Cranberry-containing products for prevention of urinary tract infections in susceptible populations

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CRD summary
The authors concluded that cranberry-containing products were associated with protective effect against urinary tract infection. The authors advised cautious interpretation of this result given substantial variation across the included trials. Together with methodological concerns in the included trials, this tentative conclusion seems justified.

Authors' objectives
To evaluate the effect of cranberry-containing products for the prevention of urinary tract infection.

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to November 2011. Search terms were reported. There were no language restrictions. Bibliographies of relevant studies, reviews and meta-analyses were scanned and attempts were made to contact authors to identify further articles. The authors did not search conference proceedings or clinical trial registries.

Study selection
Eligible randomised controlled trials compared cranberry-containing products with placebo or a non-placebo control group, in any population. The primary outcome was incidence of urinary tract infection.

Most trials were carried out in North America; one trial was located in the United Kingdom. Study duration ranged from 35 days to 12 months. Most of the included participants lived in the community and were women; three trials involved children. Most included trials comprised patients with neuropathic bladder or women with recurrent urinary tract infections. Where reported, the average age ranged from 21 to 79 years. Cranberry-containing products varied in terms of type (juice, capsules and tablets), dose (range 0.4g to 194.4g), frequency of administration and proanthocyanidin content. Control groups contained formulated placebo, water or no placebo. Definitions of urinary tract infection varied.

Two independent reviewers selected the studies for inclusion. Disagreements were resolved by consensus, or with involvement from a third reviewer.

Assessment of study quality
Trial quality was assessed using the Cochrane Risk of Bias tool, which covered random sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting. Studies were scored as high risk, low risk or unclear.

Two independent reviewers carried out the quality assessment. Disagreements were resolved by discussion, or in consultation with a third reviewer.

Data extraction
Data were extracted to calculate risk ratios (RR) and 95% confidence intervals (CI). Where it was impossible to express the outcome data as incidence or cumulative incidence rate of urinary tract infection, the original data from the study were presented.

Two independent reviewers carried out the data extraction.

Methods of synthesis
Where possible, results were pooled in a meta-analysis. In the presence of substantial heterogeneity (where I² exceeded 50%; or p≤0.05) a random-effects (Der Simonian and Laird) model was used; otherwise a fixed-effect analysis was carried out. Galbraith and influential plots were constructed to identify potential sources of heterogeneity and assess the
impact of heterogeneity. The influence of risk of bias for randomisation, study characteristics and definitions of urinary tract infection were explored in sensitivity analyses. Pre-specified sub-group analyses (reported in the paper) were also carried out. Publication bias was assessed with a funnel plot.

Results of the review
Thirteen randomised controlled trials (1,616 participants across nine parallel group and four crossover designs) were included in the review. Six trials had a high risk of bias for at least two out of the five criteria assessed. Many aspects of trial quality were unclear; only four studies had a low risk of bias for three or more of the five criteria assessed. Loss to follow up ranged from 0 to 48%. None of the crossover trials had washout periods.

Ten trials (1,494 participants) that reported cumulative incidence of urinary tract infection were included in the meta-analysis as follows:

After excluding one outlying trial, results showed that cranberry-containing products were effective in preventing urinary tract infections (RR 0.62, 95% CI 0.49 to 0.80; moderate heterogeneity: $I^2=43\%$). The estimate was robust in sensitivity analysis, although the protective effect of the intervention was greatest in trials without placebo in the control group (RR 0.36, 95% CI 0.21 to 0.62; two trials; no heterogeneity).

Subgroup analyses showed that cranberry-containing products were most effective in women with recurrent urinary tract infection (two trials); females (four trials); children (mean age under 18 years; two trials) those using cranberry juice (five trials); and when products were used more than twice a day (four trials).

The authors stated that there was no evidence of publication bias.

Authors' conclusions
Cranberry-containing products were associated with protective effect against urinary tract infection. The authors advise cautious interpretation of this result given substantial variation across the included trials.

CRD commentary
The review question was clear and inclusion criteria were sufficiently detailed to enable replication. The inclusion of any population did not reflect the title of the review. Appropriate data sources were searched, but the apparent focus on published articles might have meant that relevant studies were missed. Although the authors reported no evidence of publication bias, this was difficult to verify from the sparsely-populated funnel plot. The review process was conducted with adequate attempts to minimise error and bias. An appropriate quality assessment tool was applied and results of this indicated some methodological concerns in the included trials. The chosen method of synthesis seemed justified and this was supplemented by sensitivity and sub-group analyses. Study characteristics were supplied, and substantial variation supports the authors' conclusion advising cautious interpretation of the review findings.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that a further trial is underway to investigate the optimal dosage of cranberry for the prevention of urinary tract infection.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.