The prevention of urinary tract infections

Background

Urinary tract infection (UTI) is one of the most commonly acquired bacterial infections. It is the second most frequent bacterial infection in residents of long-term–care facilities. Most infections are asymptomatic, with a prevalence of asymptomatic bacteriuria of 15%–50% among care home residents (Nicolle, 2013; Nicolle, 2000).

Summary and key findings

The use of antibiotics has generally been shown to be effective in the prevention of recurrent urinary tract infection. A 3-day course of antibiotics may not be significantly less effective than a 7-day course (Vogel et al, 2004) and, since the over-use of antibiotics is to be avoided to maintain their overall effectiveness, other solutions have been sought. One study (Bleidorn et al, 2010) has shown that treating symptoms with ibuprofen is not significantly less effective than the use of antibiotics.

Probiotic interventions have shown variable results in preventing the recurrence of UTIs depending on the type of probiotic used. Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 may be effective but Lactobacillus GG drink less so.

A number of small scale studies, over the years, have shown that cranberry derivatives, particularly tablets, and to a lesser extent juice, can be effective in preventing UTI, particularly for people at higher risk. A recently updated systematic review of cranberry treatments (Jepson, Williams and Craig, 2012) has however concluded that cranberry juice is not as effective as previously thought and suffers from a very high withdrawal/dropout rate.

Other interventions that may be effective include oral immunotherapy with Uro-Vaxom Escherichia coli (E. coli) extract, the use of vaginal oestrogens and HA-CS intravesical instillations.

Urinary tract infection is commonly associated with the use of catheters in care homes and hospitals. Guidelines to prevent infection indicate that the most effective measure is to avoid the use of catheters wherever possible (not using them as a routine intervention), to constantly monitor their use and to remove catheters at the earliest opportunity. Alternative catheter designs and the use of anti-microbial materials to reduce the formation of biofilm show promise but have not yet been conclusively proved to be effective.

Review of evidence

The reviewed evidence is listed in reverse chronological order with the most recent evidence first.

a) Reviews, overviews and comparative studies

Study	Findings	
Eells S J, Bharadwa K, McKinnell J A and Miller L G (2014) Recurrent Urinary Tract Infections Among Women: Comparative Effectiveness of 5 Prevention and Management Strategies Using a Markov Chain Monte Carlo Model, *Clinical Infectious Diseases* 58 (2) : 147-160	A systematic literature review of management of women experiencing 3 or more UTIs per year was carried out. The study then developed a Markov chain Monte Carlo model of recurrent UTI for each management strategy with 2 or more adequate trials published. The model simulated a cohort that experienced 3 UTIs/year and a secondary cohort that experienced 8 UTIs/year. Model outcomes were treatment efficacy, patient and payer cost, and health-related quality of life.	Five strategies had 2 or more clinical trials published: (1) daily antibiotic (nitrofurantoin) prophylaxis; (2) daily estrogen prophylaxis; (3) daily cranberry prophylaxis; (4) acupuncture prophylaxis; and (5) symptomatic self-treatment. In the 3 UTIs/year model, nitrofurantoin prophylaxis was most effective, reducing the UTI rate to 0.4 UTIs/year, and the most expensive to the payer ($821/year). All other strategies resulted in payer cost savings but were less efficacious. Symptomatic self-treatment was the only strategy that resulted in patient cost savings, and was the most favourable strategy in term of cost per quality-adjusted life-year (QALY) gained. Conclusions: Daily antibiotic use is the most effective strategy for recurrent UTI prevention compared to daily cranberry pills, daily estrogen therapy, and acupuncture. Cost savings to payers and patients were seen for most regimens, and improvements in QALYs were seen with all.

Beerepoot M A J, Geerlings S E, van Haarst E P, van Charante N M and ter Riet G (2013) Nonantibiotic Prophylaxis for Recurrent Urinary Tract Infections: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, *The Journal of Urology* 190 (6) : 1981-1989	This review identified 5,413 records and included 17 studies with data for 2,165 patients. The oral immunostimulant OM-89 decreased the rate of urinary tract infection recurrence (4 trials, sample size 891, median Jadad score 3, RR 0.61, 95% CI 0.48–0.78) and had a good safety profile. The vaginal vaccine Urovac® slightly reduced urinary tract infection recurrence (3 trials, sample size 220, Jadad score 3, RR 0.81, 95% CI 0.68–0.96) and primary immunization followed by booster immunization increased the time to reinfection. Vaginal estrogens showed a trend toward preventing urinary tract infection recurrence (2 trials, sample size 201, Jadad score 2.5, RR 0.42, 95% CI 0.16–1.10) but vaginal irritation occurred in 6% to 20% of women. Cranberries decreased urinary tract infection recurrence (2 trials, sample size 250, Jadad score 4, RR 0.53, 95% CI 0.33–0.83) as did acupuncture (2 open label trials, sample size 165, Jadad score 2, RR 0.48, 95% CI 0.29–0.79). Oral estrogens and lactobacilli prophylaxis did not decrease the rate of urinary tract infection recurrence. Authors' conclusions: The evidence of the effectiveness of the oral immunostimulant OM-89 is promising. Although sometimes statistically significant, pooled findings for the other interventions should be considered tentative until corroborated by more research.
Nicolle L E (2013) Urinary tract infection in long-term care facilities, *Healthcare Infection* 19 (1) : 4-12	Asymptomatic bacteriuria and pyuria are pervasive in the long-term care population. Optimal management of urinary infection for residents of long-term care facilities requires knowledge of the unique features of the infection in this setting, together with critical evaluation of each episode of potential urinary infection in the individual resident. The author carried out a non-structured review of current knowledge and recommendations relevant to urinary infection in long-term care facilities. Urinary infection is the second most common infection occurring in long-term care facility residents. For residents without chronic indwelling catheters, acute, localising, genitourinary symptoms should be present to support a clinical diagnosis of symptomatic infection. Inappropriate antimicrobial use for urinary tract infection, particularly treatment of asymptomatic bacteriuria and prophylaxis of urinary infection, is a consistent observation in reviews of antimicrobial use in these facilities. Management approaches to improve treatment include observation and reassessment when symptoms are questionable or the diagnosis is unclear, limiting the use of chronic indwelling catheters, and early identification of complications, such as obstruction, of indwelling catheters. Conclusions: Clinical diagnostic imprecision and a high prevalence of asymptomatic bacteriuria means these infections are over-diagnosed and over-treated, leading to adverse events from excess antimicrobial use. Antimicrobial stewardship programs to improve antimicrobial use for this indication need to be developed in long-term care facilities.

McMurdo M E T, Argo I, Phillips G, Daly F and Davey P (2009) Cranberry or trimethoprim for the prevention of recurrent urinary tract infections? A randomized controlled trial in older women, *Journal of Antimicrobial Chemotherapy* 63 (2) : 389-395	To compare the effectiveness of cranberry extract with low-dose trimethoprim in the prevention of recurrent urinary tract infections (UTIs) in older women. One hundred and thirty-seven women with two or more antibiotic-treated UTIs in the previous 12 months were randomized to receive either 500 mg of cranberry extract or 100 mg of trimethoprim for 6 months. There were 17/137 (12%) withdrawals from the study, 6/69 (9%) from the cranberry group and 11/68 (16%) from the trimethoprim group (P = 0.205), with a relative risk of withdrawal from the cranberry group of 0.54 (95% CI: 0.19, 1.37).	Thirty-nine of 137 participants (28%) had an antibiotic-treated UTI (25 in the cranberry group and 14 in the trimethoprim group); difference in proportions relative risk 1.616 (95% CI: 0.93, 2.79) P = 0.084. The time to first recurrence of UTI was not significantly different between the groups (P = 0.100). The median time to recurrence of UTI was 84.5 days for the cranberry group and 91 days for the trimethoprim group (U = 166, P = 0.479). Conclusions: Trimethoprim had a very limited advantage over cranberry extract in the prevention of recurrent UTIs in older women and had more adverse effects.

Fihn S D (2003) Acute Uncomplicated Urinary Tract Infection in Women, *New England Journal of Medicine* 349 (3) : 259-268	This study presents an overview of urinary tract infection: The probability of cystitis in a woman with dysuria, urinary frequency, or gross hematuria is about 50 percent in primary care settings. Symptoms suggesting vaginitis or cervicitis, such as vaginal irritation or discharge, reduce the likelihood of a diagnosis of cystitis by about 20 percent. Specific combinations of symptoms (e.g., dysuria and frequency without vaginal discharge or irritation) raise the probability of cystitis to more than 90 percent. When a woman who has previously had cystitis has symptoms suggesting a recurrence, there is an 84 to 92 percent chance that an infection is present. The most important risk factors for acute cystitis in young women are a history of previous episodes of cystitis and frequent or recent sexual activity. Celibate women rarely have cystitis. The relative odds of acute cystitis during the 48 hours after sexual intercourse increase by a factor as great as 60. The use of spermicidal agents elevates the odds of infection by E. coli or by S. saprophyticus by a factor of two to three, irrespective of whether the exposure occurs with the use of a diaphragm or a spermicide-coated condom. Women with frequent recurrences are more likely to have a maternal history of cystitis and to have had cystitis at an early age. E. coli that encode the type 1 pilus, an organelle containing the adhesin FimH, which recognizes a wide range of cell types, are commonly associated with cystitis as well as sepsis and meningitis. Among elderly women living in institutional settings, the risk of urinary infection increases with age and debility, especially in those with conditions associated with impaired voiding or poor perineal hygiene (e.g., neurologic disease or dementia). Estrogen deficiency may also contribute. Among generally healthy postmenopausal women, sexual activity is a less important predictor of cystitis than it is in younger women, and women with diabetes that requires pharmacologic treatment have approximately twice as high a risk of cystitis as nondiabetic women. Recurrent cystitis in this age group is more likely in women who have cystoceles or urinary incontinence or who have previously undergone genitourinary surgery than in other women.

