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Cranberry Reduces the Risk of Urinary Tract Infection Recurrence in Otherwise Healthy Women: A Systematic Review and Meta-Analysis

Zhuxuan Fu,[1] DeAnn Liska,[2] David Talan,[3] and Mei Chung[1]

[1]Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA; [2]Nutrition Science and Biostatistics, Biofortis Research, Addison, IL; and [3]University of California, Los Angeles School of Medicine, UCLA–Olive View Medical Center, Sylmar, CA

Abstract

Background: Cranberry (*Vaccinium* spp.) has been advocated for treatment of urinary tract infection (UTI); however, its efficacy is controversial. Women have a 50% risk of UTI over their lifetime, and ~20–30% experience a subsequent UTI recurrence.

Objective: We conducted this meta-analysis to assess the effect of cranberry on the risk of UTI recurrence in otherwise healthy women.

Methods: Literature published before January 2011 was obtained from 2 published systematic reviews, and we conducted updated searches in EMBASE and MEDLINE (through July 2017). We included randomized controlled trials that were conducted in generally healthy nonpregnant women aged ≥18 y with a history of UTI, compared cranberry intervention to a placebo or control, and reported the outcome as the number of participants experiencing a UTI. Two researchers conducted abstract and full-text screenings, data extractions, and risk of bias assessments independently, and discrepancies were resolved by group consensus. Meta-analyses were performed by using Stata SE software (version 13). We employed a fixed-effect model using the Mantel-Haenszel method to estimate the summary risk if the heterogeneity was low to moderate (I^2 < 50%). Otherwise, we applied a random-effects model using the DerSimonian-Laird method.

Results: We identified 7 randomized controlled trials conducted in healthy women at risk of UTI (n = 1498 participants). Results of the meta-analysis showed that cranberry reduced the risk of UTI by 26% (pooled risk ratio: 0.74; 95% CI: 0.55, 0.98; I^2 = 54%). Risk of bias indicated that 2 studies had high loss to follow-up or selective outcome reporting. Overall, the studies were relatively small, with only 2 having >300 participants.

Conclusion: These results suggest that cranberry may be effective in preventing UTI recurrence in generally healthy women; however, larger high-quality studies are needed to confirm these findings. This trial was registered at crd.york.ac.uk/prospero as CRD42015024439. *J Nutr* 2017;147:2282–8.

Keywords: meta-analysis, *Vaccinium*, urinary tract infection, prevention, proanthocyanidin

Introduction

Urinary tract infection (UTI) affects >150 million people/y worldwide and is the most common urologic disease in the United States, accounting for >$2.6 billion in annual health care expenditures (1). The most common form of UTI is cystitis, a sporadic uncomplicated UTI in the bladder of otherwise healthy individuals (2, 3). Complicated UTI is less common and is associated with a structural or functional abnormality (e.g., urinary obstruction, neurologic disease, immunosuppression, renal dysfunction, or catheterization) as well as those that occur in women during pregnancy (4).

Uncomplicated UTI is more common in women. Women have a 50% risk of a UTI episode over their lifetime, and ~20–30% experience a subsequent UTI recurrence (4, 5). For example, using MarketScan data for 2003–2011, Suskind et al. (1) reported an overall incidence of UTI recurrence of 102 in 100,000 women, with

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Address correspondence to MC (e-mail: mei_chun.chung@tufts.edu).

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the highest incidence in women aged 55–65 y (189 in 100,000) compared with those aged 18–54 y (76–77 in 100,000) (1).

The most common therapeutic approach to UTI is the use of antibiotics (e.g., fluoroquinolones); however, women with recurrent UTI often require multiple antibiotic regimens within short periods of time, and antibiotics are also employed as a prophylactic. This use of antibiotics increases women's risk of developing antibiotic resistance (5, 6). Currently, rates of fluoroquinolone resistance are >20% in many parts of the world, and multiple-resistant strains of the Enterobacteriaceae that produce extended-spectrum β-lactamases are now present or emerging in many communities, including the United States (7). Moreover, the FDA stated in 2016 that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with an uncomplicated UTI (8). Therefore, nonantibiotic methods for UTI prevention are of interest to clinicians, particularly in the treatment of uncomplicated UTI (9).

