Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"In older adults with recurrent urinary tract infections (RUTIs), how effective is fluid intake, specifically cranberry juice, compared to antibiotics in reducing frequency and duration of RUTIs?"

Clarification of question using PICO structure

Patients:	Older adults with recurrent urinary tract infections
Intervention:	Fluid intake, specifically cranberry juice
Comparator:	Antibiotics
Outcome:	Reducing frequency and duration of recurrent urinary tract infections.

Clinical and research implications

One high quality Cochrane systematic review included a small number of studies which were considered to be of partial relevance to this evidence summary, but none which fully matched the specified PICO. The limited available evidence suggests that cranberry juice or cranberry capsules have no significant treatment effect (compared to placebo) in reducing incidence of recurrent UTI in elderly in-patient populations. Limited evidence also suggests that there is no significant difference between cranberry tablets and trimethoprim or trimethoprim/sulfamethoxazole when used to reduce recurrent UTI in adult females.

No systematic reviews or primary studies were identified, which assessed the effectiveness of cranberry juice compared to antibiotics in reducing recurrent UTI in older adults. Therefore further studies are needed to specifically address the comparative preventative effect of fluid intake in the form of cranberry juice in this population.

What does the evidence say?

Number of included studies/reviews (number of participants)
We identified one Cochrane systematic review, which was of partial relevance to this evidence summary. The review aimed to compare the effectiveness of cranberry juice/cranberry products with placebo and other treatments and to compare the effectiveness of different cranberry products. None of the studies included in this review assessed the effectiveness of cranberry juice compared to antibiotics in reducing recurrent UTI in older adults. However, of the 24 studies included in the review, six were considered to have partial relevance to this evidence summary. Four RCTs compared cranberry juice/cranberry tablets with placebo in elderly populations and two RCTs compared cranberry tablets with antibiotics in adult populations.

Main Findings
Of the four randomised, placebo-controlled trials conducted in elderly populations, two reported sufficient data for analysis. One of these compared cranberry juice with placebo in hospitalised patients over 60 years of age, with a treatment duration of six months, and the other compared cranberry capsules with placebo in nursing home residents over 60 years with dementia and did not report treatment duration. The pooled risk ratio for recurrent UTI (participants with one or more UTIs at follow up) derived from these two studies was 0.75 (95% CI: 0.39 to 1.44), n=413 participants. Neither individual study reported a significant treatment effect for cranberry juice/capsules. The two remaining partially relevant RCTs compared cranberry tablets with trimethoprim or trimethoprim/sulfamethoxazole, in women ≥ 45 years and premenopausal women, respectively, who had experienced recurrent UTI in the year prior to the study. The pooled risk ratio for recurrent UTI (participants with one or more UTIs at follow up) derived from these two studies was 1.31 (95% CI: 0.85 to 2.02), n=344 participants.

Authors Conclusions
The authors concluded that, “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."

Reliability of conclusions/Strength of evidence
One high quality Cochrane systematic review included a small number of studies which were considered to be of partial relevance to this evidence summary, but none which fully matched the specified PICO. No systematic reviews or primary studies were identified, which assessed the effectiveness of cranberry juice compared to antibiotics in reducing recurrent UTI in older adults. The limited available evidence suggests that cranberry juice or cranberry capsules have no significant treatment effect (compared to placebo) in reducing incidence of recurrent UTI in elderly in-patient populations. Limited evidence also suggests that there is no significant difference between cranberry tablets and trimethoprim or trimethoprim/sulfamethoxazole when used to reduce recurrent UTI in adult females.

What do guidelines say?

The following guidelines were identified in SIGN 88 (Updated July 2012):

Page 1:
"The diagnosis of UTI is particularly difficult in elderly patients, who are more likely to have asymptomatic bacteriuria as they get older. The prevalence of bacteriuria may be so high that urine culture ceases to be a diagnostic test. Elderly institutionalised patients frequently receive unnecessary antibiotic treatment for asymptomatic bacteriuria despite clear evidence of adverse effects with no compensating clinical benefit."

Page 13-14:
"Cranberry products (juice, tablets, capsules) are not regulated and the concentration of active ingredients is not known. Concentrations may also fluctuate between batches of the same product. Most of the high strength preparations (tablet/capsule form) in the UK quote 200 mg of cranberry extract, equivalent to 5,000 mg of fresh cranberries (25:1 concentration). There is evidence that cranberry products significantly reduce 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 in reducing the incidence of UTIs in women with recurrent UTIs, than in elderly men and women or people requiring catheterisation. The optimal dose and route of administration has not been addressed.

One study has shown that trimethoprim had a very limited advantage over cranberry extract in the prevention of recurrent UTIs in older women and had more adverse effects. The NNTs for cranberry products are higher than for nightly antibiotic prophylaxis for six months, or postcoital antibiotic prophylaxis for six months.

