Can Cranberry Extract Prevent UTI?
A Meta-Analysis of Randomized Controlled Trials

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Introduction/Background

Urinary tract infections are among the most common bacterial infections, responsible for over $2.5 billion in health-care cost. More importantly, up to 30% of patients with a UTI, mostly females, suffer recurrences, necessitating repeated antimicrobial treatments. Given the cost, rising anti-microbial resistance, and adverse effects of such treatment, non-antimicrobial prophylaxis against recurrent UTIs is being avidly researched. Several studies suggest that cranberry extract may lower the incidence of recurrent UTIs, albeit inconsistently. Hence, we undertook a meta-analysis of randomized-controlled trials (RCTs) to evaluate the role of cranberry extract in preventing UTIs.

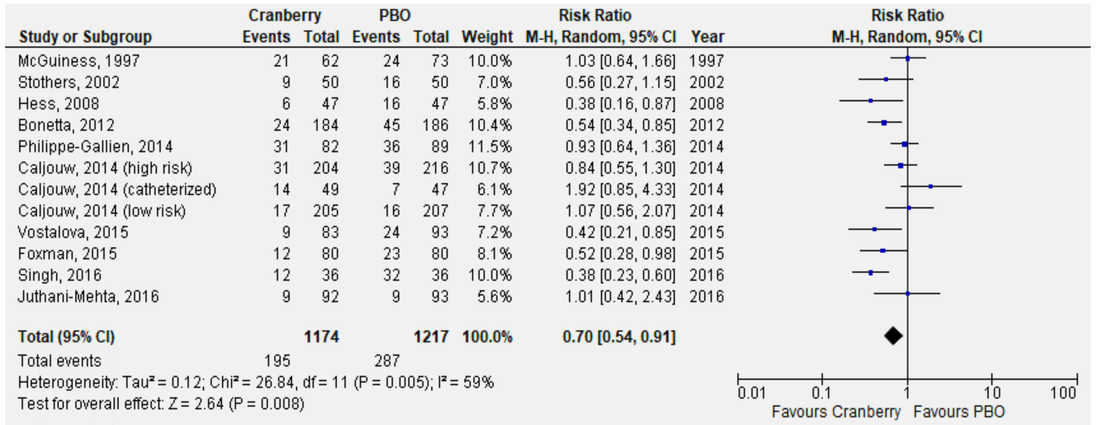

Figure 1: Forest plot depicting pooled relative risk (RR) of recurrent UTI after cranberry extract versus placebo for the three outcomes of culture-confirmed UTI