Cranberry is often used by women to prevent UTI (10, 11). Several clinical studies suggest that consumption of cranberry juice or cranberry supplements may decrease UTI occurrence in healthy women (12–15). These observations have been supported by results from in vitro research, which show that cranberry-derived compounds (e.g., polyphenolics and A-type proanthocyanidins) may interfere with the adhesion of bacteria to urinary tract epithelial cells, attenuate the uropathogen reservoir in the gastrointestinal tract, and suppress the inflammatory cascade (16–19). However, a recent clinical trial conducted in institutionalized elderly women showed no effect of cranberry capsules on bacteriuria with pyuria (20). Although this population included cases of complicated UTI, an accompanying editorial concluded that cranberry should not be considered for women at risk of UTI (21).

Published meta-analyses have also been inconclusive regarding the efficacy of cranberry on UTI risk. For example, a 2012 Cochrane review by Jepson et al. (22) indicated that cranberry had no benefit in UTI compared with placebo. By contrast, another meta-analysis published that same year by Wang et al. (23) indicated the opposite, stating that cranberry products were associated with a protective effect. These reports, however, combined complicated and uncomplicated UTIs, and it is not clear whether the findings can be generalized to healthy women at risk of an uncomplicated UTI (24). Most recently, a systematic review by the Canadian Agency for Drugs and Technologies in Health (11) found 5 studies with evidence of clinical efficacy for a reduced risk of UTI with cranberry, and it included several studies that were not available for the previously reported meta-analyses. The agency concluded that the data on cranberry and UTI remain mixed; however, the review did not provide a quantitative analysis of the data on uncomplicated UTI alone.

We undertook this systematic review and meta-analysis to evaluate the evidence of cranberry in the prevention of UTI among generally healthy women. In this analysis, we applied strict inclusion criteria to select trials that enrolled healthy women only and assessed uncomplicated UTI as the outcome.

Methods

This review was registered at crd.york.ac.uk/prospero as CRD42015024439 and was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations (25).

Identification of trials. Literature published before January 2011 was obtained from 2 published systematic reviews with search dates of November 2011 (23) and July 2012 (22). Updated searches for clinical trials were conducted using the following terms with the search date from January 2010 to July 2017 in MEDLINE and EMBASE: UTI, urinary tract infection(s), uncomplicated UTI, uncomplicated urinary tract infection, bacteriuria, pyelonephritis, cystitis, pyuria, dysuria, *Escherichia coli*, *coli* AND cranberry, *Vaccinium macrocarpon*, *Vaccinium microcarpum*, *Vaccinium oxycoccus*, and *Vaccinium erythrocarpum* (**Supplemental Table 1**). Hand searches were also conducted. Searches of international and US clinical trial registries were conducted to locate unpublished data. The authors of 2 studies identified in the clinical trial registries were contacted but no response was received. Three published abstracts were identified: 2 appeared to be duplicates of a published full-text report (13) and 1 was a report of one of the unpublished studies identified in the clinical trials database search (26). This abstract, however, did not include information on dosing and was thus excluded.

We included randomized controlled trials that were conducted in generally healthy nonpregnant women aged ≥18 y with a history of UTI, compared a cranberry intervention to a placebo or nontreatment control group, and reported the outcome as the number of participants experiencing a UTI. We excluded studies that were not published as peer-reviewed full-text articles or were conducted in special groups (elderly persons, children, or pregnant women), institutionalized subjects, and participants with diagnosed diseases or a complicated UTI (e.g., severe renal impairment, multiple sclerosis, dementia, spinal cord injury, abnormalities of the urinary tract, neuropathic bladder, in-dwelling catheter, stones, or anatomic abnormalities of the urinary tract) (4).

