0\%$) or discontinuation due to adverse reactions (Analysis 4.6: RR 0.33, 95% CI 0.01 to 7.87) between single dose and short-course or long-course treatment.

Treatment acceptability/dissatisfaction

Guibert 1993 and Guibert 1996 reported less patients were dissatisfied with single dose compared to short-course or long-course treatment, however this was not significant (Analysis 4.7: RR 0.58, 95% CI 0.27 to 1.25; I² = 48%).

Antibiotics used

When the four studies comparing the same antibiotic in each group were analysed (Andersen 1986; Flanagan 1991; Gellermann 1988; Lacey 1981), there was no statistical difference between the single dose group and short-course or long-course treatment group for persistent UTI at short-term follow-up (≤ 2 weeks post-treatment) (Analysis 4.1.2: RR 1.87, 95% CI 0.91 to 3.83; I² = 41%) or at long-term follow-up (Analysis 4.2.2: RR 1.06, 95% CI 0.50 to 2.24; I² = 16%).

Only one of the four studies reported adverse drug reactions (Flanagan 1991). There was no statistical difference between the single dose group and the short-course or long-course treatment group (Analysis 4.5: RR 0.14, 95% CI 0.01 to 2.85). Other clinical outcomes were not available.

Healthcare settings

Of the four studies comparing the same antibiotic two studies were undertaken in hospitals (Flanagan 1991; Lacey 1981) and two included ambulatory women (Andersen 1986; Gellermann 1988). There was no significant difference between single dose treatment and short-course or long-course treatment for either hospital patients (Analysis 4.1.3: RR 2.57, 95% CI 0.64 to 10.37; $I^2 = 67\%$) or ambulatory women (Analysis 4.1.4: RR 1.35, 95% CI 0.64 to 2.86; $I^2 = 0\%$).

There were insufficient studies to analyse clinical cure or adverse drug reactions.

The other subgroup analyses planned in the protocol (e.g. antibiotic classes and patients' age) were not done due to the low number and heterogeneity of included studies. The planned sensitivity analyses were also not undertaken because of the same reasons. There were insufficient studies to analyse for publication bias.

Three versus 5-day treatment

We included one study identified at our last update in this separate comparison group (van Merode 2005).

Persistent UTI

van Merode 2005 found more persistent UTI in the 3-day than in the 5-day treatment group, however this difference was not statistically significant (Analysis 5.1: RR 2.72, 95% CI 0.90 to 8.27). This subgroup analysis of older patients included only 26 patients (12 and 14 in each group). The authors had calculated that they needed 142 patients/treatment regimen to detect a difference in efficacy of 10%. Therefore sample size was too small to detect a significant difference.

The rate of trimethoprim-resistant *E. coli* reported in this study was high (16%).

Clinical failure

The self-reported rate of clinical failure was similar in both treatment regimens (Analysis 5.2: RR 1.17, 95% CI 0.29 to 4.74). Interestingly, it took the same time to recover from symptoms of UTI as the rate of recovery increased from day 1 to day 3 after the end of therapy, regardless of the duration of treatment (van Merode 2005).

DISCUSSION

The discussion will focus on the results and their clinical interpretation but also on important methodological quality issues.

Methodological Issues

The methodological quality of most studies was low, as only a few studies reported an adequate method of allocation concealment (five studies) and blinding of patients and outcome assessors (four studies). Only one more recent study (Vogel 2004) met high methodological quality standards (overall quality ranking A).

While all studies showed results of bacteriological cure rate, clinically important outcomes such as cure of symptoms or kidney complications were rarely described. Again, the more recent studies (van Merode 2005; Vogel 2004) did report on improvement of symptoms such as nocturia, urgency, frequency, burning on micturition and suprapubic pain after treatment.

Other quality issues pertain to the many sources of heterogeneity between included studies. Two studies included men, and one of these also included patients with urinary catheters (Lacey 1981). These patients are usually more difficult to treat and need longer treatment durations (i.e. 10 to 14 days) (Nicolle 1992; Nygaard 1996; Stamm 1993; Wood 1996). Lacey 1981 included patients with asymptomatic bacteriuria. This is a frequent and usually

benign infection in elderly patients which often resolves spontaneously and does not need antimicrobial treatment (Humbert 1992; Kasviki-Charvati1982; Sourander 1972).

Another possible source of heterogeneity between studies is the different handling of patients with organisms resistant to the study drugs. Some studies excluded those patients. In clinical practice, patients with uncomplicated lower UTI are usually treated empirically. Norrby 1992 recommended in his overview on study design in UTI to continue treatment of cystitis even if the causative organism is reported as being resistant to one or more of the study drugs. Therefore patients with resistant pathogens should be included in studies on UTI and also evaluated for efficacy. In the more recent study by Vogel 2004 none of the identified bacteria were resistant to ciprofloxacin.

In nine studies we were able to do a subgroup analysis of elderly patients. However, not all authors reported the outcomes for elderly patients, and we are unsure if these subgroups were stratified and/or comparable a priori. Most of the studies included relatively young women (e.g. > 50 years), whereas only three studies enrolled older patients (mean age > 78 years) who are often more fragile and present multiple comorbidities.

The setting of studies in elderly patients is very important, because the prevalence of UTI in older people depends on the place of living which may influence the outcome of UTI. Our results suggest that longer treatment durations may be necessary for hospitalised patients. However, the two studies taking place in hospital only included much older patients (mean age 80 and 82) than the other studies. This may also affect the response to treatment. Unfortunately, none of the studies took place in nursing homes where recurrent UTI is a frequent problem (Nicolle 1983; Nicolle 1993). One geriatric study (Vogel 2004) included elderly women from both ambulatory clinics and hospital acute care units.

Eight of the 15 studies compared different treatment durations and different antibiotics. These may not be necessarily equivalent - neither in their bacterial efficacy nor in half-life or adverse drug reactions. For example, several studies showed that trimethoprim, pivmecillinam, amoxicillin and certain cephalosporins are less effective than fluoroquinolones, co-amoxiclav or cotrimoxazole given the same treatment duration (Ewer 1988; Gallacher 1986; Hooton 1995; Jonsson 1990). These findings may explain the better bacterial efficacy of a 3-day course of ofloxacin compared to a 7-day course with cephalexin (Raz 1996).

Some antibiotics may not be appropriate for short-course treatment for pharmacokinetic reasons. Several penicillins and cephalosporins have a relatively short half-life (1 to 2 hours in young people, 2 to 4 hours in older people), whereas the fluoroquinolones, cotrimoxazole and fosfomycin have longer half-lives (4 to 12 hours, 8 to 13 hours, 4 to 50 hours respectively) (Compendium 1998; McCue 1992). Indeed, Norrby 1990 has shown in his systematic review, that the optimal treatment duration for lower, uncomplicated UTI in women (of all ages) depends on the type of antibiotic: three days for cotrimoxazole and the

fluoroquinolones and five days for beta-lactam antibiotics. Due to these findings we included the seven studies comparing the same antibiotic for a different length of time in a separate meta-analysis. Unfortunately, clinical outcomes like persistence of symptoms (our primary outcome) or patients' acceptability were not reported. The other results were similar to the meta-analyses of all 15 studies.

Discussion of results

There was a significant difference for persistent UTI between single dose and short-course treatment in the short-term (< 2 weeks post-treatment) (RR 2.01, 95% CI 1.05 to 3.84), but not at the long-term follow-up (RR 1.18, 95% CI 0.59 to 2.32) or on clinical outcomes. However sample size of the last two outcome parameters was small.

There was a significant decrease in persistent UTI for long-course treatment compared to single dose for short-term (RR 1.93, 95% CI 1.01 to 3.70) but not long-term follow-up (RR 1.28, 95% CI 0.89 to 1.84).There was no statistically significant difference adverse drug reactions. Patients preferred single dose treatment (RR 0.73, 95% CI 0.60 to 0.88) to longer treatments (7 to 14 days), but this was based on only one study comparing different antibiotics.

Short versus longer treatments showed no significant difference in efficacy. Rate of adverse drug reactions increased significantly with longer treatment durations in only one study (Vogel 2004). This study suggested a safety advantage for three day therapy. However ciprofloxacin can cause central side effects in geriatric patients which are rare with antibiotics which do not permeate tissues and remain concentrated in the urine (norfloxacin for example). Other studies in our review with other antibiotics did not cause higher side effects rates in the longer treatment arms.

In one study (which we analysed separately) a three day treatment was compared with a five day regimen of trimethoprim (van Merode 2005). There was no statistically significant difference in bacterial and clinical outcomes, but the sample size was very small. Two other systematic reviews, which mainly included studies with younger patients, found that single dose therapy was less effective than longer treatment durations (Norrby 1990; Warren 1999). The same systematic reviews showed that most antimicrobials given for three days (e.g. trimethoprim, cotrimoxazole or a fluoroquinolone) were as effective as the same antibiotic given for a longer duration. Therefore, a three day course is recommended in younger patients with uncomplicated lower UTI (Warren 1999). These results seem also to apply to older patients, but further investigations are needed to determine the optimal treatment duration in relation to specific antibiotics.

AUTHORS' CONCLUSIONS

Implications for practice

This review suggests that single dose antibiotic treatment is less effective but may be better accepted by the patients than longer treatment durations (3 to 6 days). In addition, there was no difference between short-course (3 to 6 days) and long-course (7 to 14 days) antibiotics in regards to treatment efficacy. Longer courses may be associated with more adverse drug events. The evidence suggests the optimal treatment duration in elderly women is 3 to 6 days.