Advise women with recurrent UTI to consider using cranberry products to reduce the frequency of recurrence. Women should be advised that cranberry capsules may be more convenient than juice and that high strength capsules may be most effective. There is no evidence to support the effectiveness of cranberry products for treating symptomatic episodes of UTI.

No serious adverse effects to cranberry products were reported, although the high drop-out rate in clinical trials suggests that long term treatment with cranberry products may not be well tolerated. The mechanism of action of cranberry products is unclear.

Advise patients taking warfarin to avoid taking cranberry products unless the health benefits are considered to outweigh any risks. Consider increased medical supervision and INR monitoring for any patient taking warfarin with a regular intake of cranberry products.

Advise women with recurrent UTI that cranberry products are not available on the NHS, but are readily available from pharmacies, health food shops, herbalists and supermarkets."

Page 20:
"Recurrent UTI is a common reason for referral to urologists. There are no trials about the effectiveness of antibiotics or cranberry products for preventing recurrent UTI in men."

The SIGN guidance summarised above appears more favourable towards cranberry products than is supported by the evidence presented in, or the conclusions of, the Cochrane systematic review (published in the same year) indentified for this summary.

Date question received: 08/05/2013
Date searches conducted: 13/05/13
Date answer completed: 20/05/2013

REFERENCES:

SRs

Jepson, R.G., Williams, G., Craig, J.C. (2012) Cranberries for preventing urinary tract infections. *Cochrane Database of Systematic Reviews Issue 10*.

Guidelines

Scottish Intercollegiate Guidelines Network (2012) Management of suspected bacterial urinary tract infection in adults. A national clinical guideline. CG88. Scottish Intercollegiate Guidelines Network.

Results

SRs

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Jepson, Williams and Craig (2013)	07/2012	RCTs of quasi-RCTs comparing cranberry juice (or derivatives) with placebo or any other treatment for the prevention of urinary tract infections (UTIs) in susceptible populations were eligible for inclusion. Susceptible populations were defined as: history of recurrent lower UTI (> 2 in previous 12 months); elderly men and women; patients needing intermittent catheterisation; pregnant women; patients with indwelling catheters; patients with abnormalities of the urinary tract; children with first or subsequent UTI. The primary outcome was number (incidence) of UTIs (confirmed by a catheter specimen of urine (CSU), midstream specimen of urine (MSU) if possible, or a 'clean catch' specimen). Secondary outcomes were adherence to therapy and side effects. Studies of the treatment of UTI and studies of any urinary tract condition not caused by bacterial infection were eexcluded.	24 Studies were included in this review, of which only 6 were of partial relevance to this evidence summary.	This review aimed to compare the effectiveness of cranberry juice/cranberry products with placebo and other treatments and to compare the effectiveness of different cranberry products. No study included in this review assessed the effectiveness of cranberry juice compared to antibiotics in reducing recurrent UTI in older adults. Six studies were considered of partial relevance to this evidence summary. Randomised placebo controlled trials of cranberry juice/cranberry products in elderly populations: Three studies with a total of 590 participants compared the effectiveness of cranberry juice versus placebo for reducing recurrence of UTI in elderly populations. One additional three arm study (n=56) compared cranberry capsules once or twice daily with placebo. Only two studies reported sufficient data for analysis.	The objectives of the review were clearly stated and inclusion criteria were specified for all components of PICOS. Six bibliographic databases were searched for relevant studies. In addition, trial registries and relevant conference proceedings were searched, companies involved I the distribution of cranberry products were approached and the bibliographies of review articles and

				The first study was a parallel group RCT conducted in Scotland, which randomised 376 hospitalised patients, aged ≥ 60 years, to receive 300 mL of cranberry juice or matching placebo daily; treatment duration 6 months. The second study, conducted in the USA, randomised 56 elderly (> 60 years) nursing home residents with dementia to receive 1 x 650 mg cranberry capsule daily, 1x 650 mg cranberry capsule twice daily, or no treatment; treatment duration was not reported. The pooled risk ratio for recurrent UTI (participants with one or more UTIs at follow up) derived from these two studies was 0.75 (95% CI: 0.39 to 1.44), n=413 participants. Randomised controlled trials of cranberry juice/cranberry products versus antibiotics in adult populations: Two studies, with a total of 358 participants, compared the effectiveness of cranberry derivatives versus antibiotics for reducing recurrence of UTI in adults. One study, conducted in Scotland, randomised 137 community dwelling women, aged ≥ 45 years, who had experienced at least 2 antibiotic treated UTIs in the previous 12 months, to receive either 500 mg cranberry tablet or 100 mg trimethoprim; treatment duration was not reported. The second study was conducted in	relevant studies were screened. Study selection, data extraction and assessment of the methodological quality of included studies were undertaken independently by two reviewers, with any disagreements resolved through discussion and consultation with a third reviewer. This approach minimises the potential for error and/or bias in the review process. Meta-analyses were undertaken using a random effects model. The validity of generating pooled estimates which include different interventions (e.g.