Study selection, data extraction, and quality assessment. The cumulative incidence of participants with ≥1 UTI was used for pooled risk ratio estimates. The risk of bias assessment for each study included random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other bias (e.g., source of funding) (**Table 1**). Each risk of bias item was scored as low, high, or unclear. Abstract and full-text screenings, data extraction, and quality assessment, which used the Cochrane risk of bias assessment guideline (22), were conducted by 2 independent researchers and discrepancies were resolved by group consensus.

TABLE 1 Risk of bias assessment of included randomized controlled trials

Reference	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Kontiokari et al. (27)	Low	Low	Low	Low	High	Low	Unclear
Stothers (28)	Low	Low	High	Unclear	Low	Unclear	Unclear
Barbosa-Cesnik et al. (29)	Unclear	Low	Low	Low	Low	Unclear	High
Stapleton et al. (14)	Low	Low	Low	Low	High	Low	Low
Takahashi et al. (15)	Unclear	Low	Low	Low	Low	Low	Low
Vostalova et al. (13)	Unclear	Low	Low	Unclear	Low	High	High
Maki et al. (12)	Low	Unclear	Low	Low	Low	Low	Low

Data synthesis and analysis. Meta-analyses were performed using Stata SE software (version 13). Statistical significance was defined as $P < 0.05$ (2-sided), unless otherwise stated. Heterogeneity was quantified using both the I^2 statistic and the chi-square test, with an I^2 value of $\geq 50\%$ (P value for heterogeneity test ≤ 0.10) considered substantial heterogeneity. We employed a fixed-effect model using the Mantel-Haenszel method to estimate the summary risk if the heterogeneity was low to moderate ($I^2 < 50\%$). Otherwise, we applied a random-effects model using the DerSimonian-Laird method (30). As the primary summary risk estimate, the risk ratio was calculated as a measure of effect for dichotomous outcomes in individual studies. If there was >1 time point for UTI measures (e.g., 6 and 12 mo), UTI data reported as the primary outcome in the publication were used for the main risk ratio estimate. A funnel plot was drawn to visually evaluate small-study effects, formerly known as "publication bias" testing (**Supplemental Figure 1**). Because of the small number of included studies ($n < 10$), the interpretations of funnel plot symmetry are limited and thus no statistical testing (e.g., Egger's test) was done.

Results

Study characteristics. Seven RCTs met the inclusion criteria for qualitative synthesis (**Figure 1**). Three studies (27–29) were included in the previous meta-analyses, and 4 studies (12–15) were published after the analyses and represent new data. A quality review indicated that 3 trials (12, 15, 28) did not provide the randomization information, 1 trial (13) did not provide the allocation concealment information, and 2 trials (14, 28) had high rates of loss to follow-up (28–32%). In addition, 4 studies were subject to other biases, which included funding source (12, 29), lack of information on UTI diagnosis (15), or poor compliance response (27) (Table 1).

Characteristics of the trials are provided in **Table 2.** Briefly, 4 trials (12–14, 28) enrolled participants who were free of UTI at study entry; the other 3 trials (15, 27, 29) included participants who had a UTI at enrollment and were treated and the UTI resolved before the start of the intervention. Five trials (12, 14, 15, 27, 29) administered cranberry juice, whereas 1 trial (28) used both juice and tablets and 1 trial (13) used powder capsules. Six trials (12–15, 28, 29) used a formulated placebo, whereas 1 trial (27) had an open control. Most notable were the differences in the definition of UTI. Clinical symptoms to define UTI were required in most trials. Four trials also required confirmed bacteriuria; however, the thresholds varied from $\geq 10^3$ (31) to $\geq 10^5$ CFU/mL (13, 27, 28) (**Supplemental Table 2**). In addition, 1 trial (14) included 2 options for designation of UTI, including both a culture-confirmed UTI outcome ($\geq 10^3$ CFU/mL) and a clinical UTI that did not require culture confirmation but included clinical exclusion of other diagnoses and pyuria. Another trial (12) reported clinically confirmed UTI (requiring a pelvic examination) as the primary outcome and reported the culture-confirmed UTI ($\geq 10^5$ CFU/mL) as a subanalysis. Finally, 1 trial (15) did not define the outcome except as the point when antibiotics were administered after a UTI diagnosis.