Nicolle L E (2000) Urinary Tract Infection in Long-Term–Care Facility Residents, *Clinical Infectious Disease* 31 : 757-761 [see also Nicolle L E (2013) above]	Overview: Urinary tract infection is the most frequent bacterial infection in residents of long-term–care facilities. Most infections are asymptomatic, with a remarkable prevalence of asymptomatic bacteriuria of 15%–50% among all residents. The major reasons for this high prevalence are chronic comorbid illnesses with neurogenic bladder and interventions to manage incontinence. Prospective, randomized, comparative trials of therapy and no therapy for asymptomatic bacteriuria among nursing home residents have repeatedly documented that antimicrobial treatment had no benefits. However, there is substantial diagnostic uncertainty in determining whether an individual with a positive urine culture has symptomatic or asymptomatic infection when there is clinical deterioration and there are no localized findings. In the non-catheterized resident, urinary infection is an infrequent source of fever but may not be definitively excluded. The use of antimicrobials for treatment of urinary infection is part of the larger concern about appropriate antimicrobial use in long-term–care facilities and the impacts of the selective pressure of antimicrobials on colonization and infection with resistant organisms.

b) The use of antibiotics

Study	Methods	Findings
Bleidorn J, Gágyor I, Kochen M M, Wegscheider K and Hummers-Pradier E (2010) Symptomatic treatment (ibuprofen) or antibiotics (ciprofloxacin) for uncomplicated urinary tract infection?-results of a randomized controlled pilot trial, *BMC Medicine* 8 (30)	A double-blind, randomized controlled pilot trial in 29 German general practices. Eighty otherwise healthy women aged 18 to 85 years, presenting with at least one of the main UTI symptoms dysuria and frequency and without any complicating factors, were randomly assigned to receive either ibuprofen 3 × 400 mg oral or ciprofloxacin 2 × 250 mg (+1 placebo) oral, both for three days. Intensity of main symptoms - dysuria, frequency, low abdominal pain - was recorded at inclusion and after 4, 7 and 28 days, scoring each symptom from 0 (none) to 4 (very strong). The primary endpoint was symptom resolution on Day 4. Secondary outcomes were the burden of symptoms on Days 4 and 7 (based on the sum score of all symptoms), symptom resolution on Day 7 and frequency of relapses. Equivalence margins for symptom burden on Day 4 were prespecified as +/- 0.5 sum score points. Data analysis was done by intention to treat and per protocol. Randomization was carried out on patient level by computer programme in blocks of six.	Seventy-nine patients were analyzed (ibuprofen n = 40, ciprofloxacin n = 39). On Day 4, 21/36 (58.3%) of patients in the ibuprofen-group were symptom-free versus 17/33 (51.5%) in the ciprofloxacin-group. On Day 4, ibuprofen patients reported fewer symptoms in terms of total sum score (1; SD 1,42) than ciprofloxacin patients (1,3; SD 1,9), difference -0,33 (95% CI (-1,13 to +0,47)), PP (per protocol) analysis. During Days 0 and 9, 12/36 (33%) of patients in the ibuprofen-group received secondary antibiotic treatment due to ongoing or worsening symptoms, compared to 6/33 (18%) in the ciprofloxacin-group (non significant). A total of 58 non-serious adverse events were reported, 32 in the ibuprofen group versus 26 in the ciprofloxacin group (non significant). Conclusions: Our results support the assumption of non-inferiority of ibuprofen compared to ciprofloxacin for treatment of symptomatic uncomplicated UTI, but need confirmation by further trials.

Little P, Moore M V, Turner S, Rumsby K, Warner G, Lowes J A, Smith H, Hawke C, Leydon G, Arscott A, Turner D and Mullee M (2010) Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial, *British Medical Journal* 340 : c199	A randomised controlled trial to assess the impact of different management strategies in urinary tract infections in primary care. Participants: 309 non-pregnant women aged 18-70 presenting with suspected urinary tract infection. Patients were randomised to five management approaches: empirical antibiotics; empirical delayed (by 48 hours) antibiotics; or targeted antibiotics based on a symptom score (two or more of urine cloudiness, urine smell, nocturia, or dysuria), a dipstick result (nitrite or both leucocytes and blood), or a positive result on midstream urine analysis. Self help advice was controlled in each group. Main outcome measures were symptom severity (days 2 to 4) and duration, and use of antibiotics.	Patients had 3.5 days of moderately bad symptoms if they took antibiotics immediately. There were no significant differences in duration or severity of symptoms (mean frequency of symptoms on a 0 to 6 scale: immediate antibiotics 2.15, midstream urine 2.08, dipstick 1.74, symptom score 1.77, delayed antibiotics 2.11; likelihood ratio test for the five groups P=0.177). There were differences in antibiotic use (immediate antibiotics 97%, midstream urine 81%, dipstick 80%, symptom score 90%, delayed antibiotics 77%; P=0.011) and in sending midstream urine samples (immediate antibiotics 23%, midstream urine 89%, dipstick 36%, symptom score 33%, delayed antibiotics 15%; P<0.001). Patients who waited at least 48 hours to start taking antibiotics re-consulted less (hazard ratio 0.57 (95% confidence interval 0.36 to 0.89), P=0.014) but on average had symptoms for 37% longer than those taking immediate antibiotics (incident rate ratio 1.37 (1.11 to 1.68), P=0.003), particularly the midstream urine group (73% longer, 22% to 140%; none of the other groups had more than 22% longer duration). Conclusion: All management strategies achieve similar symptom control. There is no advantage in routinely sending midstream urine samples for testing, and antibiotics targeted with dipstick tests with a delayed prescription as backup, or empirical delayed prescription, can help to reduce antibiotic use.

McMurdo M E T, Argo I, Phillips G, Daly F and Davey P (2009) Cranberry or trimethoprim for the prevention of recurrent urinary tract infections? A randomized controlled trial in older women, *Journal of Antimicrobial Chemotherapy* 63 (2) : 389-395	See comparative studies

Albert X, Huertas I, Pereiro I, Sanfélix J, Gosalbes V and Perrotta C (2008) *Antibiotics for preventing recurrent urinary tract infection in*, The Cochrane Collaboration. Published by John Wiley & Sons, Ltd	To determine the efficacy (during and after) and safety of prophylactic antibiotics used to prevent uncomplicated RUTI in adult non-pregnant women. A review of published randomised controlled trial where antibiotics were used as prophylactic therapy in RUTI. Two reviewers independently assessed trial quality and extracted data. Statistical analyses were performed using the random effects model and the results expressed as relative risk (RR) with 95% confidence intervals (CI). Nineteen studies involving 1120 women were eligible for inclusion.	During active prophylaxis the rate range of microbiological recurrence patient-year (MRPY) was 0 to 0.9 person-year in the antibiotic group against 0.8 to 3.6 with placebo. The RR of having one microbiological recurrence (MR) was 0.21 (95% CI 0.13 to 0.34), favouring antibiotic and the NNT was 1.85. For clinical recurrences (CRPY) the RR was 0.15 (95% CI 0.08 to 0.28). The NNT was 1.85. The RR of having one MR after prophylaxis was 0.82 (95% CI 0.44 to 1.53). The RR for severe side effects was 1.58 (95% CI 0.47 to 5.28) and for other side effects the RR was 1.78 (CI 1.06 to 3.00) favouring placebo. Side effects included vaginal and oral candidiasis and gastrointestinal symptoms. Weekly perfloxacin was more effective than monthly. The RR for MR was 0.31(95% CI 0.19 to 0.52). There was no significant difference in MR between continuous daily and post-coital iprofloxacin. Authors' conclusions Continuous antibiotic prophylaxis for 6-12 months reduced the rate of UTI during prophylaxis when compared to placebo. After prophylaxis two studies showed no difference between groups. There were more adverse events in the antibiotic group. One RCT compared post-coital versus continuous daily ciprofloxacin and found no significant difference in rates of UTIs, suggesting that post-coital treatment could be offered to woman who have UTI associated with sexual intercourse.

Richards D, Toop L, Chambers S and Fletcher L (2005) Response to antibiotics of women with symptoms of urinary tract infection but negative dipstick urine test results: double blind randomised controlled trial., *British Medical Journal* 331 (7509) : 143-146	To assess the effectiveness of antibiotic treatment of women with symptoms of urinary tract infection but negative urine dipstick testing. A prospective, double blind, randomised, placebo controlled trial in primary care, among a randomly selected group of general practitioners in Christchurch, New Zealand. Participants: 59 women aged 16-50 years presenting with a history of dysuria and frequency in whom a dipstick test of midstream urine was negative for both nitrites and leucocytes. Participants with complicated urinary tract infection were excluded. Intervention: Trimethoprim 300 mg daily for three days or placebo. Main outcome measures: Self reported diary of symptoms for seven days, recording the presence or absence of individual symptoms each day, followed by a structured telephone questionnaire after seven days. The main clinical outcome was resolution of dysuria at three and seven days and median time to resolution. Secondary outcomes were resolution of other symptoms.	The median time for resolution of dysuria was three days for trimethoprim compared with five days for placebo (P = 0.002). At day 3, five (24%) of patients in the treatment group had ongoing dysuria compared with 20 (74%) in the placebo group (P = 0.005). This difference persisted until day 7: two patients (10%) in the treatment group v 11 (41%) in the placebo group; P = 0.02). The number needed to treat was 4. The median duration of constitutional symptoms (feverishness, shivers) was reduced by four days. Conclusions: Although a negative dipstick test for leucocytes and nitrites accurately predicted absence of infection when standard microbiological definitions were used (negative predictive value 92%), it did not predict response to antibiotic treatment. Three days' treatment with trimethoprim significantly reduced dysuria in women whose urine dipstick test was negative. These results support the practice of empirical antibiotic use guided by symptoms.

Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, and Rochette L (2004) Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: a double-blind randomized controlled trial, *Canadian Medical Association Journal* 170 (4) : 469-473	The aim of this randomized controlled double-blind noninferiority trial was to compare the efficacy and safety of 3-day and 7-day courses of oral ciprofloxacin for uncomplicated symptomatic UTI in older women. A total of 183 women at least 65 years of age with acute uncomplicated UTI were recruited from ambulatory clinics and hospital acute care units. Patients with pyelonephritis, contraindications to fluoroquinolones, recent use of antibiotics, urinary tract abnormalities and diabetes mellitus were excluded. Women were randomly assigned to receive either ciprofloxacin 250 mg twice daily orally for 3 days followed by placebo for 4 days (the 3-day group, 93 patients) or ciprofloxacin 250 mg twice daily orally for 7 days (the 7-day group, 90 patients). Bacterial eradication, clinical improvement and occurrence of adverse events were determined 2 days after completion of treatment, and occurrence of re-infection or relapse were determined 6 weeks after completion of treatment. Bacterial eradication and relapse were determined by urine culture. Double-blind procedures were maintained throughout data collection.	The proportion of patients with bacterial eradication at 2 days after treatment was 98% (91/93) in the 3-day group and 93% (83/89) in the 7-day group (p = 0.16). The frequency of adverse events, including drowsiness, headache, nausea or vomiting, and loss of appetite, was significantly lower in the 3-day group. These results suggest that a 3-day course of antibiotic therapy is not inferior to a 7-day course for treatment of uncomplicated symptomatic UTI in older women, and that the shorter course is better tolerated.

Christiaens T C M, De Meyere M, Verschraegen G, Peersman W, Heytens S and De Maeseneer J M (2002) Randomised controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women, *British Journal of General Practice* 52 (482) : 729-734	To measure the symptomatic and bacteriological short-term effect of nitrofurantoin treatment versus placebo, in the treatment of uncomplicated UTI in adult non-pregnant women. A randomised placebo-controlled trial in general practice of non-pregnant women, aged between 15 and 54 years old, consulting a general practitioner for symptoms suggestive of uncomplicated lower UTI and with pyuria (positive for leucocyte esterase test). A dipslide was inoculated in first-void midstream urine and sent for examination. The patients were randomised to receive nitrofurantoin 100 mg or placebo four times daily for three days. After three, seven, and 14 days a new dipslide was inoculated and symptoms of UTI were checked for the disappearance or improvement of symptoms and bacteriuria. Of 166 women consulting with symptoms suggestive for UTI, 78 had pyuria and agreed to participate in the study (the clinically suspected UTI group); of these, 40 received nitrofurantoin and 38 received placebo.	The result for combined symptomatic improvement and cure after three days was 27/35 in the nitrofurantoin group and 19/35 in the placebo group (c2 with Yates' correction P =0.08; number needed to treat [NNT] = 4.4, 95% confidence interval [CI] = 2.3 to 79). After seven days, combined improvement and cure was observed in 30/34 and 17/33 respectively (P = 0.003, NNT = 2.7, 95% CI = 1.8 to 6.0). At inclusion, 56 women had bacteriuria of 105 CFU/ml (the bacteriologically proven UTI group). Of these, 29 received nitrofurantoin and 27 received placebo. After three days the bacteriological cure was 21/26 in the treatment group, compared with 5/25 in the placebo group (P<0.001; NNT = 1.6, 95% CI = 1.2 to 2.6). After seven days the bacteriological cure rate was 17/23 in the intervention group and 9/22 in the placebo group (P = 0.05, NNT = 3, 95% CI = 1.7 to 17). Conclusion: In women with bacteriologically proven UTI, nitrofurantoin was significantly more effective than placebo in achieving bacteriological cure and symptomatic relief in just three days; this was still present after seven days. In patients with clinically suspected UTI the symptomatic effect was statistically significant after seven days; after three days there was a trend towards significance.

c) The use of probiotics

Study	Methods	Findings
Stapleton A E, Au-Yeung M, Hooton T M, Fredricks D N, Roberts P L, Czaja C A, Yarova-Yarovaya Y, Fiedler T, Cox M and Stamm W E (2011) Randomized, Placebo-Controlled Phase 2 Trial of a Lactobacillus crispatus Probiotic Given Intravaginally for Prevention of Recurrent Urinary Tract Infection, *Clinical Infectious Diseases* 52 (10) : 1212-1217	Depletion of vaginal lactobacilli is associated with UTI risk, which suggests that repletion may be beneficial. This study conducted a double-blind placebo-controlled trial of a Lactobacillus crispatus intravaginal suppository probiotic (Lactin-V; Osel) for prevention of recurrent UTI in premenopausal women. One hundred young women with a history of recurrent UTI received antimicrobials for acute UTI and then were randomized to receive either Lactin-V or placebo daily for 5 days, then once weekly for 10 weeks. Participants were followed up at 1 week and 10 weeks after intervention and for UTIs; urine samples for culture and vaginal swabs for real-time quantitative 16S ribosomal RNA gene polymerase chain reaction for L. crispatus were collected.	Recurrent UTI occurred in 7/48 15% of women receiving Lactin-V compared with 13/48 27% of women receiving placebo (relative risk [RR], .5; 95% confidence interval, .2–1.2). High-level vaginal colonization with L. crispatus (=106 16S RNA gene copies per swab) throughout follow-up was associated with a significant reduction in recurrent UTI only for Lactin-V (RR for Lactin-V, .07; RR for placebo, 1.1; P < .01). Conclusions. Lactin-V after treatment for cystitis is associated with a reduction in recurrent UTI.

Falagas M E, Betsi G I, Tokas T and Athanasiou S (2006) Probiotics for Prevention of Recurrent Urinary Tract Infections in Women, *Drugs* 66 (9) : 1253-1261	The use of probiotics, especially lactobacilli, has been considered for the prevention of UTIs. Since lactobacilli dominate the urogenital flora of healthy premenopausal women, it has been suggested that restoration of the urogenital flora, which is dominated by uropathogens, with lactobacilli may protect against UTIs. This review is based on a search for relevant articles.	Many in vitro studies, animal experiments, microbiological studies in healthy women, and clinical trials in women with UTIs have been carried out to assess the effectiveness and safety of probiotics for prophylaxis against uropathogens. Most of them had encouraging findings for some specific strains of lactobacilli. Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 (previously called L. fermentum RC-14) seemed to be the most effective among the studied lactobacilli for the prevention of UTIs. L. casei shirota and L. crispatus CTV-05 have also shown efficacy in some studies. L. rhamnosus GG did not appear to be quite as effective in the prevention of UTIs. The evidence from the available studies suggests that probiotics can be beneficial for preventing recurrent UTIs in women; they also have a good safety profile.
Reid G and Bruce A W (2006) Probiotics to prevent urinary tract infections: the rationale and evidence, *World Journal of Urology* 24 (1) : 28-32	Overview: For over 30 years, urologists have recognized in females, that urinary pathogens almost always infect the host through ascension from the rectum, vagina to the urethra and bladder. Likewise, the Lactobacillus organisms that predominate in the vagina of healthy women, spread from the rectum and perineum and form a barrier in the vagina to bladder entry by uropathogens. The concept of artificially boosting the lactobacilli numbers through probiotic instillation has long been conceived, but only in recent years shown to be possible. Not all lactobacilli are effective, and to date clinical efficacy only exists for Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri B-54 and RC-14. These strains are only commercially available in Austria, and therefore for most urologists, while some probiotic organisms may reduce the recurrences of bladder cancer or oxaluria, no probiotics can be recommended widely to prevent UTI at present.	

Kontiokari T, Sundqvist K, Nuutinen M, Pokka T, Koskela M and Uhari M (2001) Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women, *British Medical Journal* 322 (7302) : 1-5	To determine whether recurrences of urinary tract infection can be prevented with cranberry-lingonberry juice or with Lactobacillus GG drink. An open, randomised controlled 12 month follow up trial in health centres for university students and staff of university hospital. Participants: 150 women with urinary tract infection caused by Escherichia coli randomly allocated into three groups. Interventions: 50 ml of cranberry-lingonberry juice concentrate daily for six months or 100 ml of lactobacillus drink five days a week for one year, or no intervention. Main outcome measure: First recurrence of symptomatic urinary tract infection, defined as bacterial growth 105 colony forming units/ml in a clean voided midstream urine specimen.	The cumulative rate of first recurrence of urinary tract infection during the 12 month follow up differed significantly between the groups (P=0.048). At six months, eight (16%) women in the cranberry group, 19 (39%) in the lactobacillus group, and 18 (36%) in the control group had had at least one recurrence. This is a 20% reduction in absolute risk in the cranberry group compared with the control group (95% confidence interval 3% to 36%, P=0.023, number needed to treat=5, 95% confidence interval 3 to 34). Conclusion: Regular drinking of cranberry juice but not lactobacillus seems to reduce the recurrence of urinary tract infection.

d) Cranberry derivatives

Study	Methods	Findings
van den Hout W B, Caljouw M A A, Putter H, Cools H J M and Gussekloo J (2014) Cost-Effectiveness of Cranberry Capsules to Prevent Urinary Tract Infection in Long-Term Care Facilities: Economic Evaluation with a Randomized Controlled Trial, *Journal of the American Geriatrics Society* 62 (1) : 111-116	Economic evaluation with a randomized controlled trial to investigate whether the preventive use of cranberry capsules in long-term care facility (LTCF) residents is cost-effective depending on urinary tract infection (UTI) risk. Participants: LTCF residents (N = 928, 703 female, median age 84), stratified according to UTI risk. Measurements: UTI incidence (clinically or strictly defined), survival, quality of life, quality-adjusted life years (QALYs), and costs.	In the weeks after a clinical UTI, participants showed a significant but moderate deterioration in quality of life, survival, care dependency, and costs. In high-UTI-risk participants, cranberry costs were estimated at €439 per year (1.00 euro = 1.37 U.S. dollar), which is €3,800 per prevented clinically defined UTI (95% confidence interval = €1,300–infinity). Using the strict UTI definition, the use of cranberry increased costs without preventing UTIs. Taking cranberry capsules had a 22% probability of being cost-effective compared with placebo (at a willingness to pay of €40,000 per QALY). In low-UTI-risk participants, use of cranberry capsules was only 3% likely to be cost-effective. Conclusion: In high-UTI-risk residents, taking cranberry capsules may be effective in preventing UTIs but is not likely to be cost-effective in the investigated dosage, frequency, and setting. In low-UTI-risk LTCF residents, taking cranberry capsules twice daily is neither effective nor cost-effective.