				the Netherlands and randomised 221 premenopausal women, who had experienced at least 3 symptomatic UTIs in the previous year, to receive either 500 mg of cranberry extract twice daily plus 1 placebo tablet at night, or 480 mg trimethoprim/sulfamethoxazole at night + 1 placebo tablet at night; treatment duration 12 months. The pooled risk ratio for recurrent UTI (participants with one or more UTIs at follow up) derived from these two studies was 1.31 (95% CI: 0.85 to 2.02), n=344 participants.	cranberry juice and cranberry tablets) is questionable.

Risk of Bias: SRs

Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Jepson, Williams and Craig (2012)	☺	☺	☺	☺	?

☺Low Risk ☹High Risk ? Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
SRs and Guidelines			
NICE	UTI Cranberry	101	1
DARE	(UTI) IN DARE 46 Delete 2 ((urin* OR kidney* OR renal*) AND (infect* OR inflam*)) IN DARE 599 Delete 3 (urin*) IN DARE 1003 Delete 4 (urin* ADJ2 tract*) IN DARE 294 Delete 5 (pyelonephritis) IN DARE 23 Delete 6 (bacteriuria) IN DARE 41 Delete 7 (pyuria) IN DARE 7 Delete 8 (antibiot* OR (anti ADJ2 biot*) OR anti-biot*) IN DARE 1170 Delete 9 MeSH DESCRIPTOR Urinary Tract Infections EXPLODE ALL TREES 176 Delete 14 ((water* or fluid* or liquid* or beverage* or cranberr*) ADJ3 (increase* or intake* or take* or give* or drink* or consume*)) IN DARE 74 Delete 15 (fluid ADJ3 therap*) IN DARE 79 Delete 16 ((water* or fluid*) ADJ3 deprivat*) IN DARE 1 Delete 17 (cranberr*) IN DARE 9 Delete 18 MeSH DESCRIPTOR Fluid Therapy EXPLODE ALL TREES 84 Delete 19 MeSH DESCRIPTOR Vaccinium macrocarpon EXPLODE ALL TREES 5 Delete 20 MeSH DESCRIPTOR Viburnum EXPLODE ALL TREES 0 Delete 21 MeSH DESCRIPTOR Drinking EXPLODE ALL TREES 4 Delete 22 MeSH DESCRIPTOR Water Deprivation EXPLODE ALL TREES 0 Delete 23 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #9 1357 Delete 24 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 184 Delete 25 #23 AND #24		
DARE	(UTI) IN DARE 46 Delete 2 ((urin* OR kidney* OR renal*) AND (infect* OR inflam*)) IN DARE 599 Delete		

	3 (urin*) IN DARE 1003 Delete 4 (urin* ADJ2 tract*) IN DARE 294 Delete 5 (pyelonephritis) IN DARE 23 Delete 6 (bacteriuria) IN DARE 41 Delete 7 (pyuria) IN DARE 7 Delete 8 (antibiot* OR (anti ADJ2 biot*) OR anti-biot*) IN DARE 1170 Delete 9 MeSH DESCRIPTOR Urinary Tract Infections EXPLODE ALL TREES 176 Delete 10 (antibiotics) IN DARE 878 Delete 11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #9 1357 Delete 12 #8 OR #10 1170 Delete 13 #11 AND #12		
Primary studies			
CENTRAL	#1 "Urinary Tract Infections":ti,ab,kw (Word variations have been searched) 3032 #2 Enter terms for search UTIUTI 628 #3 MeSH descriptor: [Urinary Tract Infections] explode all trees 1984 #4 Enter terms for search CystitisCystitis 682 #5 MeSH descriptor: [Cystitis] explode all trees 300 #6 Enter terms for search #1 or #2 or #3 or #4 or #5#1 or #2 or #3 or #4 or #5 3925 #7 Enter terms for search antibiotic*antibiotic* 15868 #8 MeSH descriptor: [Anti-Bacterial Agents] explode all trees 8388 #9Enter terms for searc#7 or #820177 #10Enter terms for searcfluid* or liquid* or water or drink* or drank or juice38653 #11Enter terms for searc#6 and #9 and #10 111	44	
Embase	3. EMBASE; "Urinary Tract Infection".ti,ab; 18867 results. 4. EMBASE; PYELONEPHRITIS/; 15692 results. 5. EMBASE; PYELONEPHRITIS/ OR ACUTE PYELONEPHRITIS/ OR CHRONIC PYELONEPHRITIS/; 17787 results. 6. EMBASE; exp CYSTITIS/; 16088 results. 7. EMBASE; BACTERIURIA/; 6636 results. 8. EMBASE; ASYMPTOMATIC BACTERIURIA/; 744 results. 9. EMBASE; UTI.ti,ab; 7753 results. 10. EMBASE; cystitis.ti,ab; 10265 results. 11. EMBASE; pyelonephritis.ti,ab; 11576 results.	59	