Implications for research

The more recent ciprofloxacin study (Vogel 2004) offers a high quality model for designing new geriatric RCTs with clinically relevant outcomes, testing the efficacy of different treatment durations of a given antibiotic in elderly women. Indeed it would be clinically relevant, to verify the optimal treatment duration of other antibiotics especially those with narrow spectrum antibacterial activity and less systemic side effects.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

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* Indicates the major publication for the study

Andersen 1986

Methods	Multicentre, double-blind RCT	
Participants Ambulatory patients >15 years old with symptoms of lower UTI and significant bacteriuria		
Interventions	Sulfamethizole 3 g single dose versus 2 x 1 g for 6 days	
Outcomes	For subgroup \geq 60: bacterial eradication after 8 days	
Notes	Subgroup of patients > 60 years old	
Risk of bias		
Item	Authors' judgement I	Description
Allocation concealment??	Unclear H	3 - Unclear

Ferraro 1990

Methods

Open RCT Method of randomisation not specified

Participants	Age: > 50 Uncomplicated symptomatic lower UTI with \geq 100,000 bacteria/mL of germs susceptible to Gender: 5/60 (25%) men	study drugs.
Interventions Fosfomycin trometamol single dose 3 g versus norfloxacin 2 x 400 mg for 7 da		
Outcomes	 Bacterial eradication Side effects 	
Notes		
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Ferraro 1990 (Continued)

Flanagan 1991

Methods	Open, single centre RCT	
Participants	Hospitalised elderly women, with significant bacteriuria, without catheter	
Interventions	single dose versus 7-10 days Various AB, if resistance ≥ other antibiotic	
Outcomes	 Bacterial eradication rate for subgroup with urinary symptoms available No clinical outcome 	
Notes		
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	No	C - Inadequate

Gellermann 1988

Methods	Multicentre, open RCT
Participants	Women, outpatients, with acute lower uncomplicated UTI
Interventions	Ciprofloxacin single dose 1 x 250 mg versus 2 x 250 mg for 3 days
Outcomes	Bacterial eradication and clinical cure after 1 week and 4 weeks
Notes	Subgroup of patients > 65 years old

Gellermann 1988 (Continued)

Risk of bias

Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Guibert 1993

Methods	Multicentre, open RCT	
Participants	Ambulatory women age > 50 with acute uncomplicated bacterial cystitis and positive dipstick test	
Interventions	Pefloxacin 1 x 800 mg single dose versus 10 days norfloxacin 2 x 400 mg	
Outcomes	 Bacterial eradication rate Clinical cure Side effects Acceptability 	
Notes	Also data for patients over 75 years available, resistant bacteria excluded from efficacy evaluation	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Guibert 1996

Methods	Multicentre, open RCT Concealment by telephone	
Participants	ticipants Ambulatory women > 18, with acute uncomplicated cystitis + positive dipstick test and urinary	
Interventions	Pefloxacin 800 mg single dose versus 3-day lomefloxacin, 1 x 400 mg	
Outcomes	 For subgroup ≥ 50 1. Bacterial eradication 2. acceptability 3. Side effects 	
Notes	Subgroup of patients \geq 50 years old	
Risk of bias		
Item	Authors' judgement Des	cription
Allocation concealment??	Yes A -	Adequate

Guibert 1997

Methods	Multicentre, open RCT Concealment by telephone	
Participants Ambulatory women > 18, with acute recurrent uncomplicated cystitis + positive dipstick test		
Interventions	Lomefloxacin 1x 400mg 3 days versus norfloxacin 2x 400mg, 10 days	
Outcomes	for subgroup \geq 50: acceptability	
Notes	Subgroup of patients \geq 50 years old	
Risk of bias		
Item	Authors' judgement Des	scription
Allocation concealment??	Yes A -	Adequate

Jardin 1990

Methods	Multicentre, open RCT	
Participants	Women, outpatients, with symptoms of uncomplicated lower UTI and significant bacteriuria	
Interventions	Fosfomycin trometamol 3 g single dose versus pipemidic acid 2 x 400 mg 5 days	
Outcomes	Bacterial eradication at 5-10 days and 28 days post treatment	
Notes	Subgroup of patients \geq 58 years old	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Lacey 1981

Methods	Multicentre single-blind RCT
Participants	Elderly patients (age 63-97, men: 33/96), with UTI: 2 urine cultures with significant bacteriuria, susceptible to trimethoprim, and significant pyuria (> 100 pus cells /mm ³)
Interventions	Trimethoprim 2 x 100 mg single dose versus 2 x 200 mg for 5 days
Outcomes	
	1. Bacterial eradication rate
	2. Side effects
	3. Selection of resistance
	Time points: 1 and 2 weeks post treatment

Lacey 1981 (Continued)

Notes	Catheter 35% symptoms ? Complicated UTI?	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Matsumoto 1994

Methods	Open RCT	
Participants	Women, 18-69, with acute uncomplicated cystitis	
Interventions	Isepamicin 400mg single dose versus ofloxacin 2x 200mg for 3 days	
Outcomes	Clinical cure at 5 days post treatment	
Notes	Subgroup of patients ≥ 50 or postmenopausal women	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Piipo 1990

Methods	Double blind RCT, 2 centres	
Participants	Female outpatients, 18-80 years old, with acute lower uncomplicated UTI (\geq 100,000 cfu/mL)	
Interventions	Norfloxacin 2 x 400 mg for 3 days versus 7 days	
Outcomes	Accumulated bacterial eradication rate (day 3 to day 45)	
Notes	Subgroup of patients > 65 years All initial bacteria sensitive to norfloxacin.	
Risk of bias		
Item	Authors' judgement Descrip	tion
Allocation concealment??	Yes A - Adec	quate

Raz 1996

Methods	Single centre, open RCT	
Participants	articipants Postmenopausal ambulatory women with lower UTI: pyuria (> 8 WBC/field) + positive urine cult 100,000 cfu/mL) sensitive to antibiotics. Mean age: 66	
Interventions	Ofloxacin 1 x 200 mg 3 days versus cefalexin 4 x 500 mg 7 days	
Outcomes	 Bacterial eradication Short/long term Resolution of symptoms Adverse drug reactions 	
Notes	Age range unknown	
Risk of bias		
Item	Authors' judgement Desc	ription
Allocation concealment??	Unclear B - U	Jnclear

Stein 1992

Methods	Multicentre double-blind RCT	
Participants	Ambulatory women \geq 18 years, with symptoms of lower UTI, pyuria (> 5 WBC/field), \geq 10,000 cfu/mL susceptible to both drugs	
Interventions	Temafloxacin 1 x 400 mg 3 days versus ciprofloxacin 2 x 250 mg for 7 days	
Outcomes	 Bacterial eradication Clinical cure Side effects 	
Notes	Clinical cure rate subgroup of patients ≥ 65 years, no raw data available, resistant bacteria excluded from efficacy analysis Clinical cure rate subgroup of patients 65 years, no raw data available, resistant bacteria excluded from efficacy analysis	
Risk of bias		
Item	Authors' judgement Description	
Allocation concealment??	Yes A - Adequate	

van Merode 2005

Methods	Multicentre single-blind (physicians) RCT	
Participants	Ambulatory women (GPs) 13-77 years with symptoms of lower UTI	
Interventions	ons Trimethoprim (dosage?) 3 days versus 5 days	
Outcomes	 Bacterial cure Self-stated clinical cure rate Trimethoprim-resistant bacteria 	
Notes	Subgroup of patients 60 years old	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment??	Unclear	B - Unclear

Vogel 2004

Methods	 chods Multicentre double-blind RCT icipants Hospitalised and ambulatory women ≥ 65 years with at least 1 symptom of lower UTI and bacteriuria ≥ 100,000 cfu/mL 	
Participants		
Interventions	Ciprofloxacin 2 x 250 mg P.O. 3 days versus 7 days	
Outcomes	 Bacterial eradication at 2 days after end of treatment and at 6 weeks Clinical cure Side effects 	
Notes		
Risk of bias		
Item	Authors' judgement Description	on
Allocation concealment??	Yes A - Adequ	ate

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Abadi 1986	Unable to separate/determine population group/s included in this study
Abadi 1987	Unable to separate/determine population group/s included in this study
Abbas 1984	No control group
Allgulander 1979	All groups 14-day treatment
Ancill 1987	Both groups 7-day treatment
Anderson 1979	Unable to separate/determine population group/s included in this study
Anderson 1980	Leading article, no trial
Andrewes 1981	All groups 7-day treatment
Aragones 1990	Unable to separate/determine population group/s included in this study
Arredondo 2004	Pre-menopausal women
Auquer 2002	Two different antibiotics, two different treatment durations, population ranged from 18-65 years and unable to separate data
Backhouse 1989	Unable to separate/determine population group/s included in this study
Bailey 1977	Age 16-56
Bailey 1978	Age 17-55, not only symptomatic lower UTI, but also asymptomatic and upper UTI
Bailey 1980	Age 17-64, majority < 21 years old
Bailey 1982	Unable to separate/determine population group/s included in this study
Bailey 1984	Age 18-55
Bailey 1985a	Not RCT
Bailey 1985b	Unable to separate/determine population group/s included in this study
Basista 1991	Unable to separate/determine population group/s included in this study
Bergan 1990	Healthy volunteers, no control
Bitsch 1985	Unable to separate/determine population group/s included in this study
Boerema 1990	Age 16-50
Bordier 1978	All groups 10-day treatment
Brosof 1980	Unable to separate/determine population group/s included in this study
Brouhard 1981	Not RCT
Brumfitt 1993	The trial included only 10 patients over 50 years old. Details on these patients were not available

(Continued)	
Study	Reason for exclusion
Buckwold 1982	All groups single dose
Capalbi 1987	All groups 7-day treatment, age 16-63
Capri 1991	Not RCT
Carmignani 2005	Complicated UTI, mixed population
Charlton 1976	Not RCT, treatment assigned according to the month (odd- or even-numbered) the patient attended the doctor
Charlton 1981	Not RCT, treatment assigned according to the month (odd- or even-numbered) the patient attended the doctor
Cheung 1988	Not RCT, both groups 7-day treatment
Compton 1983	Not RCT "Treatment was alternated from one woman to the next as the woman entered the study".
Cooper 1990a	Unable to separate/determine population group/s included in this study
Cooper 1990b	Unable to separate/determine population group/s included in this study
Cosmi 1996	Unable to separate/determine population group/s included in this study
Counts 1982	Unable to separate/determine population group/s included in this study
Cox 1992	Unable to separate/determine population group/s included in this study
Craft 1991	Unable to separate/determine population group/s included in this study
Crocchiolo 1990	Unable to separate/determine population group/s included in this study
Daengsvang 1990	Unable to separate/determine population group/s included in this study
de Almeida 1994	Unable to separate/determine population group/s included in this study
de Jong 1991	Unable to separate/determine population group/s included in this study
del Rio 1996	Unable to separate/determine population group/s included in this study
Dickie 1986	No control group
Dickreuter 1984	Unable to separate/determine population group/s included in this study
Dubois 1984	Age 18-45
Elhanan 1994	Unable to separate/determine population group/s included in this study
Fair 1980	Unable to separate/determine population group/s included in this study
Fairley 1970	Recurrent UTI, age 18-65
Falck 1984	All groups 3 days, not different duration
Falck 1988	Unable to separate/determine population group/s included in this study
Fang 1978	Age 18-54