Shin C-N (2014) *The Effects of Cranberries on Preventing Urinary Tract Infections*, 23 (1) : 54-79	A review of research-based information regarding the ability of cranberries to prevent UTIs in adults at risk for UTIs.	Author's summary: Current evidence suggests that cranberries decrease bacterial adherence to uroepithelial cells and thus decrease the incidence of UTIs without adverse effects in most individuals. Thus clinicians may safely advise patients that cranberries are helpful in preventing UTIs. Cranberries may be a viable adjunct to antibiotics for patients with repeated UTIs.
Takahashi S, Hamasuna R, Yasuda M, Arakawa S, Tanaka K, Ishikawa K, Kiyota H, Hayami H, Yamamoto S, Kubo T and Matsumoto T (2013) A randomized clinical trial to evaluate the preventive effect of cranberry juice (UR65) for patients with recurrent urinary tract infection, *Journal of Infection and Chemotherapy* 19 (1) : 112-117	This study examined the rate of relapse, as a variable index, in patients with urinary tract infection (UTI) who suffered from multiple relapses when using cranberry juice (UR65). A randomized, placebo-controlled, double-blind study was conducted from October 2007 to September 2009 in Japan. The subjects were outpatients aged 20 to 79 years who were randomly divided into two groups. One group received cranberry juice (group A) and the other a placebo beverage (group P). To keep the conditions blind, the colour and taste of the beverages were adjusted. The subjects drank 1 bottle (125 mL) of cranberry juice or the placebo beverage once daily, before going to sleep, for 24 weeks. The primary endpoint was relapse of UTI.	In the group of females aged 50 years or more, there was a significant difference in the rate of relapse of UTI between groups A and P (log-rank test; p = 0.0425). In this subgroup analysis, relapse of UTI was observed in 16 of 55 (29.1 %) patients in group A and 31 of 63 (49.2 %) in group P. In this study, cranberry juice prevented the recurrence of UTI in a limited female population with 24-week intake of the beverage

Sánchez Ballester F S, Vidal V R, Alcina E L, Perez C D, Fontano E E, Oltra Benavent A M, García A M and Bustamante M A S (2013) Cysticlean® a highly pac standardized content in the prevention of recurrent urinary tract infections: an observational, prospective cohort study, *BMC Urology* 13 (28)	This study was aimed at determining the prophylactic efficacy of American cranberry (AC) extract (Cysticlean®) in women with recurrent symptomatic post-coital urinary tract infections (PCUTI), non-consumer of AC extract in the past 3 months before inclusion, and to determine changes in their quality of life (QoL). This was a single centre, observational, prospective study in a total of 20 women (mean age 35.2 years; 50.0% were married). Patients were followed up for 3 and 6 months during treatment.	The number of PCUTIs in the previous 3 months prior to start the treatment with Cysticlean® was 2.8±1.3 and it was reduced to 0.2±0.5 at Month 6 (P<0.0001), which represent a 93% improvement. At baseline, the mean score on the VAS scale (range from 0 to 100) for assessing the QoL was 62.4±19.1, increasing to 78.2±12.4 at Month 6 (P=0.0002), which represents a 20% improvement. All patients had an infection with positive urine culture at baseline, after 6 months there were only 3 symptomatic infections (P<0.001). The most common bacterium was Escherichia coli. Conclusions: Prophylaxis with American cranberry extract (Cysticlean®) could be an alternative to classical therapies with antibiotics.
Lorenzo A J and Braga L H P (2013) Systematic review and meta-analysis: Use of cranberry products does not appear to be associated with a significant reduction in incidence of recurrent urinary tract infections, *Evidence-Based Medicine* 18 (5) : 181-182	Commentary on systematic review by Jepson, Williams and Craig (2012): A total of 24 studies (14 added to the 2008 paper), of which 11 were not included in the MA due to design or data-extraction issues, povided information on4473 participants. Compared to placebo, water or no treatment, intake of CP was not associated with a significant reduction in occurrence of symptomatic UTIs both overall and for all evaluated sub-groups. An important number of studies reported problems with compliance and withdrawals. Ultimately there is now more uncertainty than clarity on the role of CP as a prophylactic agent against UTIs.	

Jepson R G, Williams G and Craig J C; The Cochrane Collaboration (2012) *Cranberries for preventing urinary tract infections (Review)*, John Wiley & Sons, Ltd	This updated review includes a total of 24 studies (six cross-over studies, 11 parallel group studies with two arms; five with three arms, and two studies with a factorial design) with a total of 4473 participants. Ten studies were included in the 2008 review, and 14 studies have been added to this update. Thirteen studies (2380 participants) evaluated only cranberry juice/concentrate; nine studies (1032 participants) evaluated only cranberry tablets/capsules; one study compared cranberry juice and tablets; and one study compared cranberry capsules and tablets. The comparison/control arms were placebo, no treatment, water, methenamine hippurate, antibiotics, or lactobacillus. Eleven studies were not included in the meta-analyses because either the design was a cross-over study and data were not reported separately for the first phase, or there was a lack of relevant data. Data included in the meta-analyses showed that, compared with placebo, water or not treatment, cranberry products did not significantly reduce the occurrence of symptomatic UTI overall (RR 0.86, 95% CI 0.71 to 1.04) or for any the subgroups: women with recurrent UTIs (RR 0.74, 95% CI 0.42 to 1.31); older people (RR 0.75, 95% CI 0.39 to 1.44); pregnant women (RR 1.04, 95% CI 0.97 to 1.17); children with recurrent UTI (RR 0.48, 95% CI 0.19 to 1.22); cancer patients (RR 1.15 95% CI 0.75 to 1.77); or people with neuropathic bladder or spinal injury (RR 0.95, 95% CI: 0.75 to 1.20). Overall heterogeneity was moderate (I^2 = 55%). The effectiveness of cranberry was not significantly different to antibiotics for women (RR 1.31, 95% CI 0.85, 2.02) and children (RR 0.69 95% CI 0.32 to 1.51). There was no significant difference between gastrointestinal adverse effects from cranberry product compared to those of placebo/no treatment (RR 0.83, 95% CI 0.31 to 2.27). Many studies reported low compliance and high withdrawal/dropout problems which they attributed to palatability/acceptability of the products, primarily the cranberry juice. Most studies of other cranberry products (tablets and capsules) did not report how much of the 'active' ingredient the product contained, and therefore the products may not have had enough potency to be effective. Authors' conclusions Prior to the current update it appeared there was some evidence that cranberry juice may decrease the number of symptomatic UTIs over a 12 month period, particularly for women with recurrent UTIs. The addition of 14 further studies suggests that cranberry juice is less effective than previously indicated. Although some of small studies demonstrated a small benefit for women with recurrent UTIs, there were no statistically significant differences when the results of a much larger study were included. Cranberry products were not significantly different to antibiotics for preventing UTIs in three small studies. Given the large number of dropouts/withdrawals from studies (mainly attributed to the acceptability of consuming cranberry products particularly juice, over long periods), and the evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTIs. Other preparations (such as powders) need to be quantified using standardised methods to ensure the potency, and contain enough of the 'active' ingredient, before being evaluated in clinical studies or recommended for use.

Wang C-H, Fang C-C, Chen N-C, Liu S S-H, Yu P-H, Wu T-Y, Chen W-T, Lee C-C and Chen S-C (2012) Cranberry-Containing Products for Prevention of Urinary Tract Infections in Susceptible Populations: A Systematic Review and Meta-analysis of Randomized Controlled Trials, *JAMA Internal Medicine (formerly Archives of Internal Medicine)* 172 (13) : 988-996	The aims of this study were to evaluate cranberry-containing products for the prevention of UTI and to examine the factors influencing their effectiveness. A review was carried out of randomized controlled trials that compared prevention of UTIs in users of cranberry-containing products vs placebo or non-placebo controls. Thirteen trials, including 1616 subjects, were identified for qualitative synthesis from 414 potentially relevant references; 10 of these trials, including a total of 1494 subjects, were further analyzed in quantitative synthesis.	The random-effects pooled risk ratio (RR) for cranberry users vs nonusers was 0.62 (95% CI, 0.49-0.80), with a moderate degree of heterogeneity (I2 = 43%) after the exclusion of 1 outlier study. On subgroup analysis, cranberry-containing products seemed to be more effective in several subgroups, including women with recurrent UTIs (RR, 0.53; 95% CI, 0.33-0.83) (I2 = 0%), female populations (RR, 0.49; 95% CI, 0.34-0.73) (I2 = 34%), children (RR, 0.33; 95% CI, 0.16-0.69) (I2 = 0%), cranberry juice drinkers (RR, 0.47; 95% CI, 0.30-0.72) (I2 = 2%), and subjects using cranberry-containing products more than twice daily (RR, 0.58; 95% CI, 0.40-0.84) (I2 = 18%). Author's Conclusion: Our findings indicate that cranberry-containing products are associated with protective effect against UTIs. However, this result should be interpreted in the context of substantial heterogeneity across trials.

