A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against urinary tract infection in women

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined two different ways of giving cranberry to women who had suffered from urinary tract infection in the preceding calendar year. One was juice based (250ml of pure unsweetened cranberry juice 3 times a day and one placebo tablet twice a day), and one was tablet based (one tablet of concentrated cranberry juice twice a day and 250ml of placebo juice 3 times a day). The comparator was a placebo consisting of juice (250ml of filtered water with food colouring and 20ml pineapple juice 3 times a day), and tablets (placebo tablets twice a day). The treatment lasted for 12 months.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised sexually active women who had in the preceding calendar year suffered from two symptomatic, single-organism, culture-positive urinary tract infections in the prior calendar year but who were now free of infection according to urinanalysis and culture.

Patients were excluded if they had neurogenic bladder dysfunction, were pregnant, allergic to cranberry products, had insulin dependent diabetes, had immunosuppressive disease, took steroids or had intermittent or indwelling catheterisation.

Patients had to give written informed consent.

Setting
The setting appeared to be secondary care. The economic study was conducted at the University of British Columbia, Vancouver, Canada.

Dates to which data relate
No dates were given for effectiveness or resource evidence. No price year given.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Prospective costing was carried out on the same patient sample as provided the effectiveness evidence.

**Study sample**
The authors reported that power calculations were performed but did not report the sample size that these calculations implied would be necessary. Only women satisfying the inclusion criteria were included, but it was not stated how they were selected. There were 150 women in the study, 50 were allocated to each of the three groups, cranberry juice, cranberry tablet and placebo. There was no evidence that the study sample was representative of the study population.

**Study design**
The study design was a randomised controlled trial conducted at a single centre in which women were allocated in blocks of ten to each treatment group. The randomisation was concealed from the study health care workers. The patients were blinded to the treatment through the use of placebo tablets and juice. The treatment was scheduled for 12 months. There was no follow-up after the 12 months. Two patients in the juice group dropped out because of symptoms of reflux. The assessor of patient symptoms was unaware of the treatment that the patients had received.

**Analysis of effectiveness**
The analysis was based on intention to treat. The primary health outcome was the number of patients experiencing at least 1 UTI and the mean number of UTIs in each group. Compliance with the treatment was also recorded. Groups were shown to be comparable in terms of age, whether they were pre- or post-menopause, the mean number of UTIs in the preceding year and their mean annual income.

**Effectiveness results**
In the preceding calendar year the mean number of UTIs was 2.8, (range: 2 - 5).

During the treatment year, 16 (32%) of the placebo group, 10 (20%; p<0.05) in the juice group and 9 (18%), (p<0.05) in the tablet group experienced at least 1 UTI.

During the year following the study, the mean number of UTIs was 0.72 in the placebo group, 0.30 in the juice group, (p<0.05), and 0.39 in the tablet group, (p<0.05).

In terms of side effects 2 patients in the placebo group experienced headache and 2 patients experienced mild nausea. In the juice group, 3 patients experienced reflux. In the tablet group 4 patients experienced mild nausea and 1 experienced increased frequency of bowel movements. Eight patients complained about the size of the tablets.

Monthly compliance data showed that the compliance with the regimes was lowest in the juice group, dropping below 80% during 5 of the 12 months.

**Clinical conclusions**
Women taking cranberry either as juice or tablet can reduce the frequency of UTIs.

**Measure of benefits used in the economic analysis**
The summary measure of benefit used in the economic analysis was the number of UTIs avoided.

**Direct costs**
Patient and hospital direct costs were calculated. Costs were not discounted as costs were incurred over a one-year period. Costs were based on actual data. Patients' medical records were used to provide hospital cost data. Patients provided data on taxi expenses and parking receipts for their appointments. The breakdown of costs into components and into prices and quantities was partial. The price of cranberry tablets and cranberry juice was given; the cost of the
prophylaxis was calculated by the specifications of the protocol. The cost of antibiotics including dispensing fees was given in the three groups but this was not broken down into quantities and costs. No price year was given.

**Statistical analysis of costs**
No statistical analysis of costs was carried out.

**Indirect Costs**
No discounting was carried out, as it was not relevant. The authors included time lost from work based on the mean pre-study weekly income. No price year was given.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
The incremental benefits of the cranberry juice and tablet strategies compared to the 'do nothing' strategy (placebo) were calculated from the effectiveness results reported earlier, but were not reported in the study.

**Cost results**
During the year of treatment the cost of the prophylaxis with tablets was Can$624 and the cost with juice Can$1,400.

**Synthesis of costs and benefits**
The cost per UTI avoided was Can$3,333 for the juice patients compared to 'do nothing' and Can$1,890 for the tablet patients compared to 'do nothing'.

**Authors' conclusions**
The authors concluded that cranberry prophylaxis does reduce the incidence of UTIs in women. They also noted that the placebo group had a lower incidence of UTIs than in the preceding year concluding that the increased fluid intake in the placebo fluid must have had a beneficial effect. They acknowledged that the cost per UTI avoided was high.

**CRD COMMENTARY - Selection of comparators**
The authors chose a placebo as a comparator for the cranberry prophylaxis in order to evaluate the effectiveness of the prophylaxis.

**Validity of estimate of measure of effectiveness**
The study design, a randomised controlled trial, was appropriate for the study question. Both the study team and the patients were blind to the treatment groups. The patient groups were shown to be comparable at analysis. The analysis of effectiveness was handled credibly. The internal validity of this study should, therefore, be quite high. However, the study sample was not shown to be representative of the study population.

**Validity of estimate of measure of benefit**
The measure of health benefit was proxied by a single effectiveness estimate.
Validity of estimate of costs
The authors reported the cost categories that had been included but the information in their study did not show how the total were costs broken down into their components. There was also limited information about breaking down costs into prices and quantities. It was not clear in the cost-effectiveness analysis whether all costs had been included. Any omission of costs would imply that the case in favour of prophylaxis had been understated, as fewer UTIs would imply less time off work and fewer antibiotics. The resource quantities were taken from a single study, no statistical or sensitivity analysis of quantities was carried out. The price of cranberry, antibiotic and mean wages were taken from the authors' setting. No statistical or sensitivity analyses of prices were carried out.

Other issues
The authors did make comparisons of their results with the findings of other studies. The authors addressed the issue of whether or not the results could be generalised to men, children or pregnant women. Generalisability to other settings was not addressed. The authors reported several limitations of the study: the placebo juice did not taste the same as the cranberry juice, the cranberry products may have varied between batches as their composition is not controlled in the same way as drugs are, compliance was measured by the patients and therefore may not be accurate.

Implications of the study
Cranberry prophylaxis as described in this study can reduce the incidence of UTIs in women who have experienced this problem. Further research is necessary to determine whether similar results can be achieved with different amounts of cranberry and with lower cost cranberry.

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None stated.

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