(Continued)	
Study	Reason for exclusion
Ferry 2007	Different durations with different doses (200mg x 3 x 7days versus 200mg x 2 x 7 days versus 400mg x 2 x
Fihn 1988	None of the participants were over age of 65 (email from the author)
Fischer 1982	Both groups 10-day treatment
Flavell-Matts 1985	Both groups 7-day treatment
Fünfstück 1990	Chronic pyelonephritis
Gallego Gomez 1987	Both groups 10-day treatment
Gippert 1981	All groups 7-day treatment
Gordin 1987	Age 17-63, mostly young women
Gordon 1978	Both groups same treatment duration (\geq 5 days)
Gossius 1984a	Age 16-60
Gossius 1984b	Age 16-60
Gossius 1986	Age 16-60
Goto 1999	Unable to separate/determine population group/s included in this study
Greenberg 1981	Trial included mostly young adult females who were sexually active, most patients were less than 60 years (author's information)
Greenberg 1986	Trial included mostly young adult females who were sexally active, most patients were less than 60 years (author's information)
Greenwood 1994	Not RCT
Grüneberg 1967	Unable to separate/determine population group/s included in this study
Hansen 1981	Unable to separate/determine population group/s included in this study
Heer 1980	No control group
Henning 1981	Age 16-65, inclusion criteria: significant bacteriuria $\geq 10^8$
Henry 1999	Age range 18-64, mean age 34
Hill 1985	Both groups 10-day treatment
Hinnah 1991	Both groups single dose
Hoigne 1977	All groups \geq 14-day treatment
Hooton 1985	Age 18-56, all groups single dose
Hooton 1989	Unable to separate/determine population group/s included in this study
Hooton 1991	Students, mean age 25
Hoover 1982	Only young women
Hoyme 1993	Unable to separate/determine population group/s included in this study
Huang 2002	Study is not on uncomplicated UTI or treatment duration
Humbert 1987	Review article
Iravani 1985	College women, mean age 22

Iravani 1989	College women, mean age 22 and 23 respectively
Iravani 1991a	Unable to separate/determine population group/s included in this study
Iravani 1991b	Unable to separate/determine population group/s included in this study
Iravani 1993	Unable to separate/determine population group/s included in this study
Iravani 1995	Unable to separate/determine population group/s included in this study
Iravani 1999	Unable to separate/determine population group/s included in this study
Ishihara 1998	Unable to separate/determine population group/s included in this study
Johansen 1981	All groups 10-day treatment
Jones 1983	Unable to separate/determine population group/s included in this study
Jordan 1986	Not RCT
Khatib 1981	Age 14-57
Kirby 1984	No control group
Kiyota 1992	Unable to separate/determine population group/s included in this study
Kosmidis 1988	Both groups single dose, age 18-50
Koyama 2000	Unable to separate/determine population group/s included in this study
Kumamoto 1992	No control groups, 5 trials, all single dose
Källenius 1979	Girls 6-14 years
Lecomte 1991	Review article
Leelarasamee 1995	No patients > 60 included (email from the author)
Leigh 1980	Unable to separate/determine population group/s included in this study
Lewis 1980	Dose comparison, same treatment duration, also patients with upper UTI
Lightstone 1988	Unable to separate/determine population group/s included in this study
Lockey 1980	Unable to separate/determine population group/s included in this study
Ludwig 1987	Unable to separate/determine population group/s included in this study
Mabeck 1980a	All groups same duration
Mabeck 1980b	All groups 1-week treatment
Mallo 1979	No control group
Marsh 1980	Age 15-55
Martin 1983	Both groups 7-day treatment
Masterton 1995	Unable to separate/determine population group/s included in this study
Matsumoto 1991	Unable to separate/determine population group/s included in this study

(Continued)	
Study	Reason for exclusion
Menday 2000	Unable to separate/determine population group/s included in this study
Minassian 1998	Age 18-65, mean age 40
Mompo 1986	Both groups single dose
Musierowicz 1980	No control group
Naber 2004	Population of women > 18 years, no separation based on age
Neringer 1992	Age 18-65, mean age 39
Neu 1990	All groups single dose, no duration trial
Norrby 1993	Unable to separate/determine population group/s included in this study
Ode 1987	Unable to separate/determine population group/s included in this study
Olsovsky 1988	Unable to separate/determine population group/s included in this study
Onodera 1980	No control group (7-day treatment)
Oosterlinck 1980	All groups 15-day treatment, recurrent UTI
Osterberg 1990	Unable to separate/determine population group/s included in this study
Otieno 1988	All groups 7-day treatment, age 20-57
Patrick 1991	Unable to separate/determine population group/s included in this study
Pawelczyk 2002	Does not look at duration of antibiotics
Peddie 1981	Both groups 5-day treatment, age ?
Petersen 1990	Unable to separate/determine population group/s included in this study
Pfau 1984	Unable to separate/determine population group/s included in this study
Pitkäjärvi 1990	Age range 18-65, mean age 35
Polubiec 1988	All groups 10-day treatment
Pontzer 1983	Age 19-49 and 18-62 respectively
Porpaczy 1984	Unable to separate/determine population group/s included in this study
Prat 1986	No control group
Prentice 1985	Age 18-65, mean 27.2 years
Ranno 1986	No control group
Rapoport 1981	Letter from Dr Slack: elderly patients were excluded and the majority of patients were under 65 years
Raz 1991	Unable to separate/determine population group/s included in this study
Reeves 1981	Not RCT
Reynaert 1990	Unable to separate/determine population group/s included in this study
Richard 2002	Age group 18-88 years, unable to separate/obtain data on women over 60 years
Richards 1984	Age 18-55
Rosenstock 1985	Unable to separate/determine population group/s included in this study

Rubin 1980	Age 18-55
Russ 1980	Patients included without symptoms of UTI and with renalkidney transplantation, mean age unknown, raw data not available
Saginur 1992	Unable to separate/determine population group/s included in this study
Sanchez 1988	Probably not randomised (randomisation not mentioned, both groups same size), very small subgroup of elderly patients (11)
Sandberg 1985	Unable to separate/determine population group/s included in this study
Savard-Fenton 1982	Unable to separate/determine population group/s included in this study
Schultz 1984	Age 18-55
Sigurdsson 1983	Both groups 3-day treatment
Slade 1972	Unable to separate/determine population group/s included in this study
Staszewska 1995	Duration > 14 days (3, 6, and 18 months), no information if patients had symptoms of UTI
Stein 1987	Unable to separate/determine population group/s included in this study
Sturm 1984	Only 2 patients > 60 years
Sutlieff 1982	Age 18-55
Tolkoff-Rubin 1982	Age 18-55
Trienekens 1993	Age 18-65
UTI Study Group 1987	All groups 7-day treatment
van Balen 1990	Unable to separate/determine population group/s included in this study
van Pienbroek 1993	Unable to separate/determine population group/s included in this study
Vogel 1984	Four trials: one: no control group, others: both groups same treatment duration
Winwick 1981	Age 18-65, mean age 38 and 30 respectively
Zorbas 1995	Only patients with asymptomatic bacteriuria included

DATA AND ANALYSES

Comparison 1. Single dose versus short-course treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Persistent UTI: short-term	5	356	Risk Ratio (M-H, Random, 95% CI)	2.01 [1.05, 3.84]
2 Persistent UTI: long-term	3	95	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.59, 2.32]
3 Clinical failure (persistence of symptoms): short-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Clinical failure (persistence of symptoms): long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Adverse drug reactions			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Discontinuation due to adverse reactions			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
7 Reinfection rate: short-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
8 Reinfection rate: long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Acceptability (little or not satisfied with treatment)			Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 2. Single dose versus long-course treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Persistent UTI: short-term	6	628	Risk Ratio (M-H, Random, 95% CI)	1.93 [1.01, 3.70]
2 Persistent UTI: long-term	5	523	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.89, 1.84]
3 Clinical failure (persistence of symptoms): short-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Clinical failure (persistence of symptoms): long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Adverse drug reactions	3	595	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.45, 1.41]
6 Discontinuation due to adverse reactions	3	595	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
7 Acceptability (little or not satisfied with treatment)			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
8 Reinfection rate: short-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Reinfection rate: long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 3. Short-course versus long-course treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Persistent UTI: short-term			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 All trials	3	431	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.29, 2.47]
1.2 Trials comparing the same antibiotic in each group	2	208	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.12, 8.57]
2 Persistent UTI: long-term			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 All trials	3	470	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.54, 1.32]
2.2 Trials comparing the same antibiotic in each group	2	247	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.50, 2.81]
3 Clinical failure (persistence of symptoms): short-term			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 All trials	4	395	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.62, 1.54]
3.2 Trials comparing the same antibiotic in each group	2	91	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.27, 3.47]
4 Clinical failure (persistence of symptoms): long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Adverse drug reactions			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Discontinuation due to adverse reactions	2	406	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.01, 1.97]
7 Reinfection rate: short-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
8 Reinfection rate: long-term	2	405	Risk Ratio (M-H, Random, 95% CI)	1.30 [0.42, 4.01]
9 Acceptability (little or not satisfied with treatment)			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10 Mean number of adverse events/patient (day 5)			Mean Difference (IV, Random, 95% CI)	Totals not selected
11 Mean number of adverse events/patient (day 9)			Mean Difference (IV, Random, 95% CI)	Totals not selected

Comparison 4. Single dose versus short-course or long-course treatment (3 to 14 days)