Stapleton A E, Dziura J, Hooton T M, Cox M E, Yarova-Yarovaya Y, Chen S and Gupta K (2012) Recurrent Urinary Tract Infection and Urinary Escherichia coli in Women Ingesting Cranberry Juice Daily: A Randomized Controlled Trial, *Mayo Clinic Proceedings* 87 (2) : 143-150	To compare the time to urinary tract infection (UTI) and the rates of asymptomatic bacteriuria and urinary P-fimbriated Escherichia coli during a 6-month period in women ingesting cranberry vs placebo juice daily. Premenopausal women with a history of recent UTI were enrolled from November 16, 2005, through December 31, 2008, at 2 centres and randomized to 1 of 3 arms: 4 oz of cranberry juice daily, 8 oz of cranberry juice daily, or placebo juice. Time to UTI (symptoms plus pyuria) was the main outcome. Asymptomatic bacteriuria, adherence, and adverse effects were assessed at monthly visits. A total of 176 participants were randomized (120 to cranberry juice and 56 to placebo) and followed up for a median of 168 days.	The cumulative rate of UTI was 0.29 in the cranberry juice group and 0.37 in the placebo group (P=.82). The adjusted hazard ratio for UTI in the cranberry juice group vs the placebo group was 0.68 (95% confidence interval, 0.33-1.39; P=.29). The proportion of women with P-fimbriated urinary E coli isolates during the intervention phase was 10 of 23 (43.5%) in the cranberry juice group and 8 of 10 (80.0%) in the placebo group (P=.07). The mean dose adherence was 91.8% and 90.3% in the cranberry juice group vs the placebo group. Minor adverse effects were reported by 24.2% of those in the cranberry juice group and 12.5% in the placebo group (P=.07). Conclusion: Cranberry juice did not significantly reduce UTI risk compared with placebo. The potential protective effect we observed is consistent with previous. The concurrent reduction in urinary P-fimbriated E coli strains supports the biological plausibility of cranberry activity.

Barbosa-Cesnik C, Brown M B, Buxton M, Zhang L, DeBusscher J and Foxman B (2011) Cranberry Juice Fails to Prevent Recurrent Urinary Tract Infection: Results From a Randomized Placebo-Controlled Trial, *Clinical Infectious Diseases* 52 (1) : 23-30	A double-blind, placebo-controlled trial of the effects of cranberry on risk of recurring UTI among 319 college women presenting with an acute UTI. Participants were followed up until a second UTI or for 6 months, whichever came first. A UTI was defined on the basis of the combination of symptoms and a urine culture positive for a known uropathogen. The study was designed to detect a 2-fold difference between treated and placebo groups, as was detected in unblinded trials. We assumed 30% of participants would experience a UTI during the follow-up period.	Overall, the recurrence rate was 16.9% (95% confidence interval, 12.8%–21.0%), and the distribution of the recurrences was similar between study groups, with the active cranberry group presenting a slightly higher recurrence rate (20.0% vs 14.0%). The presence of urinary symptoms at 3 days, 1–2 weeks, and at =1 month was similar between study groups, with overall no marked differences. Conclusions. Among otherwise healthy college women with an acute UTI, those drinking 8 oz of 27% cranberry juice twice daily did not experience a decrease in the 6-month incidence of a second UTI, compared with those drinking a placebo.

Guay D R P (2009) Cranberry and urinary tract infections, *Drugs* 69 (7) : 775-807	Overview: At present, there is no evidence that cranberry can be used to treat UTIs. Hence, the focus has been on its use as a preventative strategy. Cranberry has been effective in vitro and in vivo in animals for the prevention of UTI. Cranberry appears to work by inhibiting the adhesion of type I and P-fimbriated uro-pathogens (e.g. uropathogenic E. coli) to the uroepithelium, thus impairing colonization and subsequent infection. The isolation of the component(s) of cranberry with this activity has been a daunting task, considering the hundreds of compounds found in the fruit and its juice derivatives. Reasonable evidence suggests that the anthocyanidin/proanthocyanidin moieties are potent antiadhesion compounds. However, problems still exist with standardization of cranberry products, which makes it extremely difficult to compare products or extrapolate results. Unfortunately, most clinical trials have had design deficiencies and none have evaluated specific key cranberry-derived compounds considered likely to be active moieties (e.g. proantho-cyanidins). In general, the preventive efficacy of cranberry has been variable and modest at best. Meta-analyses have established that recurrence rates over 1 year are reduced approximately 35% in young to middle-aged women. The efficacy of cranberry in other groups (i.e. elderly, paediatric patients, those with neurogenic bladder, those with chronic indwelling urinary catheters) is questionable. Withdrawal rates have been quite high (up to 55%), suggesting that these products may not be acceptable over long periods. Adverse events include gastrointestinal intolerance, weight gain (due to the excessive calorie load) and drug-cranberry interactions (due to the inhibitory effect of flavo-noids on cytochrome P450-mediated drug metabolism). The findings of the Cochrane Collaboration support the potential use of cranberry products in the prophylaxis of recurrent UTIs in young and middle-aged women. However, in light of the heterogeneity of clinical study designs and the lack of consensus regarding the dosage regimen and formulation to use, cranberry products cannot be recommended for the prophylaxis of recurrent UTIs at this time.
McMurdo M E T, Argo I, Phillips G, Daly F and Davey P (2009) Cranberry or trimethoprim for the prevention of recurrent urinary tract infections? A randomized controlled trial in older women, *Journal of Antimicrobial Chemotherapy* 63 (2) : 389-395	See comparative studies

Jepson R G and Craig J C; The Cochrane Collaboration (2008) *Cranberries for preventing urinary tract infections (Review)*, John Wiley & Sons, Ltd	To assess the effectiveness of cranberry products in preventing UTIs in susceptible populations. A review of randomised controlled trials (RCTs) or quasi-RCTs of cranberry products for the prevention of UTIs in all populations. Ten studies (n = 1049, five cross-over, five parallel group) were included. Cranberry/cranberry-lingonberry juice versus placebo, juice or water was evaluated in seven studies, and cranberries tablets versus placebo in four studies (one study evaluated both juice and tablets).	Cranberry products significantly reduced the incidence of UTIs at 12 months (RR 0.65, 95% CI 0.46 to 0.90) compared with placebo/control. Cranberry products were more effective reducing the incidence of UTIs in women with recurrent UTIs, than elderly men and women or people requiring catheterisation. Six studies were not included in the meta-analyses due to methodological issues or lack of available data. However, only one reported a significant result for the outcome of symptomatic UTIs. Side effects were common in all studies, and dropouts/withdrawals in several of the studies were high. Authors' conclusions: There is some evidence that cranberry juice may decrease the number of symptomatic UTIs over a 12 month period, particularly for women with recurrent UTIs. It's effectiveness for other groups is less certain. The large number of dropouts/withdrawals indicates that cranberry juice may not be acceptable over long periods of time. It is not clear what is the optimum dosage or method of administration (e.g. juice, tablets or capsules).

Jepson R G and Craig J C (2007) A systematic review of the evidence for cranberries and blueberries in UTI prevention, *Molecular Nutrition & Food Research Special Issue: Berry Fruits* 51 (6) : 738-745	A review to assess the effectiveness of cranberry and blueberry products in preventing symptomatic urinary tract infections (UTIs). Selection criteria were randomised or quasi-randomised controlled trials of cranberry or blueberry juice/products for the prevention of symptomatic UTIs. No relevant trials of blueberry products were identified. Nine trials of cranberry products met the inclusion criteria.	In four good quality randomised controlled trials (RCTs), cranberry products significantly reduced the incidence of symptomatic UTIs in 12 months (overall RR 0.65, 95% CI: 0.46–0.90) compared with placebo/control. Five trials were not included in the meta-analyses due to the lack of appropriate data. However, only one reported a significant result. Side effects were common, and losses to followup/withdrawals in several of the trials were high (> 40%). There is some evidence from four good quality RCTs that cranberry juice may decrease the number of symptomatic UTIs over a 12-month period, particularly in women with recurrent UTIs. It is uncertain whether it is effective in other susceptible groups.
Howell A B (2007) Bioactive compounds in cranberries and their role in prevention of urinary tract infections, *Molecular Nutrition & Food Research Special Issue: Berry Fruits* 51 (6) : 732-737	Cranberry (Vaccinium macrocarpon Ait.) ingestion has long been associated with prevention of urinary tract infections. The beneficial mechanism was historically thought to be due to the fruit acids causing a bacteriostatic effect in the urine. However, recently, a group of proanthocyanidins (PACs) with A-type linkages were isolated from cranberry which exhibit bacterial antiadhesion activity against both antibiotic susceptible and resistant strains of uropathogenic P-fimbriated Escherichia coli bacteria. The link between cranberry ingestion and maintenance of urinary tract health as well as the structural diversity, pharmacokinetics, quantification, and bacterial antiadhesion bioactivity of the A-linked cranberry PACs were reviewed. Only cranberry juice with A-type PACs prevents bacterial adhesion.	

McMurdo M E T, Bissett L Y, Price R J G, Phillips G and Crombie I K (2005) Does ingestion of cranberry juice reduce symptomatic urinary tract infections in older people in hospital? A double-blind, placebo-controlled trial, *Age and Ageing* 34 (3) : 256-261	A randomised, placebo-controlled, double-blind trial to assess whether cranberry juice ingestion is effective in reducing UTIs in older people in hospital. Participants: 376 older patients in medicine for the Elderly assessment and rehabilitation hospital wards. Participants were randomised to daily ingestion of 300 ml of cranberry juice or matching placebo beverage. The primary outcome was time to onset of first UTI. Secondary outcomes were adherence to beverage drinking, courses of antibiotics prescribed, and organisms responsible for UTIs.	A total of 21/376 (5.6%) participants developed a symptomatic UTI: 14/189 in the placebo group and 7/187 in the cranberry juice group. These between-group differences were not significant, relative risk (RR) 0.51 [95% CI 0.21–1.22, P=0.122). Although there were significantly fewer infections with Escherichia coli in the cranberry group (13 versus 4) RR 0.31 [95% CI 0.10–0.94, P=0.027], this should be interpreted with caution as it was a secondary outcome. Conclusion: despite having the largest sample size of any clinical trial yet to have examined the effect of cranberry juice ingestion, the actual infection rate observed was lower than anticipated, making the study underpowered. This study has confirmed the acceptability of cranberry juice to older people.