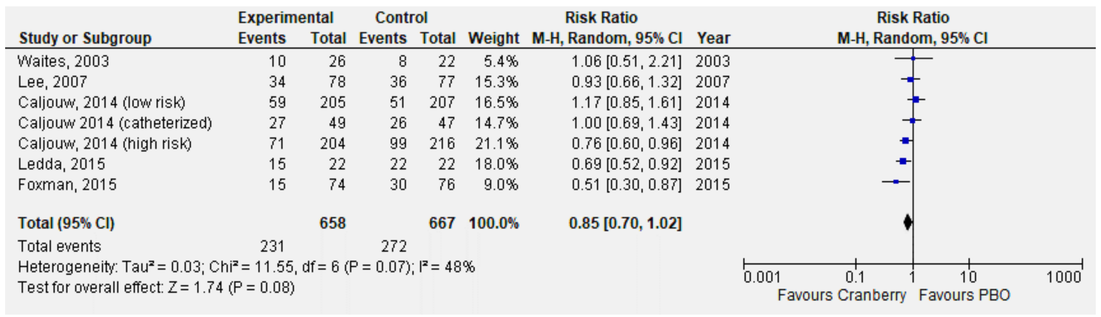

Figure 2 Symptomatic UTI

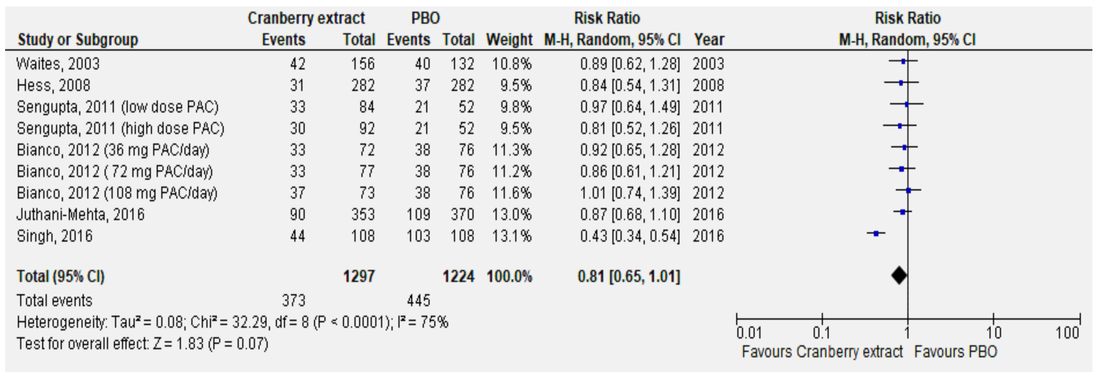

Figure 3 Asymptomatic pyuria and bacteriuria

Methodology and Statistical Approach

We performed a PUBMED/MEDLINE search using search terms “cranberry” AND “urinary tract infection”, “UTI”, “dysuria”, “pyuria”, “bacteriuria” or “cystitis”. We included RCTs using cranberry extract in tablet/capsule form in adults. Studies reporting incidence of symptomatic UTI, culture-confirmed UTI, and/or pyuria/bacteriuria were included. Meta-analysis was performed using RevMan version 5.3 *(*Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.*)*.

Results

12 trials including a total of 2391(1174 cranberry/1217 placebo) subjects were analyzed for impact of cranberry on culture confirmed UTI incidence. The random-effects pooled risk ratio (RR) for cranberry vs placebo was significant (RR 0.70, 95% CI 0.54-0.91, p=0.008), albeit with moderate heterogeneity (I^2=59%) (Figure 1). Heterogeneity was significantly attenuated (I^2=36%) while RR reduction remained significant (RR 0.72, 95% CI, 0.57-0.90, p=0.004) after excluding two outliers (Caljouw, 2014-catheterized cohort, and Singh 2016) identified in the Funnel plot.

5 trials examined impact of cranberry on symptomatic UTI, yielding 7 comparison groups, totaling 1325 patients (658 cranberry/667 placebo). There was no benefit of cranberry over placebo overall (RR 0.85, 95% CI 0.70-1.02, p=0.08). However, excluding one study with low-risk patients, i.e. those with no history of recurrent UTI (Caljouw 2014, low-risk cohort), revealed a significant benefit of cranberry over placebo (RR 0.79, 95% CI 0.67-0.94), while at the same time reducing heterogeneity among studies (I^2 = 24% versus 48%).

6 trials examined the impact of cranberry on reducing incidence of pyuria and bacteriuria, yielding 9 discreet datasets, totaling 2521 urine cultures (1297 cranberry/1224 placebo). There was no significant benefit, or at best a trend towards benefit, of cranberry over placebo (RR 0.81, 95%CI 0.65-1.01, p=0.07) though heterogeneity was high (I^2=75%) (Figure 3). However, excluding one outlier trial (Singh 2016) eliminated heterogeneity (I^2=0%) while maintaining non-significant pooled effect (RR 0.90, 95% CI, 0.79-1.01, p=0.07).

Discussion and Conclusion

A large number of RCTs have shown inconsistent benefit of cranberry in preventing UTI, likely stemming from several factors including sample size, population characteristics, duration of treatment, outcome definition, and formulation of cranberry used. Our meta-analysis, restricted to adult RCTs and those using cranberry extract in capsule/tablet form shows a significant benefit of cranberry extract in preventing UTIs, both culture confirmed and symptomatic. However, there was significant heterogeneity among studies, with patient characteristics, in terms of baseline UTI risk, being a major source of this heterogeneity.

References

1. Simmering JE, Tang F, Cavanaugh JE, Polgreen LA, Polgreen PM. The increase in hospitalizations for urinary tract infections and the associated costs in the United States, 1998-2011. Open Forum Infect Dis. 2017;4(1):1–7.
2. Gupta K, Chou MY, Howell A, Wobbe C, Grady R, Stapleton AE. Cranberry Products Inhibit Adherence of P-Fimbriated Escherichia Coli to Primary Cultured Bladder and Vaginal Epithelial Cells. J fo Urol. 2007;177(6):2357–60.