Outcome or subgroup title	No. of No. of studies participants		Statistical method	Effect size
1 Persistent UTI: short-term			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 All trials	8	809	Risk Ratio (M-H, Random, 95% CI)	1.51 [0.92, 2.49]
1.2 Trials comparing the same antibiotic in each group	4	162	Risk Ratio (M-H, Random, 95% CI)	1.87 [0.91, 3.83]
1.3 Hospital setting	2	114	Risk Ratio (M-H, Random, 95% CI)	2.57 [0.64, 10.37]
1.4 Ambulatory patients	2	48	Risk Ratio (M-H, Random, 95% CI)	1.35 [0.64, 2.86]
2 Persistent UTI: long-term			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 All trials	5	521	Risk Ratio (M-H, Random, 95% CI)	1.14 [0.80, 1.63]
2.2 Trials comparing the same antibiotic in each group	2	39	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.50, 2.24]
3 Clinical failure (persistence of symptoms): short-term	2	411	Risk Ratio (M-H, Random, 95% CI)	1.91 [0.70, 5.19]

4 Clinical failure (persistence of symptoms): long-term			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Adverse drug reactions	3	595	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.45, 1.41]
6 Discontinuationsdue to adverse reactions	3	595	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.01, 7.87]
7 Acceptability (little or not satisfied with treatment)	2	546	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.27, 1.25]

Comparison 5. 3 days versus 5 days

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Persistent UTI: short term (3 days after treatment)			Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Clinical failure (not recovered): short term (3 days after treatment)			Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis I.I. Comparison I Single dose versus short-course treatment, Outcome I Persistent UTI: short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: I Single dose versus short-course treatment

Outcome: I Persistent UTI: short-term

Study or subgroup	Single dose	3-6 days	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Random,95% Cl		M-H,Random,95% Cl
Andersen 1986	4/10	3/15		17.8 %	2.00 [0.56, 7.09]
Gellermann 1988	5/11	5/12		25.9 %	1.09 [0.43, 2.77]
Guibert 1996	7/79	6/79	_	22.7 %	1.17 [0.41, 3.32]
Jardin 1990	6/23	2/31		13.8 %	4.04 [0.90, 18.24]
Lacey 1981	6/49	3/47		19.8 %	5.12 [1.59, 16.42]
Total (95% CI)	172	184	•	100.0 %	2.01 [1.05, 3.84]
Total events: 38 (Single do	ose), 19 (3-6 days)				
Heterogeneity: Tau² = 0.2	0; Chi ² = 6.26, df = 4 (P	P = 0.18); I² =36%			
Test for overall effect: Z =	2.11 (P = 0.034)				
			0.1 10		
		Favours	single dose Favours 3-6 o	days	

Analysis I.2. Comparison I Single dose versus short-course treatment, Outcome 2 Persistent UTI: longterm.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: I Single dose versus short-course treatment Outcome: 2 Persistent UTI: long-term

Study or subgroup	Single dose	3-6 days		F	Risk Rati	0	Weight	Risk Ratio
	n/N	n/N		M-H,Ran	dom,95	% CI		M-H,Random,95% Cl
Andersen 1986	4/10	3/15					29.0 %	2.00 [0.56, 7.09]
Gellermann 1988	4/11	6/12					49.9 %	0.73 [0.28, 1.91]
Jardin 1990	3/17	3/30			-		21.1 %	1.76 [0.40, 7.80]
Total (95% CI)	38	57			-		100.0 %	1.18 [0.59, 2.32]
Total events: (Single do	se), 12 (3-6 days)							
Heterogeneity: Tau ² = 0.0;	; Chi ² = 1.94, df = 2 (P =	= 0.38); l² =0.0%						
Test for overall effect: $Z =$	0.47 (P = 0.64)							
			i			i		
			0.2	0.5	1 2	5		
			Favours	single dose	Favour	rs 3-6 days		

Analysis I.3. Comparison I Single dose versus short-course treatment, Outcome 3 Clinical failure (persistence of symptoms): short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: I Single dose versus short-course treatment

Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	Single dose n/N	dose 3-6 days /N n/N		Risk Ratio dom,95% Cl	Risk Ratio M-H,Random,95% C	
Matsumoto 1994	1/15	0/8			1.69 [0.08, 37.26]	
			0.1	1 10		
		Favo	ours single dose	Favours 3-6 days		

Analysis 1.7. Comparison I Single dose versus short-course treatment, Outcome 7 Reinfection rate: short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: I Single dose versus short-course treatment Outcome: 7 Reinfection rate: short-term

Study or subgroup	Single dose n/N	3-6 days n/N	R M-H,Rand	isk Ratio dom,95% Cl	Risk Ratio M-H,Random,95% CI
Lacey 1981	7/49	10/47			0.67 [0.28, 1.62]
			0.2 0.5 I Favours single dose	2 5 Favours 3-6 days	

Analysis 1.8. Comparison I Single dose versus short-course treatment, Outcome 8 Reinfection rate: longterm.

Comparison: I Single de Outcome: 8 Reinfection	ose versus short-course treatm rate: long-term	ent	,, ,	
Study or subgroup	Single dose n/N	3-6 days n/N	Risk Ratio M-H,Random,95% Cl	Risk Ratio M-H,Random,95% Cl
Lacey 1981	8/36	3/38		2.81 [0.81, 9.79]
			0.2 0.5 2 5 Favours single dose Favours 3-6 day	s

Analysis I.9. Comparison I Single dose versus short-course treatment, Outcome 9 Acceptability (little or not satisfied with treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: I Single dose versus short-course treatment Outcome: 9 Acceptability (little or not satisfied with treatment) 3-6 days Risk Ratio Risk Ratio Study or subgroup Single dose M-H,Random,95% CI M-H,Random,95% Cl n/N n/N Guibert 1996 3/79 10/79 0.30 [0.09, 1.05] 0.1 10 Favours single dose Favours 3-6 days

Analysis 2.1. Comparison 2 Single dose versus long-course treatment, Outcome 1 Persistent UTI: shortterm.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 2 Single dose versus long-course treatment Outcome: I Persistent UTI: short-term

Study or subgroup	Single dose	7-14 days		Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H	1,Random,95% Cl		M-H,Random,95% Cl
Andersen 1986	4/10	3/15			17.8 %	2.00 [0.56, 7.09]
Ferraro 1990	3/30	5/30			16.4 %	0.60 [0.16, 2.29]
Flanagan 1991	5/10	3/8			21.5 %	1.33 [0.45, 3.96]
Guibert 1993	3/189	2/186	-	•	10.7 %	1.48 [0.25, 8.73]
Jardin 1990	6/23	2/31			13.8 %	4.04 [0.90, 18.24]
Lacey 1981	16/49	3/47			19.8 %	5.12 [1.59, 16.42]
Total (95% CI)	311	317		•	100.0 %	1.93 [1.01, 3.70]
Total events: 37 (Single de	ose), 18 (7-14 days)					
Heterogeneity: Tau² = 0.2	20; Chi ² = 7.22, df = 5 (P = 0.20); I ² =31%				
Test for overall effect: Z =	= 1.99 (P = 0.047)					
			0.1	1 10		

Favours single dose

Favours 7-14 days

Analysis 2.2. Comparison 2 Single dose versus long-course treatment, Outcome 2 Persistent UTI: longterm.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 2 Single dose versus long-course treatment

Outcome: 2 Persistent UTI: long-term

Study or subgroup	Single dose	7-14 days		Risk Ratio	Weight	Risk Ratio
	n/N	n/N	٢	1-H,Random,95% Cl		M-H,Random,95% Cl
Andersen 1986	4/10	3/15			8.4 %	2.00 [0.56, 7.09]
Ferraro 1990	7/30	8/30			17.3 %	0.88 [0.36, 2.11]
Flanagan 1991	6/9	3/7			14.2 %	1.56 [0.59, 4.11]
Guibert 1993	30/189	24/186			54.1 %	1.23 [0.75, 2.02]
Jardin 1990	3/17	3/30			6.1 %	1.76 [0.40, 7.80]
Total (95% CI)	255	268		•	100.0 %	1.28 [0.89, 1.84]
Total events: 50 (Single de	ose), 41 (7-14 days)					
Heterogeneity: Tau² = 0.0); Chi² = 1.56, df = 4 (P	= 0.82); l ² =0.0%				
Test for overall effect: Z =	= 1.31 (P = 0.19)					
	· ·		1			
			0.2	0.5 1 2 5		
			Favours singl	e dose Favours 7-14 days		

Analysis 2.3. Comparison 2 Single dose versus long-course treatment, Outcome 3 Clinical failure (persistence of symptoms): short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 2 Single dose versus long-course treatment

Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	Single dose	7-14 days	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Random,95% Cl	M-H,Random,95% CI
Guibert 1993	10/197	5/191		1.94 [0.68, 5.57]
			0.2 0.5 2 5	
			Favours single dose Favours 7-14 days	

Analysis 2.5. Comparison 2 Single dose versus long-course treatment, Outcome 5 Adverse drug reactions.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 2 Single dose versus long-course treatment

Outcome: 5 Adverse drug reactions

Study or subgroup	Single dose	7-14 days	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Random,95% Cl		M-H,Random,95% Cl
Ferraro 1990	1/30	2/30		5.8 %	0.50 [0.05, 5.22]
Flanagan 1991	0/31	2/22		3.6 %	0.14 [0.01, 2.85]
Guibert 1993	19/244	21/238		90.6 %	0.88 [0.49, 1.60]
Total (95% CI)	305	290	•	100.0 %	0.80 [0.45, 1.41]
Total events: 20 (Single do	ose), 25 (7-14 days)				
Heterogeneity: Tau² = 0.0	; Chi² = 1.54, df = 2 (P	= 0.46); l ² =0.0%			
Test for overall effect: Z =	= 0.77 (P = 0.44)				

0.01 0.1 1 10 100 Favours single dose Favours 7-14 days

Analysis 2.6. Comparison 2 Single dose versus long-course treatment, Outcome 6 Discontinuation due to adverse reactions.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 2 Single dose versus long-course treatment

Outcome: 6 Discontinuation due to adverse reactions

Study or subgroup	Single dose	7-14 days	R	isk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Rand	dom,95% Cl		M-H,Random,95% Cl
Ferraro 1990	0/30	1/30			100.0 %	0.33 [0.01, 7.87]
Flanagan 1991	0/31	0/22			0.0 %	Not estimable
Guibert 1993	0/244	0/238			0.0 %	Not estimable
Total (95% CI)	305	290			100.0 %	0.33 [0.01, 7.87]
Total events: 0 (Single dose	e), I (7-14 days)					
Heterogeneity: not applica	ble					
Test for overall effect: Z =	0.68 (P = 0.50)					
			0.1 1	10		
		Favours	s single dose	Favours 7-14 days		