Raz R, Chazan B and Dan M (2004) Cranberry Juice and Urinary Tract Infection, *Clinical Infectious Diseases* 38 (10) : 1413-1419	Overview: Cranberries have long been the focus of interest for their beneficial effects in preventing urinary tract infections (UTIs). Cranberries contain 2 compounds with antiadherence properties that prevent fimbriated Escherichia coli from adhering to uroepithelial cells in the urinary tract. Approximately 1 dozen clinical trials have been performed testing the effects of cranberries on the urinary tract. However, these trials suffer from a number of limitations. Most importantly, the trials have used a wide variety of cranberry products, such as cranberry juice concentrate, cranberry juice cocktail, and cranberry capsules, and they have used different dosing regimens. Results of clinical studies suggest a possible clinical benefit of cranberry juice in preventing UTI in some populations. The strongest evidence available is for sexually active adult women with previous UTI. In this population, cranberry appears to be effective in the prophylaxis of recurrent UTI, although standard juice cocktail was not specifically tested. In elderly patients, cranberry consumption reduces the incidence of bacteriuria, although this is often not treated with antibiotics. In contrast, none of the randomized clinical studies that evaluated patients at high risk of UTI—for example, those with neurogenic bladder—found cranberries to have a beneficial effect. In the population that benefits most from the prophylactic effect of cranberry intake (sexually active women with recurrent UTI), trial results repeatedly show an ~50% reduction in disease morbidity. From a clinical point of view, this is quite a modest benefit, considering the accompanying burden of long-term daily intake of the compound. Not less significant is the inconvenience associated with the amount of juice required to assure continuous availability and the need to carry a daily supply if twice- or thrice-daily dosing is needed to work, business, or vacation travel. If one considers the understandably high rate of dropouts, the 50% efficacy rate may drop to a remarkably lower effectiveness. Furthermore, results of the reviewed studies should not be viewed as conclusive because many of the trials suffer from various limitations, including lack of randomization, no or improper blinding, small number of subjects, short trial duration, large number of dropouts, and no reported intent-to-treat analysis [43]. Perhaps the single most consistent limitation of these trials is the lack of uniformity regarding the intervention, including the particular cranberry product evaluated (juice, In women with recurrent urinary tract infections (UTIs), long-term antimicrobial prophylaxis is indicated. This method is effective but can cause adverse reactions and can increase emergence of antimicrobial resistance. Therefore, the need for alternative therapies for UTI prophylaxis is evident. Cranberries are one non-antibiotic alternative.

Stothers L (2002) A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against urinary tract infection in women, *Canadian Journal of Urology* 9 (3) : 1558-1562	To determine from a societal perspective, the effectiveness and cost effectiveness of concentrated cranberry tablets, versus cranberry juice, versus placebo used as prophylaxis against lower urinary tract infection (UTI) in adult women. One hundred fifty sexually active women aged 21 through 72 years were randomized for one year to one of three groups of prophylaxis; placebo juice + placebo tablets versus placebo juice + cranberry tablets, versus cranberry juice + placebo tablets. Tablets were taken twice daily, juice 250 ml three times daily. Outcome measures were: (1) a >50% decrease in symptomatic UTI's per year (symptoms + >_ =100,000 single organisms/ml) and (2) a >50% decrease in annual antibiotic consumption. Cost effectiveness was calculated as dollar cost per urinary tract infection prevented. Stochastic tree decision analytic modeling was used to identify specific clinical scenarios for cost savings.	Both cranberry juice and cranberry tablets statistically significantly decreased the number of patients experiencing at least 1 symptomatic UTI/year (to 20% and 18% respectively) compared with placebo (to 32%) ($p<0.05$). The mean annual cost of prophylaxis was $624 and $1400 for cranberry tablets and juice respectively. Cost savings were greatest when patients experienced >2 symptomatic UTI's per year (assuming 3 days antibiotic coverage) and had >2 days of missed work or required protective undergarments for urgency incontinence. Total antibiotic consumption was less annually in both treatment groups compared with placebo. Cost effectiveness ratios demonstrated cranberry tablets were twice as cost effective as organic juice for prevention. Conclusions: Cranberry tablets provided the most cost effective prevention for UTI.
Kontiokari T, Sundqvist K, Nuutinen M, Pokka T, Koskela M and Uhari M (2001) Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women, *British Medical Journal* 322 (7302) : 1-5	See 'Use of probiotics'	

e) Other interventions

Study	Methods	Findings
Damiano R, Quarto G, Bava I, Ucciero G, De Domenico R, Palumbo M I and Autorino R (2011) Prevention of Recurrent Urinary Tract Infections by Intravesical Administration of Hyaluronic Acid and Chondroitin Sulphate: A Placebo-Controlled Randomised Trial, *European Urology* 59 (4) : 645-651	To investigate the efficacy and tolerability of the intravesical administration of combined hyaluronic acid (HA) and chondroitin sulphate (CS) in female patients with a history of recurrent UTI. A prospective, randomised, double-blind, placebo-controlled study comparing the intravesical instillation of HA-CS with placebo in women with recurrent UTI. Participants were randomised to receive 50 ml of sterile sodium HA 1.6% and CS 2.0% solution (IALURIL®) weekly for 4 wk and then monthly for 5 mo. The primary end point of the study was defined as the mean number of UTI per patient per year. Participants were evaluated addressing UTI status/urinary symptoms and with a general health-related quality-of-life (QoL) questionnaire at baseline and after 3, 6, 9, and 12 mo. In the intention-to-treat analysis, 57 women were randomly allocated to HA-CS (n = 28) or placebo (n = 29).	The UTI rate per patient per year at the end of the study (12 mo) (mean ± SD: -86.6% ± 47.6 vs -9.6% ± 24.6; mean difference: 77%; 95% confidence interval, 72.3–80.8; p = 0.0002) and the mean time to UTI recurrence (52.7 ± 33.4 vs 185.2 ± 78.7 d; p < 0.001) were significantly increased after treatment with HA-CS compared with placebo. Overall urinary symptoms and QoL measured by questionnaires significantly improved compared with placebo (Pelvic Pain and Urgency/Frequency questionnaire symptom score: 14.53 ± 4.32 vs 9.88 ± 6.77; p = 0.004; SF-36 QoL score: 78.6 ± 6.44 vs 53.1 ± 4.72; p < 0.001). No serious adverse event was reported. Conclusions: Compared with placebo, HA-CS intravesical instillations significantly reduced UTI rate without severe side effects while improving symptoms and QoL over a 12-mo period in patients with recurrent UTI.

Perrotta C, Aznar M, Mejia R, Albert X and Ng C W (2008) *Oestrogens for preventing recurrent urinary tract infection in*, The Cochrane Collaboration. Published by JohnWiley & Sons, Ltd.	To estimate the efficacy and safety of oral or vaginal oestrogens for preventing RUTI in postmenopausal women. A search of randomised controlled trials (RCTs) in which postmenopausal women (more than 12 months since last menstrual period) diagnosed with RUTI received any type of oestrogen (oral , vaginal) versus placebo or any other intervention were included. Statistical analyses were performed using the random effects model and the results expressed as risk ratios (RR) for dichotomous outcomes or mean difference (MD) for continuous data with 95% confidence intervals (CI).	Nine studies (3345 women) were included. Oral oestrogens did not reduce UTI compared to placebo (4 studies, 2798 women: RR 1.08, 95% CI 0.88 to 1.33). Vaginal oestrogens versus placebo reduced the number of women with UTIs in two small studies using different application methods. The RR for one was 0.25 (95% CI 0.13 to 0.50) and 0.64 (95% CI 0.47 to 0.86) in the second. Two studies compared oral antibiotics versus vaginal oestrogens (cream (1), pessaries (1)). There was very significant heterogeneity and the results could not be pooled. Vaginal cream reduced the proportion of UTIs compared to antibiotics in one study and in the second study antibiotics were superior to vaginal pessaries. Adverse events for vaginal oestrogens were breast tenderness, vaginal bleeding or spotting, nonphysiologic discharge, vaginal irritation, burning and itching. Authors' conclusions: Based on only two studies comparing vaginal oestrogens to placebo, vaginal oestrogens reduced the number of UTIs in postmenopausal women with RUTI, however this varied according to the type of oestrogen used and the treatment duration.