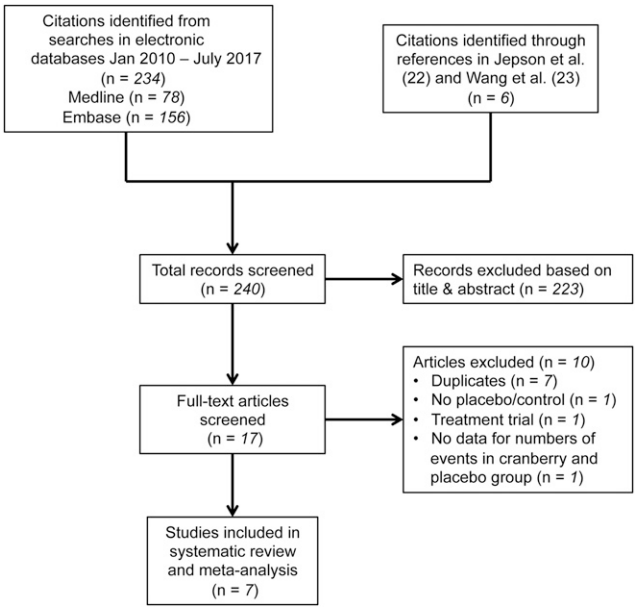

FIGURE 1 Literature search flow diagram.

All trials reported the cumulative incidence of participants with ≥1 UTI at follow-up. Four trials (12–14, 27) also reported the UTI incidence rate, and 4 trials (12, 14, 15, 29) provided data on HRs of having the first UTI during follow-up adjusted for covariates defined by individual studies.

Quantitative synthesis. Data on UTI cumulative incidence included 1498 participants across the 7 trials, with 798 in the cranberry groups and 702 in the placebo or control groups. Cranberry products (juice plus tablets or capsules) were shown to reduce the risk of UTI recurrence by 26% among otherwise healthy women compared with the placebo or control group (RR: 0.74; 95% CI: 0.55, 0.98; $I^2 = 54\%$) (**Figure 2**). Subgroup analysis also showed that cranberry significantly reduced the risk of UTI recurrence by 35% in women who were free of UTI at enrollment (RR: 0.65; 95% CI: 0.51, 0.84; $I^2 = 10\%$; $n = 4$ studies). However, the risk reduction was not statically significant, with large uncertainty and heterogeneity among women who were enrolled with confirmation of an active UTI episode and then treated with antibiotics before UTI recurrence assessment (RR: 0.84; 95% CI: 0.47, 1.50; $I^2 = 73\%$; $n = 3$ studies). The 4 studies (12–14, 28) that enrolled women free of UTI relied on a history of UTI episodes in the previous 6 or 12 mo to define UTI status at enrollment, but the definitions of UTI (i.e., based on symptoms or bacteria-positive culture) varied across the studies. Of the studies that enrolled women with an active UTI, 2 studies (27, 29) required a positive urine culture at enrollment and 1 study (15) did not indicate whether a positive culture was confirmed; however, all 3 studies indicated that women were treated with antibiotics just before or at the initiation of the intervention.

Only 2 studies (27, 28) reported the effect of cranberry after 12 mo. One study provided cranberry over 12 mo and only reported UTI data at the 12-mo time point (28). The other study was a 6-mo cranberry intervention followed by a 6-mo observation period, during which subjects were allowed prophylactic antibiotics, although this was only observed for 2% and 6% of subjects in the cranberry and control groups, respectively (27). The meta-analysis results at 12 mo (RR: 0.61; 95% CI: 0.40, 0.91; $I^2 = 0\%$; $n = 2$ studies) were similar to those at 6 mo (RR: 0.76; 95% CI: 0.55, 1.04; $I^2 = 59\%$; $n = 6$ studies) although only 2 studies reported data at 12 mo (**Table 3**).