Analysis 2.7. Comparison 2 Single dose versus long-course treatment, Outcome 7 Acceptability (little or not satisfied with treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 2 Single dose versus long-course treatment

Outcome: 7 Acceptability (little or not satisfied with treatment)

Study or subgroup	Single dose n/N	7-14 days n/N	M-H,Rai	Risk Ratio ndom,95% Cl	Risk Ratio M-H,Random,95% CI
Guibert 1993	89/197	9/ 9			0.73 [0.60, 0.88]
			0.7	I I.5	
			Favours single dose	Favours 7-14 days	

Analysis 3.1. Comparison 3 Short-course versus long-course treatment, Outcome I Persistent UTI: short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: I Persistent UTI: short-term

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Rar	ndom,95% Cl		M-H,Random,95% Cl
All trials						
Raz 1996	27/119	38/104	-	-	44.8 %	0.62 [0.41, 0.94]
van Merode 2005	7/12	3/14			31.7 %	2.72 [0.90, 8.27]
Vogel 2004	2/93	6/89			23.6 %	0.32 [0.07, 1.54]
Subtotal (95% CI)	224	207			100.0 %	0.85 [0.29, 2.47]
Total events: 36 (3-6 days), 47	7 (7-14 days)					
Heterogeneity: Tau² = 0.62; C	2hi² = 7.01, df = 2 (P	= 0.03); ² =7 %				
Test for overall effect: $Z = 0.3$	0 (P = 0.76)					
2 Trials comparing the same a	Intibiotic in each grou	qı				
van Merode 2005	7/12	3/14			53.4 %	2.72 [0.90, 8.27]
Vogel 2004	2/93	6/89			46.6 %	0.32 [0.07, 1.54]
Subtotal (95% CI)	105	103			100.0 %	1.00 [0.12, 8.57]
Total events: 9 (3-6 days), 9 (7-14 days)					
Heterogeneity: Tau² = 1.93; C	Chi² = 4.99, df = 1 (P	= 0.03); l ² =80%				
Test for overall effect: $Z = 0.0$	0 (P = 1.0)					
			0.1	1 10		
			Favours 3-6 days	Favours 7-14 day	/S	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: I Persistent UTI: short-term

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Ra	ndom,95% Cl	M-H,Random,95% Cl
All trials					
Raz 1996	27/119	38/104	-	F	0.62 [0.41, 0.94]
van Merode 2005	7/12	3/14			2.72 [0.90, 8.27]
Vogel 2004	2/93	6/89		+	0.32 [0.07, 1.54]
Subtotal (95% CI)	224	207			0.85 [0.29, 2.47]
Total events: 36 (3-6 days), 47 (7-14 days)				
Heterogeneity: Tau² = 0.62; Chi²	^e = 7.01, df = 2 (P = 0.03)	² =7 %			
Test for overall effect: $Z = 0.30$ ((P = 0.76)				
			0.1	10	
			Favours 3-6 days	Favours 7-14 days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: I Persistent UTI: short-term

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Risk Ratio
	n/N	n/N	M-H,R	andom,95% Cl	M-H,Random,95% Cl
2 Trials comparing the same an	tibiotic in each group				
van Merode 2005	7/12	3/14			2.72 [0.90, 8.27]
Vogel 2004	2/93	6/89		+	0.32 [0.07, 1.54]
Subtotal (95% CI)	105	103			1.00 [0.12, 8.57]
Total events: 9 (3-6 days), 9 (7	-14 days)				
Heterogeneity: Tau² = 1.93; Ch	$i^2 = 4.99$, $df = 1$ (P = 0.03);	I ² =80%			
Test for overall effect: $Z = 0.00$	(P = 1.0)				
			1		
			0.1	10	
			Favours 3-6 days	Favours 7-14 days	

Analysis 3.2. Comparison 3 Short-course versus long-course treatment, Outcome 2 Persistent UTI: longterm.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course	e versus long-course t	reatment				
Outcome: 2 Persistent UTI:	long-term					
Study or subgroup 3-6 days		7-14 days	F	lisk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Rand	dom,95% Cl		M-H,Random,95% Cl
All trials						
Piipo 1990	6/35	2/30	_		7.6 %	2.57 [0.56, .8]
Raz 1996	31/119	41/104	-		48.7 %	0.66 [0.45, 0.97]
Vogel 2004	27/93	28/89	-	F	43.7 %	0.92 [0.59, 1.44]
Subtotal (95% CI)	247	223	-	•	100.0 %	0.85 [0.54, 1.32]
Total events: 64 (3-6 days), 71	(7-14 days)					
Heterogeneity: Tau ² = 0.07; C	:hi² = 3.63, df = 2 (P =	= 0.16); l ² =45%				
Test for overall effect: $Z = 0.7$	3 (P = 0.46)					
2 Trials comparing the same a	ntibiotic in each group	D C				
Piipo 1990	6/35	2/30			24.1 %	2.57 [0.56, .8]
			0.1	10		
			Favours 3-6 days	Favours 7-14	days	(Continued)

(... Continued)

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Rar	idom,95% Cl		M-H,Random,95% Cl
Vogel 2004	27/93	28/89	4	<mark>-</mark> -	75.9 %	0.92 [0.59, 1.44]
Subtotal (95% CI)	128	119	-	-	100.0 %	1.18 [0.50, 2.81]
Total events: 33 (3-6 days), 30) (7-14 days)					
Heterogeneity: Tau ² = 0.21; C	Chi² = 1.63, df = 1 (P	= 0.20); I ² =39%				
Test for overall effect: $Z = 0.3$	88 (P = 0.71)					
			0.1	1 10		
			Favours 3-6 days	Favours 7-14 days		

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course versus long-course treatment

Outcome: 2 Persistent UTI: long-term

Study or subgroup	3-6 days	7-14 days	Ri	isk Ratio	Risk Ratio
	n/N	n/N	M-H,Rand	lom,95% Cl	M-H,Random,95% Cl
I All trials					
Piipo 1990	6/35	2/30		-	2.57 [0.56, .8]
Raz 1996	31/119	41/104	-		0.66 [0.45, 0.97]
Vogel 2004	27/93	28/89	-	_	0.92 [0.59, 1.44]
Subtotal (95% CI)	247	223	•	•	0.85 [0.54, 1.32]
Total events: 64 (3-6 days), 71 (7-14 days)				
Heterogeneity: Tau² = 0.07; Ch	² = 3.63, df = 2 (P = 0.16)	; I ² =45%			
Test for overall effect: $Z = 0.73$	(P = 0.46)				
				1	
			0.1	10	
			Favours 3-6 days	Favours 7-14 days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment Outcome: 2 Persistent UTI: long-term

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Risk Ratio
	n/N	n/N	M-H,R	andom,95% Cl	M-H,Random,95% Cl
2 Trials comparing the same an	tibiotic in each group				
Piipo 1990	6/35	2/30			2.57 [0.56, .8]
Vogel 2004	27/93	28/89		-	0.92 [0.59, 1.44]
Subtotal (95% CI)	128	119	-	-	1.18 [0.50, 2.81]
Total events: 33 (3-6 days), 30	(7-14 days)				
Heterogeneity: Tau ² = 0.21; Ch	ni² = 1.63, df = 1 (P = 0.20);	I ² =39%			
Test for overall effect: $Z = 0.38$	(P = 0.71)				
			0.1	10	
			Favours 3-6 days	Favours 7-14 days	

Analysis 3.3. Comparison 3 Short-course versus long-course treatment, Outcome 3 Clinical failure (persistence of symptoms): short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	3-6 days	7-14 days	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Random,95% Cl		M-H,Random,95% Cl
I All trials					
Raz 1996	27/119	24/104	-	87.6 %	0.98 [0.61, 1.59]
Stein 1992	0/37	0/44		0.0 %	Not estimable
van Merode 2005	3/12	3/14	_	10.4 %	1.17 [0.29, 4.74]
Vogel 2004	0/31	1/34		2.0 %	0.36 [0.02, 8.63]
Subtotal (95% CI)	199	196	+	100.0 %	0.98 [0.62, 1.54]
Total events: 30 (3-6 days), 28	3 (7-14 days)				
Heterogeneity: Tau² = 0.0; Ch	ni² = 0.44, df = 2 (P =	= 0.80); l ² =0.0%			
Test for overall effect: $Z = 0.0$	08 (P = 0.93)				
2 Trials comparing the same a	antibiotic in each grou	qu			
van Merode 2005	3/12	3/14		83.6 %	1.17 [0.29, 4.74]
Vogel 2004	0/31	1/34		16.4 %	0.36 [0.02, 8.63]
Subtotal (95% CI)	43	48	-	100.0 %	0.96 [0.27, 3.47]
Total events: 3 (3-6 days), 4 (7-14 days)				
Heterogeneity: Tau² = 0.0; Ch	ni² = 0.45, df = 1 (P =	= 0.50); l ² =0.0%			
Test for overall effect: $Z = 0.0$	06 (P = 0.96)				
			0.1 10		
			Favours 3-6 days Favours 7-14 c	days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course versus long-course treatment

Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	3-6 days	7-14 days	R	isk Ratio	Risk Ratio
	n/N	n/N	M-H,Rand	lom,95% Cl	M-H,Random,95% Cl
All trials					
Raz 1996	27/119	24/104		ł	0.98 [0.61, 1.59]
Stein 1992	0/37	0/44			Not estimable
van Merode 2005	3/12	3/14		—	1.17 [0.29, 4.74]
Vogel 2004	0/31	1/34			0.36 [0.02, 8.63]
Subtotal (95% CI)	199	196	•	•	0.98 [0.62, 1.54]
Total events: 30 (3-6 days), 28 (7-14 days)				
Heterogeneity: Tau ² = 0.0; Chi ²	= 0.44, df = 2 (P = 0.80);	¹² =0.0%			
Test for overall effect: $Z = 0.08$	(P = 0.93)				
			0.1 1	10	
			Favours 3-6 days	Favours 7-14 days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course versus long-course treatment

Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	3-6 days	7-14 days		Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Rar	ndom,95% Cl	M-H,Random,95% Cl
2 Trials comparing the same ant	ibiotic in each group				
van Merode 2005	3/12	3/14		•	1.17 [0.29, 4.74]
Vogel 2004	0/31	1/34			0.36 [0.02, 8.63]
Subtotal (95% CI)	43	48			0.96 [0.27, 3.47]
Total events: 3 (3-6 days), 4 (7-	14 days)				
Heterogeneity: Tau ² = 0.0; Chi ²	= 0.45, df = 1 (P = 0.50); l ²	2 =0.0%			
Test for overall effect: $Z = 0.06$	(P = 0.96)				
			0.1	10	
			Favours 3-6 days	Favours 7-14 days	

Analysis 3.4. Comparison 3 Short-course versus long-course treatment, Outcome 4 Clinical failure (persistence of symptoms): long-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: 4 Clinical failure (persistence of symptoms): long-term



Analysis 3.5. Comparison 3 Short-course versus long-course treatment, Outcome 5 Adverse drug reactions.