Loeb M, Brazil K, Lohfeld L, McGeer A, Simor A, Stevenson K, Zoutman D, Smith S, Liu X and Walter S D (2005) Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomised controlled trial, *British Medical Journal* 331 (7518) : 669	A randomised controlled trial to assess whether a multifaceted intervention can reduce the number of prescriptions for antimicrobials for suspected urinary tract infections in residents of nursing homes. Setting: 24 nursing homes in Ontario, Canada, and Idaho, United States. Participants: 12 nursing homes allocated to a multifaceted intervention and 12 allocated to usual care. Outcomes were measured in 4217 residents. Interventions: Diagnostic and treatment algorithm for urinary tract infections implemented at the nursing home level using a multifaceted approach—small group interactive sessions for nurses, videotapes, written material, outreach visits, and one on one interviews with physicians. Main outcome measures: Number of antimicrobials prescribed for suspected urinary tract infections, total use of antimicrobials, admissions to hospital, and deaths.	Fewer courses of antimicrobials for suspected urinary tract infections per 1000 resident days were prescribed in the intervention nursing homes than in the usual care homes (1.17 v 1.59 courses; weighted mean difference -0.49, 95% confidence intervals -0.93 to -0.06). Antimicrobials for suspected urinary tract infection represented 28.4% of all courses of drugs prescribed in the intervention nursing homes compared with 38.6% prescribed in the usual care homes (weighted mean difference -9.6%, -16.9% to -2.4%). The difference in total antimicrobial use per 1000 resident days between intervention and usual care groups was not significantly different (3.52 v 3.93; weighted mean difference -0.37, -1.17 to 0.44). No significant difference was found in admissions to hospital or mortality between the study arms. Conclusion: A multifaceted intervention using algorithms can reduce the number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes.
Darouiche R O, Thornby J I, Stewart C C, Donovan W H and Hull R A (2005) Bacterial Interference for Prevention of Urinary Tract Infection: A Prospective, Randomized, Placebo-Controlled, Double-Blind Pilot Trial, *Clinical Infectious Diseases* 41 (10) : 1531-1534	This prospective, randomized, placebo-controlled, double-blind pilot trial examined the efficacy of bacterial interference in preventing urinary tract infection (UTI) in 27 patients with spinal cord injury.	Patients whose bladders became colonised with Escherichia coli 83972 were half as likely (P=.01) than non-colonised patients to develop UTI during the subsequent year

Kontiokari T, Laitinen J, Järvi L, Pokka T, Sundqvist K and Uhari M (2003) Dietary factors protecting women from urinary tract infection, *American Journal of Clinical Nutrition* 77 (3) : 600-604	To study dietary and other risk factors for UTI in fertile women in a case-control setting. Design: One hundred thirty-nine women from a health centre for university students or from the staff of a university hospital (mean age: 30.5 y) with a diagnosis of an acute UTI were compared with 185 age-matched women with no episodes of UTIs during the past 5 y. Data on the women's dietary and other lifestyle habits were collected by questionnaire. A risk profile for UTI expressed in the form of adjusted odds ratios (ORs) with 95% CIs was modelled in logistic regression analysis for 107 case-control pairs with all relevant information.	Frequent consumption of fresh juices, especially berry juices, and fermented milk products containing probiotic bacteria was associated with a decreased risk of recurrence of UTI: the OR for UTI was 0.66 (95% CI: 0.48, 0.92) per 2 dL juice. A preference for berry juice over other juices gave an OR of 0.28 (95% CI: 0.14, 0.56). Consumption of fermented milk products 3 or more times/wk gave an OR of 0.21 (95% CI: 0.06, 0.66) relative to consumption < 1 time/wk. Intercourse frequency was associated with an increased risk of UTI (OR for 3 or more times/wk compared with < 1 time/wk: 2.7; 95% CI: 1.16, 6.2). Conclusion: Dietary habits seem to be an important risk factor for UTI recurrence in fertile women, and dietary guidance could be a first step toward prevention.

Bauer H W, Rahlfs V W, Lauener P A and Bleßmann G S S (2002) Prevention of recurrent urinary tract infections with immuno-active E. coli fractions: a meta-analysis of five placebo-controlled double-blind studies, *International Journal of Antimicrobial Agents* 19 (6) : 451-456	A meta-analysis was performed on five studies conducted over the last decade to demonstrate a positive effect for the drug Uro-Vaxom® compared with Placebo in double-blind studies in patients with urinary tract infection (601 women), with special reference to the prevention of recurrences over an observation period of 6 months, the treatment being given for the first 3 months. The five studies were similar in design.	The analysis by means of the Wilcoxon–Mann–Whitney test showed superiority of Uro-Vaxom in all five studies, (P<1%). The summarising Mann–Whitney (MW) statistics also indicated superiority with the Mann–Whitney value being 0.684. In all studies, the Uro-Vaxom group was statistically significant and clinically relevant superior to control with respect to the reduction of the frequency of UTIs and to dysuria, bacteriuria and leucocyturia. The confidence intervals (CI)s were small (0.64–0.72). The drug was well tolerated and compliance of patients was excellent in all studies. Oral immunotherapy with the Uro-Vaxom Escherichia coli (E. coli) extract is an effective prophylactic approach in the prevention of UTIs.

f) Catheter acquired urinary tract infections (CAUTI)

Study	Methods	Findings
Tenke P, Köves B and Johansen T E B (2014) An update on prevention and treatment of catheter-associated urinary tract infections, *Current Opinion in Infectious Diseases* 27 (1) : 102-107	This review summarizes the latest advances in the field of catheter care and the management of catheter-associated UTIs. Recent findings: The most efficient methods to prevent catheter-associated UTIs are to avoid unnecessary catheterizations and to remove catheters as soon as possible. The use of different reminder systems and implementation of infection control programs can effectively decrease catheter-associated UTIs, although their introduction can be challenging. There is still no evidence to support the routine use of antimicrobial-impregnated catheters, but the use of hydrophilic-coated catheters for clean intermittent catheterization can effectively reduce infections. Preliminary results with chlorhexidine-coated catheters are promising. In cases of serious catheter-associated UTI in patients with a history of previous antibiotic therapy or healthcare-associated bacteraemia, empirical antibiotic treatment should be initiated with activity against multiresistant uropathogens. Suprapubic catheterization is not superior to urethral catheters in terms of reducing the rate of catheter-related bacteriuria. Summary: A technology to prevent catheter-associated UTIs is still not available; however, there are promising results with new approaches such as the use of reminder systems and infection control programs, which can effectively decrease the rate of catheter-associated UTIs. There is evidence supporting the use of hydrophilic coated catheters for clean intermittent catheterization, but an optimal catheter material or coating still has to be developed. Evidence-based catheter management is crucial for every patient in need of a catheter	

Meddings J, Rogers M A M, Krein S L, Fakih M G, Olmsted R N and Saint S (2014) Reducing unnecessary urinary catheter use and other strategies to prevent catheter-associated urinary tract infection: an integrative review, *BMJ Quality and Safety* 0 : 1-13	To summarise interventions to reduce UC use and CAUTIs, this study updated a prior systematic review (through October 2012), and a meta-analysis regarding interventions prompting UC removal by reminders or stop orders. A narrative review summarises other CAUTI prevention strategies including aseptic insertion, catheter maintenance, antimicrobial UCs, and bladder bundle implementation. 30 studies were identified and summarised with interventions to prompt removal of UCs, with potential for inclusion in the meta-analyses.	.By meta-analysis (11 studies), the rate of CAUTI (episodes per 1000 catheter-days) was reduced by 53% (rate ratio 0.47; 95% CI 0.30 to 0.64, p<0.001) using a reminder or stop order, with five studies also including interventions to decrease initial UC placement. The pooled (nine studies) standardised mean difference (SMD) in catheterisation duration (days) was -1.06 overall (p=0.065) including a statistically significant decrease in stop-order studies (SMD -0.37; p<0.001) but not in reminder studies (SMD, -1.54; p=0.071). No significant harm from catheter removal strategies is supported. Limited research is available regarding the impact of UC insertion and maintenance technique. A recent randomised controlled trial indicates antimicrobial catheters provide no significant benefit in preventing symptomatic CAUTIs. Conclusions: UC reminders and stop orders appear to reduce CAUTI rates and should be used to improve patient safety. Several evidence-based guidelines have evaluated CAUTI preventive strategies as well as emerging evidence regarding intervention bundles. Implementation strategies are important because reducing UC use involves changing well-established habits.

Al Mohajer M and Darouiche R O (2013) Prevention and Treatment of Urinary Catheter-Associated Infections, *Current Infectious Disease Reports* 15 (2) : 116-123	Overview: As is the case with all device-related infections, the biofilm plays a central role in the pathogenesis of CA-UTIs. The diagnosis is often difficult, given the lack of good diagnostic tests. The most effective way to prevent infection is to limit catheter use and discontinue the catheter when no longer needed. Catheter removal or exchange is also useful in management.
Hooton T M, Bradley S F, Cardenas D D, Colgan R, Geerlings S E, Rice J C, Saint S, Schaeffe A J, Tambayh P A, Tenke P and Nicolle L E (2010) Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America, *Clinical Infectious Diseases* 50 (5) : 625-663	Guidelines for the diagnosis, prevention, and management of persons with catheter-associated urinary tract infection (CA-UTI), both symptomatic and asymptomatic, prepared by an Expert Panel of the Infectious Diseases Society of America. The guidelines include background information on the epidemiology and pathogenesis of CA infections and evidence-based recommendations for their diagnosis, prevention and management. The most effective way to reduce the incidence of CA-ASB and CA-UTI is to reduce the use of urinary catheterization by restricting its use to patients who have clear indications and by removing the catheter as soon as it is no longer needed. Strategies to reduce the use of catheterization have been shown to be effective and are likely to have more impact on the incidence of CA-ASB and CA-UTI than any of the other strategies addressed in these guidelines. Implementing such strategies should be a priority for all health care facilities.

Gould C V, Umscheid C A, Agarwal R K, Kuntz G, Pegues D A and the Healthcare Infection Control Practices Advisory Committee (HICPAC) (2010) Guideline for Prevention of Catheter-Associated Urinary Tract Infections 2009, *Infection Control and Hospital Epidemiology* 31 (4) : 319-326	Guidelines for catheter use Including: Priority Recommendations for Appropriate Urinary Catheter Use • Insert catheters only for appropriate indications, and leave in place only as long as needed. • Avoid use of urinary catheters in patients and nursing home residents for management of incontinence. • For operative patients who have an indication for an indwelling catheter, remove the catheter as soon as possible postoperatively, preferably within 24 hours, unless there are appropriate indications for continued use. Priority Recommendations for Aseptic Insertion of Urinary Catheters • Ensure that only properly trained persons (eg, hospital personnel, family members, or patients themselves) who know the correct technique of aseptic catheter insertion and maintenance are given this responsibility. • In the acute care hospital setting, insert catheters using aseptic technique and sterile equipment. Priority Recommendations for Proper Urinary Catheter Maintenance • Following aseptic insertion of the urinary catheter, maintain a closed drainage system • Maintain unobstructed urine flow.