Only 5 studies reported on adverse events or tolerance, 3 of which (12, 28, 29) compared adverse events between groups. In 2 studies (12, 28), the number of participants reporting adverse events was higher in the placebo groups than in the cranberry groups, whereas the other study (28) found similar numbers of participants experiencing adverse events in both the placebo and cranberry groups. Gastrointestinal disturbances were the most commonly reported complaint, and no serious adverse events

TABLE 2 Study characteristics of cranberry and UTI randomized controlled trials[1]

Study (ref)	Region	Design or duration	UTI entrance criteria	Age,[2] y	Cranberry group			Placebo or control group	
					Sample size, *n*	Intervention, per day	PAC content	Sample size, *n*	Intervention, per day
Kontiokari et al. (27)	Finland	3-arm parallel[3]; 6 mo with 12 mo of follow-up (women with ≥3 UTIs/6 mo were offered antimicrobial prophylaxis)	Presence of UTI (*Escherichia coli* $\geq 10^5$ CFU/mL) at enrollment, treated and free of bacteriuria ≥3 d	Cranberry-lingonberry: 32 ± 9.8; control: 29 ± 10.5	50	7.5 g cranberry concentrate with 1.7 g lingonberry concentrate	NR	50	Open control
Stothers (28)	Canada	3-arm parallel; 12 mo	History of ≥2 symptomatic culture-positive ($\geq 10^5$ CFU/mL) UTIs in previous 12 mo	Tablet: 23–68; juice: 21–70; placebo: 21–72	Tablet: 50; juice: 50	Tablet: 2 concentrated cranberry juice tablets plus 750 mL placebo juice; juice: 750 mL unsweetened 100% cranberry juice plus 1 placebo tablet	NR	50	2 placebo tablets plus 750 mL placebo juice (water, food coloring, and pineapple juice)
Barbosa-Cesnik et al. (29)	United States	2-arm parallel; 6 mo or until a confirmed UTI	Presence of ≥3 urinary symptoms and positive urine culture ($\geq 10^3$ CFU/mL)	Cranberry: 21.2 ± 3.4; placebo: 21.2 ± 3.5	155	480 mL low-calorie cranberry juice cocktail (27% juice)	224 mg/d	164	480 mL placebo juice (similar sweetener, acidity, color, and ascorbic acid)
Stapleton et al. (14)	United States	3-arm parallel; 6 mo	History of ≥1 UTI in previous 12 mo	Cranberry: 25.3 ± 6.6; placebo: 26.4 ± 6.5	120[4]	120 or 240 mL/d low-calorie cranberry juice cocktail (27%)	NR	56	120 or 240 mL/d placebo beverage similar in color and taste
Takahashi et al. (15)	Japan	2-arm parallel; 6 mo	Acute uncomplicated UTI healed by antibiotics	Cranberry: 55 (20–79); placebo: 59 (20–79)	107	125 mL/d cranberry juice	>40 mg/125 mL	106	125 mL/d placebo beverage matched in color and taste
Vostalova et al. (13)	Czech Republic	2-arm parallel; 6 mo	History of ≥2 symptomatic UTIs in previous 12 mo	Cranberry: 35.61 ± 12.97; placebo: 38.03 ± 13.4	89	500 mg cranberry fruit powder capsules	1.4 mg 2×/d	93	Maltodextrin capsules indistinguishable in appearance
Maki et al. (12)	United States	2-arm parallel; 6 mo	History of ≥2 clinician-treated UTIs in previous 12 mo, with ≥1 in previous 6 mo	Cranberry[5]: 40.9 ± 1.1; placebo: 41.0 ± 1.0	185	240 mL low-calorie (36 kcal) cranberry cocktail (27%) juice	41.1/119 mg/d[6]	188	240 mL low-calorie (34 kcal) beverage (organic acids, sugars, noncaloric sweeteners, and colorants)