	5 0 da/5	7 1 1 day 5	INSK INDUC	Risk Ratio
Baz 1996	n/in	n/N	M-H,Random,95% Cl	M-H,Random,95% Cl
Raz 1996	5/119	5/104		0.87 [0.26, 2.93]
			02 05 1 2 5	
			Favours 3-6 days Favours 7-14 days	

Analysis 3.6. Comparison 3 Short-course versus long-course treatment, Outcome 6 Discontinuation due to adverse reactions.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: 6 Discontinuation due to adverse reactions

Study or subgroup	3-6 days n/N	7-14 days n/N	F M-H,Ran	Risk Ratio dom,95% Cl	Weight	Risk Ratio M-H,Random,95% Cl
Raz 1996	0/119	0/104			0.0 %	Not estimable
Vogel 2004	0/93	4/90		_	100.0 %	0.11 [0.01, 1.97]
Total (95% CI)	212	194	-		100.0 %	0.11 [0.01, 1.97]
Total events: 0 (3-6 days), Heterogeneity: not applica	4 (7-14 days) able					
Test for overall effect: Z =	= 1.50 (P = 0.13)					
			0.01 0.1 Favours 3-4 days	I IO IOO Favours 5-14 days		

Analysis 3.7. Comparison 3 Short-course versus long-course treatment, Outcome 7 Reinfection rate: short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment Outcome: 7 Reinfection rate: short-term

Study or subgroup	3-6 days n/N	7-14 days n/N	M-H,Rai	Risk Ratio ndom,95% Cl	Risk Ratio M-H,Random,95% CI
Raz 1996	10/119	2/104			4.37 [0.98, 19.49]
			0.1 Favours 3-6 days	10 Favours 7-14 days	

Analysis 3.8. Comparison 3 Short-course versus long-course treatment, Outcome 8 Reinfection rate: long-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment Outcome: 8 Reinfection rate: long-term

Study or subgroup	3-6 days n/N	7-14 days n/N		R M-H,Rand	lisk Ratio	s Cl	Weight	Risk Ratio M-H,Random,95% Cl
Raz 1996	4/ 9	5/104		_			44.9 %	2.45 [0.91, 6.56]
Vogel 2004	13/93	16/89					55.1 %	0.78 [0.40, 1.52]
Total (95% CI) Total events: 27 (3-6 days Heterogeneity: Tau ² = 0.4 Test for overall effect: Z =	212), 21 (7-14 days) 8; Chi ² = 3.59, df = 1 = 0.46 (P = 0.65)	193 (P = 0.06); I ² =72%			-		100.0 %	1.30 [0.42, 4.01]
			0.2 Favours	0.5 I 3-6 days	2 Favours	5 ; 7-14 days		

Analysis 3.9. Comparison 3 Short-course versus long-course treatment, Outcome 9 Acceptability (little or not satisfied with treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course versus long-course treatment

Outcome: 9 Acceptability (little or not satisfied with treatment)

Study or subgroup	3-6 days n/N	7-14 days n/N	M-H,Ra	Risk Ratio andom,95% Cl	Risk Ratio M-H,Random,95% Ci
Guibert 1997	2/49	5/43			0.35 [0.07, 1.72]
			•		
			0.1 Favours 3-6 days	I IO Favours 7-14 days	

Analysis 3.10. Comparison 3 Short-course versus long-course treatment, Outcome 10 Mean number of adverse events/patient (day 5).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 3 Short-course versus long-course treatment

Outcome: 10 Mean number of adverse events/patient (day 5)

Study or subgroup	3-6 days		7-14 days		Mea	n Difference	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	IV,Rando	om,95% Cl	IV,Random,95% CI
Vogel 2004	91	0.9 (1.1)	86	1.6 (1.5)			-0.70 [-1.09, -0.31]
					-1.2 -0.6 0	0 0.6 1.2	
					Favours 3-6 days	Favours 7-14 days	

Analysis 3.11. Comparison 3 Short-course versus long-course treatment, Outcome 11 Mean number of adverse events/patient (day 9).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 3 Short-course versus long-course treatment Outcome: 11 Mean number of adverse events/patient (day 9)

Study or subgroup	3-6 days N	Mean(SD)	7-14 days N	Mean(SD)	Mean D IV,Random,	Difference ,95% Cl	Mean Difference IV,Random,95% Cl
Vogel 2004	91	1.2 (1.3)	86	2.1 (1.6)			-0.90 [-1.33, -0.47]
					-1.48 -0.74 0 Favours 3-6 days	0.74 I.48 Favours 7-14 days	

Analysis 4.1. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 1 Persistent UTI: short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days)

Outcome: I Persistent UTI: short-term

Study or subgroup	Single dose	3-14 days	Risk Ratio	Weight	Risk Ratio
	n/IN	n/IN	M-H,Kandom,95% CI		M-H,Kandom,95% CI
Andersen 1986	4/10	3/15		11.6 %	2.00 [0.56, 7.09]
Ferraro 1990	3/30	5/30		10.6 %	0.60[016.229]
Elanagan 1991	5/10	2/9		14.2 %	1 22 [0.45 2.94]
	5/10	5/0		17.5 %	
Gellermann 1988	5/11	5/12	_	17.5 %	1.09 [0.43, 2.77]
Guibert 1993	3/189	4/186		9.0 %	0.74 [0.17, 3.25]
Guibert 1996	7/79	6/79		15.1 %	1.17 [0.41, 3.32]
Jardin 1990	6/23	2/31		8.8 %	4.04 [0.90, 18.24]
Lacey 1981	16/49	3/47		13.0 %	5.12 [1.59, 16.42]
Subtotal (95% CI)	401	408	•	100.0 %	1.51 [0.92, 2.49]
Heterogeneity: Tau ² = 0.14; (Test for overall effect: $Z = 1$.) 2 Trials comparing the same	Chi ² = 9.71, df = 7 (P = 63 (P = 0.10) antibiotic in each group	= 0.2 l); l ² =28%			
Andersen 1986	4/10	3/15		21.1 %	2.00 [0.56, 7.09]
Flanagan 1991	5/10	3/8		25.4 %	1.33 [0.45, 3.96]
Gellermann 1988	5/11	5/12	-+	30.1 %	1.09 [0.43, 2.77]
Lacey 1981	16/49	3/47		23.4 %	5.12 [1.59, 16.42]
Subtotal (95% CI) Total events: 30 (Single dose) Heterogeneity: Tau ² = 0.22; 0 Test for overall effect: Z = 1. 3 Hospital setting Flanagan 1991	80), 14 (3-14 days) Chi ² = 5.07, df = 3 (P = 71 (P = 0.086) 5/10	82 = 0.17); 1 ² =41% 3/8	-	100.0 %	1.87 [0.91, 3.83]
Lacey 1981	16/49	3/47		48.9 %	5,12 [1,59, 16,42]
Subtotal (95% CI)	59	55		100.0 %	2 57 [0 64 10 37]
Total events: 21 (Single dose) Heterogeneity: Tau ² = 0.68; 0 Test for overall effect: Z = 1. 4 Ambulatory patients), 6 (3-14 days) Chi ² = 3.06, df = 1 (P = 33 (P = 0.18)	= 0.08); I ² =67%		25 9	2.07 [0.03, 10.07]
Andersen 1706	10	Favours	0.1 10 s single dose Favours 3-14 d	avs	(Continued)

Study or subgroup	Single dose n/N	3-14 days n/N	Risk Ratio M-H,Random,95% Cl	Weight	Risk Ratio M-H,Random,95% Cl
Gellermann 1988	5/11	5/12		64.9 %	1.09 [0.43, 2.77]
Subtotal (95% CI)	21	27	-	100.0 %	1.35 [0.64, 2.86]
Total events: 9 (Single dose),	8 (3-14 days)				
Heterogeneity: Tau ² = 0.0; Cł	$hi^2 = 0.58$, $df = 1$ (P =	0.45); l² =0.0%			
Test for overall effect: $Z = 0.7$	78 (P = 0.43)				
			0.1 1 10		
		Favours s	ingle dose Favours 3	-14 days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: I Persistent UTI: short-term

-

Study or subgroup	Single dose	3-14 days	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Random,95% CI	M-H,Random,95% Cl
I All trials				
Andersen 1986	4/10	3/15		2.00 [0.56, 7.09]
Ferraro 1990	3/30	5/30		0.60 [0.16, 2.29]
Flanagan 1991	5/10	3/8		1.33 [0.45, 3.96]
Gellermann 1988	5/11	5/12		1.09 [0.43, 2.77]
Guibert 1993	3/189	4/186		0.74 [0.17, 3.25]
Guibert 1996	7/79	6/79	_	1.17 [0.41, 3.32]
Jardin 1990	6/23	2/31		4.04 [0.90, 18.24]
Lacey 1981	16/49	3/47		5.12 [1.59, 16.42]
Subtotal (95% CI)	401	408	•	1.51 [0.92, 2.49]
Total events: 49 (Single dose), 3	(3-14 days)			
Heterogeneity: Tau² = 0.14; Chi	² = 9.71, df = 7 (P = 0.21); l ²	=28%		
Test for overall effect: $Z = 1.63$	(P = 0.10)			
			0.1 1 10	
		Fav	vours single dose Favours 3-14	days

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: I Persistent UTI: short-term