Tenke P, Kovacs B, Bjerklund Johansen T E, Matsumoto T, Tambyah P A and Naber K G (2008) European and Asian guidelines on management and prevention of catheter-associated urinary tract infections, *International Journal of Antimicrobial Agents* 31 (S1) : 68-78	A literature review found that the urinary tract is the commonest source of nosocomial infection, particularly when the bladder is catheterised. Most catheter-associated UTIs are derived from the patient's own colonic flora and the catheter predisposes to UTI in several ways. The most important risk factor for the development of catheter-associated bacteriuria is the duration of catheterisation. Most episodes of short-term catheter-associated bacteriuria are asymptomatic and are caused by a single organism. Further organisms tend to be acquired by patients catheterised for more than 30 days. The clinician should be aware of two priorities: the catheter system should remain closed and the duration of catheterisation should be minimal. While the catheter is in place, systemic antimicrobial treatment of asymptomatic catheter-associated bacteriuria is not recommended, except for some special cases. Routine urine culture in an asymptomatic catheterised patient is also not recommended because treatment is in general not necessary. Antibiotic treatment is recommended only for symptomatic infection. Long-term antibiotic suppressive therapy is not effective. Antibiotic irrigation of the catheter and bladder is of no advantage. Routine urine cultures are not recommended if the catheter is draining properly. A minority of patients can be managed with the use of the non-return (flip) valve catheter, avoiding the closed drainage bag. Such patients may exchange the convenience of on-demand drainage with an increased risk of infection. Patients with urethral catheters in place for 10 years or more should be screened annually for bladder cancer. Clinicians should always consider alternatives to indwelling urethral catheters that are less prone to causing symptomatic infection. In appropriate patients, suprapubic catheters, condom drainage systems and intermittent catheterisation are each preferable to indwelling urethral catheterisation.

Saint S, Kowalski C P, Kaufman S R, Hofer T P, Kauffman C A, Olmsted R N, Forman J, Banaszak-Holl J, Damschroder L, and Krein S L (2008) Preventing Hospital-Acquired Urinary Tract Infection in the United States: A National Study, *Clinical Infectious Diseases* 46 (2) : 243-250	A written survey of infection control coordinators at a national random sample of non-federal US hospitals with an intensive care unit and 50 hospital beds (np600) and to all Veterans Affairs (VA) hospitals (np119). The survey asked about practices to prevent hospital-acquired UTI and other device-associated infections. Results. The response rate was 72%.	Overall, 56% of hospitals did not have a system for monitoring which patients had urinary catheters placed, and 74% did not monitor catheter duration. Thirty percent of hospitals reported regularly using antimicrobial urinary catheters and portable bladder scanners; 14% used condom catheters, and 9% used catheter reminders. VA hospitals were more likely than non-VA hospitals to use portable bladder scanners (49% vs. 29%; P < .001), condom catheters (46% vs. 12%; P <.001), and suprapubic catheters (22% vs. 9%; P< .001); non-VA hospitals were more likely to use antimicrobial urinary catheters (30% vs. 14%; P=.002). Conclusions. Despite the strong link between urinary catheters and subsequent UTI, we found no strategy that appeared to be widely used to prevent hospital-acquired UTI. The most commonly used practices—bladder ultrasound and antimicrobial catheters—were each used in fewer than one-third of hospitals, and urinary catheter reminders, which have proven benefits, were used in !10% of US hospitals.

Lo E, Nicolle L, Classen D, Arias K M, Podgorny K, Anderson D J, Burstin H, Calfee D P, Coffin S E, Dubberke E R, Fraser V, Gerding D N, Griffin F A, Gross P, Kaye K S, Klompas M, Marschall J, Mermel L A, Pegues D A, Perl T M, Saint S, Salgado C D, Weinstein R A, Wise R and Yokoe D S (2008) Strategies to Prevent Catheter-Associated Urinary Tract Infections in Acute Care Hospitals, *Infection Control and Hospital Epidemiology* 29 (S1)	An overview of prevention strategies including: Risk factors for development of CAUTI a. The duration of catheterization is the most important risk factor for development of infection. Limiting catheter use and, when a catheter is indicated, minimizing the duration the catheter remains in situ are primary strategies for CAUTI prevention. b. Additional risk factors include female sex, older age, and not maintaining a closed drainage system. Reservoir for transmission a. The drainage bag of the bacteriuric patient is a reservoir for organisms that may contaminate the environment and be transmitted to other patients. b. Outbreaks of infection with resistant gram-negative organisms attributable to bacteriuria in catheterized patients have been reported. Current evidence is not sufficient to support the routine use of a suprapubic catheter for short-term catheterization to prevent symptomatic urinary infection or other complications. Reviews and meta-analyses of silver-coated and other antibacterial urinary catheters consistently conclude that evidence does not support a recommendation for the uniform use of such devices. Silver-alloy catheters may decrease bacteriuria but have not been shown to decrease symptomatic infection or other undesirable outcomes.

Johnson J R, Kuskowski M A, and Wilt T J (2006) Systematic Review: Antimicrobial Urinary Catheters To Prevent Catheter-Associated Urinary Tract Infection in Hospitalized Patients, *Annals of Internal Medicine* 144 (2) : 116-126	To assess currently marketed antimicrobial urinary catheters for preventing catheter-associated urinary tract infection (UTI). Study Selection: Randomized and quasi-randomized trials of nitrofurazone-coated or silver alloy-coated antimicrobial urinary catheter use for less than 30 days; no language restriction. Data Extraction: Study design, study sample, inclusion and exclusion criteria, allocation, blinding, UTI definition, ascertainment methods, and proportion developing symptomatic UTI (primary end point) or bacteriuria (secondary end point) were extracted by using a structured data collection instrument. Twelve qualifying trials (13,392 total participants or catheters) were identified. They compared nitrofurazone-coated silicone (n= 3) or silver-coated latex (n= 9) catheters with silicone or latex catheters. No study addressed symptomatic UTI.	All trials suggested protection against bacteriuria with test catheter use. However, effect size varied considerably and post-randomisation exclusions were very common. Effect size was greatest in trials of nitrofurazone-coated catheters (all post-1995) and in pre-1995 silver alloy-coated catheter trials and was smallest in post-1995 silver alloy-coated catheter trials. Control group bacteriuria rate, control catheter type (latex vs. silicone), and patient sample (urology vs. other) also predicted effect size. Few studies addressed secondary bloodstream infection, mortality, costs, or microbial resistance. Short-term adverse effects were minimal. Conclusions: According to fair-quality evidence, antimicrobial urinary catheters can prevent bacteriuria in hospitalized patients during short-term catheterization, depending on antimicrobial coating and several other variables. Older data probably lack current relevance. Cost implications and effect on infectious complications remain undefined.

Trautner B W, Hull R A, and Darouiche R O (2005) Prevention of catheter-associated urinary tract infection, *Current Opinion in Infectious Diseases* 18 (1) : 37-41	Overview: The underlying cause of catheter-associated urinary tract infection is biofilm formation by uropathogens on the urinary catheter. Biofilm is a relatively new concept in medicine, and current measures to prevent biofilm formation are inadequate. Considerable work is being done in this area, but little clinical progress has been made. The purpose of this review is to analyze recent publications concerning prevention of catheter-associated urinary tract infection. Several recent studies have elucidated aspects of biofilm formation in catheter-associated urinary tract infection. Other researchers are working on methods to disrupt biofilm formation on catheter surfaces. At the same time, the magnitude of the problem of catheter-associated urinary tract infection has increased awareness of the effectiveness of basic infection control measures. A modern approach to infection control may include computerized ordering systems that minimize unnecessary days of catheterization. Finally, consumption of cranberry juice products and bacterial interference are two novel approaches to urinary tract infection prevention. Summary: Biofilm-disrupting strategies offer promise for the future but have little immediate applicability. Implementation of infection control measures to improve catheter function and remove unnecessary catheters can be done at the present time. In general, prevention of catheter-associated urinary tract infection remains an elusive goal. More basic research at the level of pathogenesis is needed so that novel strategies can be designed.

Tambyah P A and Maki D G (2000) Catheter-Associated Urinary Tract Infection Is Rarely Symptomatic: A Prospective Study of 1497 Catheterized Patients, *JAMA Internal Medicine (formerly Archives of Internal Medicine)* 160 (5) : 678-682	To define the clinical features of CAUTI. Setting and Patients: A university hospital; 1497 newly catheterized patients. Design: Every day that the catheter was in place, a quantitative urine culture and urine leukocyte count were obtained, and the patient was queried by a research worker regarding symptoms. To more precisely define the role of CAUTI in patients' symptoms, a subset of 1034 patients, 89 of whom developed CAUTI with more than 103 colony-forming units per millilitre, who did not have another potentially confounding site of infection besides the urinary tract, was analyzed. Outcome Measures: Presence of fever, symptoms commonly associated with community-acquired urinary tract infection, and peripheral leukocytosis.	There were 235 new cases of nosocomial CAUTI during the study period. More than 90% of the infected patients were asymptomatic; only 123 infections (52%) were detected by patients' physicians using the hospital laboratory. In the subset analysis, there were no significant differences between patients with and without CAUTI in signs or symptoms commonly associated with urinary tract infection—fever, dysuria, urgency, or flank pain—or in leukocytosis. Only 1 of the 235 episodes of CAUTI that were prospectively studied was unequivocally associated with secondary bloodstream infection. Conclusions: Whereas CAUTIs are a major reservoir of antibiotic-resistant organisms in the hospital, they are rarely symptomatic and infrequently cause bloodstream infection. Symptoms referable to the urinary tract, fever, or peripheral leukocytosis have little predictive value for the diagnosis of CAUTI.

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