[1] NR, not reported; PAC, proanthocyanidin; ref, reference; UTI, urinary tract infection.
[2] Values are means ± SDs or ranges unless otherwise indicated.
[3] This study also included a probiotic intervention (not shown).
[4] Study participants were randomly assigned to 1 of 2 cranberry arms (120 and 240 mL/d) or a placebo group (which was divided after randomization to receive the same amount of placebo).
[5] Values are means ± SEMs.
[6] This trial reported results from 2 different methods for determining proanthocyanidins.

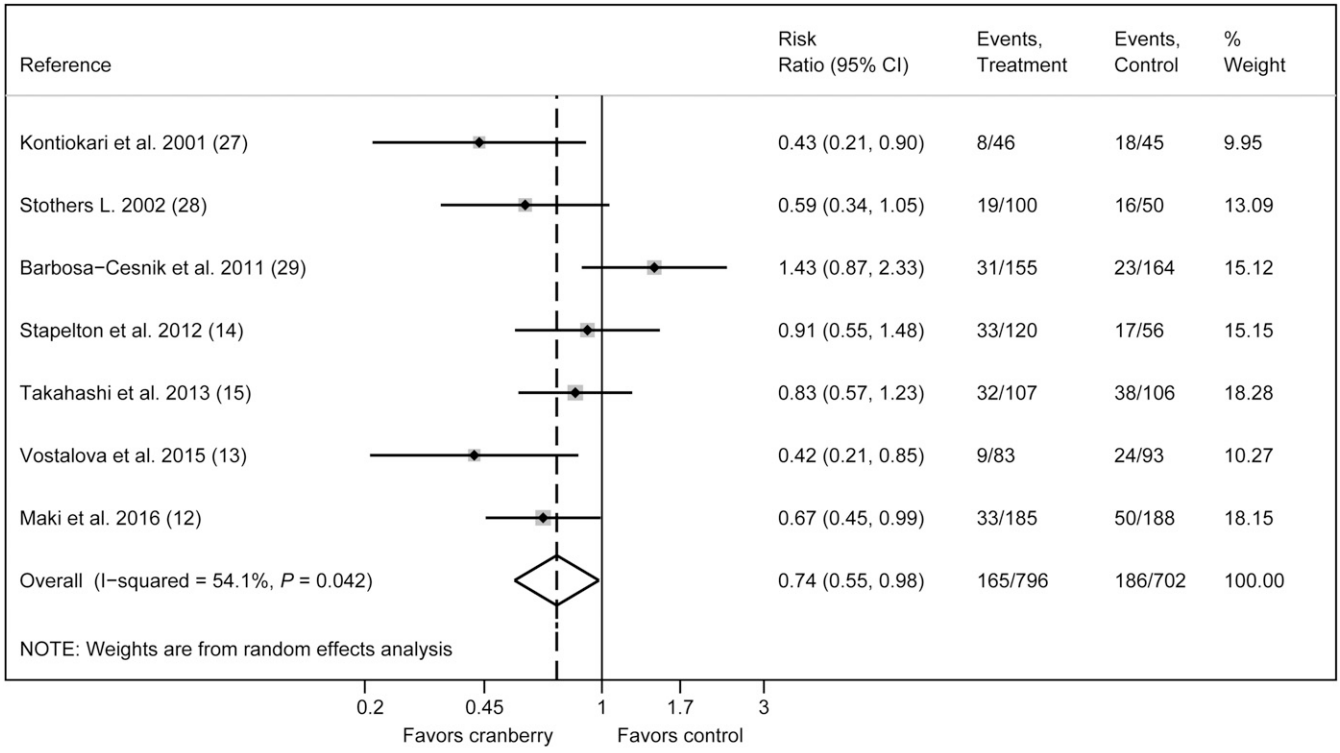

FIGURE 2 Forest plot: summary effect of cranberry in the prevention of urinary tract infection.

attributable to the intervention were noted. A few participants discontinued the interventions as a result of gastrointestinal symptoms (reflux, burning sensation from consumption of the beverage); however, the interventions were considered to be well tolerated overall.