Study or subgroup	Single dose n/N	3-14 days n/N	Risk Ratio M-H,Random,95% Cl	Risk Ratio M-H,Random,95% Cl
2 Trials comparing the same antil	piotic in each group			
Andersen 1986	4/10	3/15		2.00 [0.56, 7.09]
Flanagan 1991	5/10	3/8	_ -	1.33 [0.45, 3.96]
Gellermann 1988	5/11	5/12		1.09 [0.43, 2.77]
Lacey 1981	16/49	3/47		5.12 [1.59, 16.42]
Subtotal (95% CI)	80	82	-	1.87 [0.91, 3.83]
Total events: 30 (Single dose), 14 Heterogeneity: Tau ² = 0.22; Chi ² Test for overall effect: $Z = 1.71$ ((3-14 days) = 5.07, df = 3 (P = 0.17); I P = 0.086)	2 =41%		
		Fave	0.1 I IO burs single dose Favours 3-14 days	
Review: Antibiotic duration for Comparison: 4 Single dose vers Outcome: 1 Persistent UTI: sho	treating uncomplicated, syn sus short-course or long-co ort-term	nptomatic lower urinary trac urse treatment (3 to 14 day:	t infections in elderly women ;)	
Review: Antibiotic duration for Comparison: 4 Single dose vers Outcome: 1 Persistent UTI: sho Study or subgroup	treating uncomplicated, syn sus short-course or long-co ort-term Single dose n/N	nptomatic lower urinary trac urse treatment (3 to 14 day: 3-14 days n/N	t infections in elderly women) Risk Ratio M-H,Random,95% Cl	Risk Ratio M-H,Random,95% Cl
Review: Antibiotic duration for Comparison: 4 Single dose vers Outcome: 1 Persistent UTI: sho Study or subgroup 3 Hospital setting Flanagan 1991	treating uncomplicated, syr sus short-course or long-co ort-term Single dose n/N 5/10	nptomatic lower urinary trac urse treatment (3 to 14 day: 3-14 days n/N 3/8	t infections in elderly women ;) Risk Ratio M-H,Random,95% Cl	Risk Ratio M-H,Random,95% CI 1.33 [0.45, 3.96]
Review: Antibiotic duration for Comparison: 4 Single dose vers Outcome: 1 Persistent UTI: sho Study or subgroup 3 Hospital setting Flanagan 1991 Lacey 1981	treating uncomplicated, syr sus short-course or long-co ort-term Single dose n/N 5/10 16/49	nptomatic lower urinary trac ourse treatment (3 to 14 days 3-14 days n/N 3/8 3/47	t infections in elderly women) Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI 1.33 [0.45, 3.96] 5.12 [1.59, 16.42]
Review: Antibiotic duration for Comparison: 4 Single dose vers Outcome: 1 Persistent UTI: sho Study or subgroup 3 Hospital setting Flanagan 1991 Lacey 1981 Subtotal (95% CI) Total events: 21 (Single dose), 6 G Heterogeneity: Tau ² = 0.68; Chi ² Test for overall effect: Z = 1.33 (treating uncomplicated, syr sus short-course or long-co prt-term Single dose n/N 5/10 16/49 59 (3-14 days) = 3.06, df = 1 (P = 0.08); 1 P = 0.18)	nptomatic lower urinary trac iurse treatment (3 to 14 day: 3-14 days n/N 3/8 3/47 55 2 =67%	t infections in elderly women) Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% Cl I.33 [0.45, 3.96] 5.12 [1.59, 16.42] 2.57 [0.64, 10.37]

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: I Persistent UTI: short-term

Study or subgroup	Single dose	3-14 days	F	Risk Ratio	Risk Ratio
	n/N	n/N	M-H,Ran	dom,95% Cl	M-H,Random,95% Cl
4 Ambulatory patients					
Andersen 1986	4/10	3/15	_		2.00 [0.56, 7.09]
Gellermann 1988	5/11	5/12	_	-	1.09 [0.43, 2.77]
Subtotal (95% CI)	21	27	-	-	1.35 [0.64, 2.86]
Total events: 9 (Single dose), 8	(3-14 days)				
Heterogeneity: Tau² = 0.0; Chi²	² = 0.58, df = 1 (P = 0.45); l ²	=0.0%			
Test for overall effect: $Z = 0.78$	(P = 0.43)				
			0.1	1 10	
		Fav	ours single dose	Favours 3-14 days	

Analysis 4.2. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 2 Persistent UTI: long-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days)

Outcome: 2 Persistent UTI: long-term

Study or subgroup	Single dose	3-14 days	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Random,95% Cl		M-H,Random,95% Cl
I All trials					
Ferraro 1990	7/30	8/30		16.3 %	0.88 [0.36, 2.11]
Flanagan 1991	6/9	3/7		13.4 %	1.56 [0.59, 4.11]
Gellermann 1988	4/	6/12		13.5 %	0.73 [0.28, 1.91]
Guibert 1993	30/189	24/186		51.1 %	1.23 [0.75, 2.02]
Jardin 1990	3/17	3/30		5.7 %	1.76 [0.40, 7.80]
Subtotal (95% CI)	256	265	•	100.0 %	1.14 [0.80, 1.63]
Total events: 50 (Single dose), 44 (3-14 days)				
Heterogeneity: Tau² = 0.0; C	$Chi^2 = 2.00, df = 4 (P = 0)$	0.74); I² =0.0%			
Test for overall effect: $Z = 0$.	73 (P = 0.47)				
2 Trials comparing the same	antibiotic in each group				
Flanagan 1991	6/9	3/7		49.7 %	1.56 [0.59, 4.11]
Gellermann 1988	4/	6/12		50.3 %	0.73 [0.28, 1.91]
			0.2 0.5 2 5 Favours single dose Favours 3-14 da	iys	(Continued)

(... Continued)

Study or subgroup	Single dose	3-14 days		F	Risk Ratio	c	Weight	Risk Ratio
	n/N	n/N		M-H,Ran	dom,95%	% CI		M-H,Random,95% Cl
Subtotal (95% CI)	20	19		V			100.0 %	1.06 [0.50, 2.24]
Total events: 10 (Single dose)	, 9 (3-14 days)							
Heterogeneity: Tau ² = 0.05; 0	Chi² = 1.19, df = 1 (P =	0.28); ² = 6%						
Test for overall effect: $Z = 0$.	16 (P = 0.88)							
			l			1		
			0.2	0.5	2	5		
			Favours sin	gle dose	Favour	s 3-14 days		

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days)

Outcome: 2 Persistent UTI: long-term

Study or subgroup	Single dose	3-14 days		Risk Ratio		Risk Ratio
	n/N	n/N		M-H,Random,95% Cl		M-H,Random,95% Cl
All trials						
Ferraro 1990	7/30	8/30				0.88 [0.36, 2.11]
Flanagan 1991	6/9	3/7				1.56 [0.59, 4.11]
Gellermann 1988	4/	6/12				0.73 [0.28, 1.91]
Guibert 1993	30/189	24/186		-		1.23 [0.75, 2.02]
Jardin 1990	3/17	3/30				1.76 [0.40, 7.80]
Subtotal (95% CI)	256	265		-	•	1.14 [0.80, 1.63]
Total events: 50 (Single dose), 4	14 (3-14 days)					
Heterogeneity: Tau² = 0.0; Chi²	² = 2.00, df = 4 (P = 0.74); I ²	=0.0%				
Test for overall effect: $Z = 0.73$	(P = 0.47)					
			0.2	0.5	1 2 5	
			Favours s	ingle dose	Favours 3-14 days	

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: 2 Persistent UTI: long-term

Study or subgroup	Single dose	3-14 days	Risk F		Risk Ratic)	Risk Ratio	
	n/N	n/N	M-H,Randon		M-H,Random,95% CI		6 CI	M-H,Random,95% Cl
2 Trials comparing the same an	tibiotic in each group							
Flanagan 1991	6/9	3/7				-	1.56 [0.59, 4.11]	
Gellermann 1988	4/11	6/12					0.73 [0.28, 1.91]	
Subtotal (95% CI)	20	19					1.06 [0.50, 2.24]	
Total events: 10 (Single dose), 9	9 (3-14 days)							
Heterogeneity: Tau ² = 0.05; Ch	ni ² = 1.19, df = 1 (P = 0.28); l ² =	=16%						
Test for overall effect: $Z = 0.16$	(P = 0.88)							
						1		
			0.2	0.5	1 2	5		
			Favours sin	gle dose	Favours	s 3-14 days		

Analysis 4.3. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 3 Clinical failure (persistence of symptoms): short-term.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: 3 Clinical failure (persistence of symptoms): short-term

Study or subgroup	Single dose n/N	3-14 days n/N	Risk Ratio M-H,Random,95% Cl	Weight	Risk Ratio M-H,Random,95% Cl
Guibert 1993	10/197	5/191		89.6 %	1.94 [0.68, 5.57]
Matsumoto 1994	1/15	0/8		10.4 %	1.69 [0.08, 37.26]
Total (95% CI) Total events: 11 (Single do Heterogeneity: Tau ² = 0.0 Test for overall effect: Z =	212 ose), 5 (3-14 days) ; Chi ² = 0.01, df = 1 (P = 1.27 (P = 0.20)	199 : 0.93); l ² =0.0%		100.0 %	1.91 [0.70, 5.19]
		Favours	0.1 I 10 single dose Favours 3-14 days		

Analysis 4.5. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 5 Adverse drug reactions.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower uninary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: 5 Adverse drug reactions

Study or subgroup	Single dose	3-14 days		Risk Ratio	Weight	Risk Ratio
	n/N	n/N	٢	1-H,Random,95% Cl		M-H,Random,95% Cl
Ferraro 1990	1/30	2/30			5.8 %	0.50 [0.05, 5.22]
Flanagan 1991	0/31	2/22	_		3.6 %	0.14[0.01, 2.85]
Guibert 1993	19/244	21/238		-	90.6 %	0.88 [0.49, 1.60]
Total (95% CI)	305	290		•	100.0 %	0.80 [0.45, 1.41]
Total events: 20 (Single do	se), 25 (3-14 days)					
Heterogeneity: Tau ² = 0.0;	Chi ² = 1.54, df = 2 (P	= 0.46); l ² =0.0%				
Test for overall effect: $Z =$	0.77 (P = 0.44)					
			0.01	0.1 1 10 100		

Favours single dose Favours 3-14 days

Analysis 4.6. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 6 Discontinuationsdue to adverse reactions.