	12. EMBASE; bacteriuria.ti,ab; 5077 results. 13. EMBASE; (urin* adj3 infection*).ti,ab; 40719 results. 14. EMBASE; 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13; 77564 results. 15. EMBASE; ANTIBIOTIC AGENT/; 179790 results. 16. EMBASE; antibiotic*.ti,ab; 261595 results. 17. EMBASE; ((drink* OR drank) adj5 (water OR fluid*)).ti,ab; 45179 results. 18. EMBASE; 15 OR 16; 362320 results. 19. EMBASE; 14 AND 18; 12867 results. 20. EMBASE; 17 AND 19; 7 results. 21. EMBASE; ((fluid* OR liquid*) adj5 (drink* OR drank)).ti,ab; 1568 results. 22. EMBASE; (fluid OR liquid OR water OR drink* OR drank OR juice).ti,ab; 1140235 results. 23. EMBASE; (fluid* OR liquid* OR water OR drink* OR drank OR juice).ti,ab; 1195113 results. 24. EMBASE; 19 AND 23; 533 results. 25. EMBASE; random*.tw; 800572 results. 26. EMBASE; factorial*.tw; 20676 results. 27. EMBASE; placebo*.tw; 187993 results. 28. EMBASE; (crossover* OR cross-over*).tw; 65360 results. 29. EMBASE; (doubl* adj3 blind*).tw; 136217 results. 30. EMBASE; (singl* adj3 blind*).tw; 15356 results. 31. EMBASE; assign*.tw; 220501 results. 32. EMBASE; allocat*.tw; 75019 results. 33. EMBASE; volunteer*.tw; 166928 results. 34. EMBASE; CROSSOVER PROCEDURE/; 36827 results. 35. EMBASE; DOUBLE-BLIND PROCEDURE/; 114506 results. 36. EMBASE; SINGLE-BLIND PROCEDURE/; 17352 results. 37. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 341966 results. 38. EMBASE; 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37; 1305086 results. 39. EMBASE; 24 AND 38; 59 results.		
Medline	40. MEDLINE; "Urinary Tract Infection".ti,ab; 14797 results. 41. MEDLINE; PYELONEPHRITIS/; 12966 results. 42. MEDLINE; exp CYSTITIS/; 7667 results. 43. MEDLINE; cystitis.ti,ab; 8075 results.	356	

	44. MEDLINE; pyelonephritis.ti,ab; 10423 results. 45. MEDLINE; bacteriuria.ti,ab; 4751 results. 46. MEDLINE; (urin* adj3 infection*).ti,ab; 31969 results. 47. MEDLINE; URINARY TRACT INFECTIONS/; 31075 results. 48. MEDLINE; CYSTITIS/; 6299 results. 49. MEDLINE; BACTERIURIA/; 6892 results. 50. MEDLINE; UTI.ti,ab; 4960 results. 51. MEDLINE; 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50; 70383 results. 52. MEDLINE; ANTI-BACTERIAL AGENTS/; 226468 results. 53. MEDLINE; exp ANTI-BACTERIAL AGENTS/; 508336 results. 54. MEDLINE; antibiotic*.ti,ab; 215685 results. 55. MEDLINE; 52 OR 53 OR 54; 597179 results. 56. MEDLINE; 51 AND 55; 17456 results. 57. MEDLINE; (fluid* OR liquid* OR water OR drink* OR drank OR juice).ti,ab; 1042411 results. 58. MEDLINE; 56 AND 57; 622 results. 59. MEDLINE; "randomized controlled trial".pt; 351777 results. 60. MEDLINE; "controlled clinical trial".pt; 86248 results. 61. MEDLINE; randomi?ed.ab; 321400 results. 62. MEDLINE; placebo.ab; 145038 results. 63. MEDLINE; "drug therapy".fs; 1617872 results. 64. MEDLINE; randomly.ab; 195763 results. 65. MEDLINE; trial.ab; 278396 results. 66. MEDLINE; groups.ab; 1260542 results. 67. MEDLINE; 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66; 3146743 results. 68. MEDLINE; 58 AND 67; 356 results.		
Summary	**NA**	**NA**	

Disclaimer

BEST in MH answers to clinical questions are for information purposes only. BEST in MH does not make recommendations. Individual health care providers are responsible for assessing the applicability of BEST in MH answers to their clinical practice. BEST in MH is not responsible or liable for, directly or indirectly, any form of damage resulting from the use/misuse of information contained in or implied by these documents. Links to other sites are provided for information purposes only. BEST in MH cannot accept responsibility for the content of linked sites.