Discussion

Results of this meta-analysis suggest that cranberry can be an effective nutrition-based nonantibiotic approach to prevent UTI recurrence among generally healthy women. This meta-analysis indicates that there was a 26% reduction in the risk of UTI recurrence for healthy women who received cranberry than for those who did not (RR: 0.74; 95% CI: 0.55, 0.98; I^2 = 54%).

To our knowledge, this is the first meta-analysis to focus on cranberry as a nutritive option to reduce the risk of recurrence of uncomplicated UTI in healthy nonpregnant women. Three previous meta-analyses (22, 23, 32) included subgroup analyses in the population of healthy women with UTI recurrence as part of studies that included a broader range of participants, such as

TABLE 3 Meta-analysis of randomized controlled trials on cranberry and UTI in women[1]

Subgroup analysis	Trials, *n*	References	Pooled cumulative incidence of UTI		Risk ratio (95% CI)	Heterogeneity	
			Cranberry	Placebo/control		I^2, %	*P* value, Q test
Overall analysis	7	12–15, 27–29	165 of 796	186 of 702	0.74 (0.55, 0.98)	54	0.04
Culture-confirmed UTI	5	13, 14, 27–29	100 of 504	98 of 408	0.71 (0.45, 1.12)	68	0.01
Form of cranberry[2]							
Juice	6	12, 14, 15, 27–29	146 of 663	162 of 609	0.79 (0.59, 1.06)	50	0.075
Capsule or tablet	2	13, 28	18 of 133	40 of 143	0.48 (0.29, 0.79)	0	0.57
Follow-up duration,[3] mo							
6	6	12–15, 27, 29	146 of 696	170 of 652	0.76 (0.55, 1.04)	59	0.03
12	2	27, 28	31 of 146	35 of 95	0.61 (0.40, 0.91)	0	0.92
UTI status at baseline							
Free of UTI	4	12–14, 28	94 of 488	107 of 387	0.65 (0.51, 0.84)	10	0.35
Active UTI	3	15, 27, 29	71 of 308	79 of 315	0.84 (0.47, 1.50)	73	0.025

[1] UTI, urinary tract infection.
[2] Stothers (28) was a 3-arm trial that included both a cranberry tablet arm, a cranberry juice arm, and a placebo arm. The combined result from both cranberry tablet and cranberry juice arms compared with placebo were used for all analyses except for the subgroup analysis by form of cranberry.
[3] Kontiokari et al. (27) contained a 6-mo endpoint and a 12-mo follow-up. The 6-mo endpoint was included in all analyses except the subgroup for the 12-mo follow-up.

those with complicated UTI or as a treatment for UTI. Two of these reviews reported CIs that did not cross a null effect (RR: 1.0) for reduction with cranberry in women with UTI recurrence [RR: 0.53; 95% CI: 0.33, 0.83 (23); RR: 0.48; 95% CI: 0.29, 0.79 (32)]. A trend of RR reduction by cranberry among women was also observed in the third review (RR: 0.74; 95% CI: 0.42, 1.31) but the CI crossed 1.0, indicating that the finding was not statistically significant (22). The discrepancies in the magnitude of risk reduction among the previous meta-analyses was attributable in part to one study that was noted as contributing to substantial heterogeneity (24), which was the largest published study at the time (with 319 participants) (29).

Preventive actions are recommended as a strategy to reduce health care costs (27). This review focused on cranberry used as a preventive strategy and only included trials that enrolled participants who were either free of UTI at study entry or whose UTI was fully treated before the start of the cranberry intervention. Although relief from UTI symptoms and reduction in uropathogenic bacteria were reported in some studies (31, 33), evidence to support cranberry as a treatment is insufficient (34, 35). It is important to note that studies using cranberry as a treatment were not included in this meta-analysis.