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days)

Outcome: 6 Discontinuationsdue to adverse reactions

Study or subgroup	Single dose	3-14 days	Risk Ratio	o Weight	Risk Ratio
	n/N	n/N	M-H,Random,959	% CI	M-H,Random,95% Cl
Ferraro 1990	0/30	1/30		100.0 %	0.33 [0.01, 7.87]
Flanagan 1991	0/31	0/22		0.0 %	Not estimable
Guibert 1993	0/244	0/238		0.0 %	Not estimable
Total (95% CI) Total events: 0 (Single dos Heterogeneity: not applic Test for overall effect: Z =	305 se), I (3-14 days) able = 0.68 (P = 0.50)	290		100.0 %	0.33 [0.01, 7.87]
			0.1 1 10)	
		Favour	s single dose Favou	urs 3-14 days	

Analysis 4.7. Comparison 4 Single dose versus short-course or long-course treatment (3 to 14 days), Outcome 7 Acceptability (little or not satisfied with treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 4 Single dose versus short-course or long-course treatment (3 to 14 days) Outcome: 7 Acceptability (little or not satisfied with treatment)

Study or subgroup	single dose	3-14 days	Ri	sk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Rand	om,95% Cl		M-H,Random,95% Cl
Guibert 1993	89/197	119/191			74.6 %	0.73 [0.60, 0.88]
Guibert 1996	3/79	10/79			25.4 %	0.30 [0.09, 1.05]
Total (95% CI)	276	270	-		100.0 %	0.58 [0.27, 1.25]
Total events: 92 (single do	ose), 129 (3-14 days)					
Heterogeneity: Tau ² = 0.2	.0; Chi² = 1.94, df = 1 (l	^D = 0.16); l ² =48%				
Test for overall effect: Z =	= 1.39 (P = 0.16)					
			0.1 1	10		
		Favou	rs single dose	Favours 3-14 days		

Analysis 5.1. Comparison 5 3 days versus 5 days, Outcome I Persistent UTI: short term (3 days after treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women

Comparison: 5 3 days versus 5 days

Outcome: I Persistent UTI: short term (3 days after treatment)

Study or subgroup	3 days n/N	5 days n/N	M-H,Rar	Risk Ratio ndom,95% Cl	Risk Ratio M-H,Random,95% Cl	
van Merode 2005	7/12	3/14			2.72 [0.90, 8.27]	
			0.2 0.5	2 5		
			Favours 3 days	Favours 5 days		
Antibiotic duration for tree	ting uncomplicated as	motomatic lower urin	any tract infections i	n elderly women (Pevi		

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Analysis 5.2. Comparison 5 3 days versus 5 days, Outcome 2 Clinical failure (not recovered): short term (3 days after treatment).

Review: Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women Comparison: 5 3 days versus 5 days

Outcome: 2 Clinical failure (not recovered): short term (3 days after treatment)

Study or subgroup	3 days n/N	5 days n/N	Risk Ratio M-H,Random,95% (Risk Ratio CI M-H,Random,95% CI
van Merode 2005	3/12	3/14		1.17 [0.29, 4.74]
			0.2 0.5 2 5 Favours 3 days Favours 5	days
APPENDIC	E S			
Appendix I. Elec	tronic search strategie:	S		
Database searched	Search terms			
MEDLINE	 elderly explode "AGED"/ all st explode "AGED, 80 All old* geriatric* nursing home #1 or #2 or #3 or #4 or urinary tract infection* explode "URINARY T cystitis explode "CYSTITIS"/ UTI bacteriuria explode "BACTERIU #8 or #9 or #10 or #1 explode "ANTI-INFE explode "ANTIFIOT antibiotic* #16 or #17 or #18 #7 and #15 and #19 	ubheadings ND OVER"/ all subhe #5 or #6 RACT INFECTIONS / all subheadings 1 or #12 or #13 or #1 CCTIVE AGENTS" / : ICS"/ all subheadings	adings 3"/ all subheadings 4 all subheadings	
EMBASE	 RANDOMIZED ADJ RANDOM ADJ ALLO (SINGL\$ DOUBL\$ T PLACEBO\$1.TI,DE,A 1 2 3 4 ELDERLY AGED# AO NURSING WITH HO 	CONTROLLED AD OCAT\$5 REBL\$ TRIPL\$) WIT \B. GED GERIATRIC\$ C OME	J TRIAL\$1 TH (BLIND\$4 MASK\$4) LD	

(Continued)

8. 5 AND (6 7)
9. URINARY-TRACT-INFECTION#
10URINARY WITH INFECTION\$1
11 CYSTITIS
12. BACTERIURIA
13. 8 AND (9 10 11 12)
14. ANTI ADJ INFECTI\$5
15. ANTIBIOTIC\$4
16. 13 AND (14 15)

CENTRAL

#1. AGED #2. elderly #3. old* #4. geriatric **#5. GERIATRICS** #6. NURSING HOMES #7. HOMES FOR THE AGED #8. (#1 or #2 or #3 or #4 or #5 or #6 or #7) **#9. URINARY TRACT INFECTIONS** #10. (urinary next tract next infection*) #11. uti* #12. CYSTITIS #13. cystitis #14. BACTERIURIA #15. bacteriuria #16. (#9 or #10 or #11 or #12 or #13 or #14 or #15) #17. ANTI-INFECTIVE AGENTS #18. anti-infective* #19. antibiotic* #20. (#17 or #18 or #19) #21. (#8 and #16 and #20)

Appendix 2. Results of initial literature search

Database	System	Identified reference	Included references
MEDLINE	Knowledge Finder	2923	10
MEDLINE	Ovid	4115	10
MEDLINE	Grateful Med	5533	10
MEDLINE	PubMed	3098	10
EMBASE	Datastar	110	4
EMBASE Geriatrics	1989-99	219	1
Gerolit	DIMDI	12	0
Healthstar	DIMDI	1128	
Bioethics Line	DIMDI	0	0
Popline	GratefulMed	1	0
Cochrane CCRT		377	
ISTP 1978-95 (Index to Scientific & Technical Proceedings)	Printed index		
DAI 1991-1995 (Dissertation abstracts international)	Printed index		1
Authors and investigators	13 were contacted by letter or e-mail, 6 responded	17	0
Pharmaceutical companies	17 were contacted by letter of e-mail, 5 responded	106	2
References	Trial articles		1
References	Review articles		3

Appendix 3. Inter-individual variability of study selection

Abstract/articles	Total number	% of screened record	Different selections
Abstracts	262	ca. 5%	17 (6.5%)
Articles	166	79%	10 (6.1%)
Total	427		27 (6.3%)

Appendix 4. Sources of included studies

Trials	MEDLINE	EMBASE	Industry	Theses	References - reviews	References - trials
Andersen 1986	+					
Ferraro 1990	+	+				
Flanagan 1991	+	+	+	+	+	+
Gellermann 1988			+		+	
Guibert 1993	+	+				
Guibert 1996	+	+	+			
Guibert 1997	+		+			
Jardin 1990	+					
Lacey 1981	+	+			+	
Matsumoto 1994		+				
Piipo 1990						+
Raz 1996	+	+				
Stein 1992	+	+	+			
van Merode 2005	+					
Vogel 2004	+	+	-	-		

Trial	Allocation conceal- ment	Blinding	Random- ization method	Baseline character- istics	Power cal- culation	Sample size (old pt)	Excluded patients	Intention to treat	Overall quality
Andersen 1986	В	Double	NS	Yes ?	No	287	23, not described	No	С
Ferraro 1990	В	None	NS	NS	NS	60			С
Flanagan 1991	C (open lists)	None	Yes (random lists)	Yes, difference in mean number of drugs	No	81	30, reason described	No	С
Gellermann 1988	В	None	Yes (random list)	Yes (in detail), no difference	No	90	0	Yes (2 analyses)	С
Guibert 1993	B (NS)	None	Yes (random number table)	Yes, no difference	Yes	482	94 / 110, reasons described	No	С
Guibert 1996	A (tele- phone)	None	NS	Yes, no difference	Yes	595	213 /219, reasons described	No (efficacy), yes (ADRs)	С
Guibert 1997	A (tele- phone)	None	NS	Yes, no difference	Yes	421	81, reasons described	No (efficacy), yes (ADRs)	С
Jardin 1990	B (NS)	None	NS	Yes, difference in bio- chemical parameters	Yes (200)	386	90, reasons only partially described	No	С
Lacey 1981	B (NS)	Single (outcome assess- ment)	NS	Yes, no difference	NS	100	4, reasons described	No	С

(Continued)

Matsumoto	B (NS)	None	NS	NS					С
Piipo 1990	A (num- bered boxes)	Double	NS	No	NS	400	73, reasons described	No	С
Raz 1996	В	None	NS	Yes (difference ?)	Yes	223	27, reasons described	No	С
Stein 1992	A (num- bered boxes)	Double	Yes (computer random number generator)	Yes (difference ?)	Yes	404	184, reasons described	No	С
van Merode 2005	B (not specified envelopes)	Single (Physi- cian)	Yes (computer generated)	No	Yes	26	205/324 (all patients), reasons described	No	С
Vogel 2004	A (num- bered sealed envelopes)	Double	Yes (computer generated random- ization list, stratified by hospital laborato- ries)	Yes (only significant difference for supra- pubic pain)	Yes	183	1	Yes	A

WHAT'S NEW

Last assessed as up-to-date: 6 May 2008

Date	Event	Description		
7 May 2008	New citation required and conclusions have changed	2 new studies added, new outcomes.		
27 March 2008	Amended	Converted to new review format.		

HISTORY

Protocol first published: Issue 2, 1999

Review first published: Issue 3, 2002

Date

Event

Description

8 January 2004

New search has been performed

New search, no new trials

CONTRIBUTIONS OF AUTHORS

NV - study selection, data extraction, review writing

ML - study selection, data extraction, data analysis, review writing

DECLARATIONS OF INTEREST

None known

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Infective Agents, Urinary [*administration & dosage]; Randomized Controlled Trials as Topic; Time Factors; Treatment Outcome; Urinary Tract Infections [*drug therapy]

MeSH check words

Aged; Female; Humans; Middle Aged