The included studies required either an active UTI or history of UTI at study entry and followed participants for the development of recurrent UTI, although varying criteria to define UTI were used. The concept of "culture-negative" UTI has emerged (35), which recognizes the demonstrated effect of antibiotics to resolve UTI symptoms in women who did not demonstrate culture growth of a uropathogen or who had low-colony-count infections. In addition, it is common in clinical practice to initiate treatment without or before culture results are available. Therefore, studies that defined UTI by symptoms only compared with culture confirmation have a trade-off of the benefit of greater sensitivity to include all UTI episodes and pragmatism compared with greater specificity for UTI and exclusion of women with other causes of urethral symptoms. We conducted an analysis of the subgroup of culture-confirmed UTI and the RR was similar to the symptoms-based outcome, but the finding was not significant (RR: 0.71; 95% CI: 0.45, 1.12; I^2 = 68%). However, the heterogeneity in this analysis was substantial.

Data on the role of cranberry in decreasing the risk of complicated UTI were also generally not positive. For example, a recent study of institutionalized elderly women did not show a benefit from cranberry consumption on the presence of bacteruria with pyuria (22). The study population did not represent generally healthy individuals; rather, 66% of the participants had bladder incontinence and <7% had a history of recurrent UTI. Given the proposed mechanism of cranberry, the effects of cranberry consumption would not be expected in women with compromised health status (e.g., altered physiologic effects or immune function). However, an accompanying editorial generalized these findings to healthy women with UTI recurrence, stating that cranberry should not be considered (21). Considering the annual health care costs to diagnose and treat UTI in the United States, increasing rates of bacterial antibiotic resistance, and antibiotic side effects (including recent FDA warnings of serious adverse events associated with fluoroquinolones) (6, 8, 36), further assessment of cranberry as a potential option for healthy women with concerns of recurrent UTI may be warranted.

Data on forms of cranberry products and UTI prevention among healthy women are sparse. In our review, 5 studies used cranberry juice, 1 study used a capsule, and 1 study included both juice and tablet interventions. A few other trials have also evaluated cranberry capsules on UTI prevention, but the comparator was another intervention (i.e., antibiotics) instead of a placebo or control, and the participants were patients with pathologic conditions, not healthy women (32, 37–39). Therefore, these trials were not included in our analysis. A previous meta-analysis reported that cranberry in capsule or tablet form was not effective in preventing UTI recurrence (RR: 0.79; 95% CI: 0.44, 1.44) (22); however, the analysis included patients with conditions such as spinal cord injury and multiple sclerosis. In a broader context of UTI prevention, evidence is far from clear regarding the optimum dosage and formulation of cranberry-derived active compounds (i.e., juice, tablet, capsule, or powder).

There are several limitations to our review. First, 3 studies (13, 14, 27) either reported high rates of loss to follow-up or selective reporting. Second, although the included studies focused on healthy women at risk of UTI, differences in the study populations suggest that the baseline risk was not similar across the populations. That is, in some studies, women with an active UTI and unknown history were enrolled and the subsequent UTI was considered a recurrent UTI; other studies relied on a history of UTI in the preceding 6 or 12 mo, with a variable number of previous UTI episodes. Additional limitations include a lack of clear reporting on the randomization process in some trials and differences in definitions of UTI diagnosis. In addition, one study used of a mixture of cranberry juice and lingonberry juice, so the observed beneficial effects may not be entirely attributed to cranberry alone. However, lingonberry is in the *Vaccinium* family (*V. visit-idaea*) and likely would contain a similar phytochemical composition. Finally, we identified 2 potentially relevant trials but could not obtain any data or status update after 3 attempts to contact the authors.

In summary, our meta-analysis suggests that cranberry can be a potential nonpharmacologic approach for generally healthy women to prevent an uncomplicated recurrent UTI. However, studies were generally small, with only 2 having >300 participants, and further studies are needed to confirm these findings.

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