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# Prevention of Cystitis: Travelling between the Imaginary and Reality

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**Abstract**
As a preventive strategy, increased water intake is often recommended to women affected by recurrent cystitis; however, clinical data are sparse and conflicting. This review evaluates the preventive approaches used as alternatives to obtain relief from the burden of cystitis and focuses on the effect of fluid intake on urinary tract infection.



Cystitis is the most common lower urinary tract infection (UTI). It is a bacterial contamination of the bladder representing one of the most common infectious diseases in women, and the second most common cause of antimicrobial medicine prescriptions in primary and secondary care [1, 2].

The lifetime risk of developing cystitis has been estimated to be over 50% in women [3], with at least one third of the episodes diagnosed before the age of 24 [4]. Approximately 5% of women with initial cystitis have multiple episodes within a year; a high recurrence rate, ranging between 25 and 30%, has been shown to affect the entire female population [5, 6]. As cystitis is not a reportable disease, doctors do not necessarily report cases to local health officials, and this makes cystitis frequency in many countries difficult to measure.

Cystitis is a source of significant cost and morbidity. Most episodes are self-limiting but occasionally can be associated with significant complications such as pyelonephritis and sepsis. Composite data revealed that overall expenditures for the treatment of UTIs in women in the United States, excluding spending on outpatient prescriptions, were approximately 2.47 billion U.S. dollars in 2000 [7]. Moreover, UTI accounts for approximately 15% of all antibiotic prescriptions written [8], and concerns are rising due to its direct correlation with the development of antimicrobial resistance.

There are multiple reasons to prevent cystitis in women. The foremost is to reduce morbidity associated with the infections, which are often related to pain and general discomfort. Besides, the prevention of cystitis can potentially reduce the use of antibiotics in these subjects [9]. This reduction is particularly relevant in 3 ways. First, *Escherichia coli*, the primary causative agent of uncomplicated cystitis, gains increased resistance to a variety of antibiotics, including fluoroquinolones and β-lactams. This resistance is increasingly observed among community-ac-

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quired UTI cases [10]. Second, there can be a significant impact of short courses of antibiotics on the gut and vaginal microbiota, which can contribute to recurrence and antibiotic resistance [11]. Third, there are risks associated with antibiotic use, including allergic reactions, side effects, and vaginal *candida* infections, which occur in up to 22% of women treated for uncomplicated cystitis [12].

Non-pharmacologic antimicrobial-sparing strategies that prevent recurrent cystitis in premenopausal women generally include education about risk factors such as sexual intercourse and usage of spermicidal products. Lifestyle changes, including urination as often as needed (especially after intercourse), properly washing the vulvovaginal area, and drinking plenty of water are often suggested [13–16]. However, none of these recommendations has been scientifically validated. While the use of daily antibiotics or post-coital antibiotics is effective, the rise of bacterial resistance has made these strategies less attractive. Different approaches have been proposed, including the use of probiotic lactobacillus, functional foods, and vaccines [9]. Although promising, existing data for prevention of UTI using lactobacillus are to date insufficient and await further validation [17, 18].

The most studied functional foods thus far have been cranberries and their extracts. Some years ago, a Cochrane review of cranberry research evaluated 24 studies with a total number of 4,473 participants [19]. Meta-analyses found that (compared to placebo, water, or no treatment) cranberry products did not significantly reduce the occurrence of symptomatic UTI in the entire sample (relative risk [RR] 0.86, 95% CI 0.71–1.04) or for any of these subgroups: women with recurrent UTI (RR 0.74, 95% CI 0.42–1.31); older women (RR 0.75, 95% CI 0.39–1.44); pregnant women (RR 1.04, 95% CI 0.97–1.17); children with recurrent UTI (RR 0.48, 95% CI 0.19–1.22); cancer patients (RR 1.15 95% CI 0.75–1.77); or people with neuropathic bladder or spinal injury (RR 0.95, 95% CI 0.75–1.20). Due to these results, no recommendation can be made regarding the consumption of any cranberry-based product [20].

Abundant fluid intake may prevent recurrent episodes of infection by promoting the passage of urine and flushing of the urethra. Health care providers often recommend that women affected by recurrent cystitis drink more water. The rationale for this approach is that drinking more fluid increases voiding frequency, resulting in the dilution and flushing of bacteria from the urothelium. As such, increasing fluid intake increases the frequency and volume of voiding, and potentially reduces the risk of recurrent cystitis. Support for this hypothesis exists in a multivariate analysis that compared 791 female teachers, who deliberately restricted their fluid intake, to women drinking without restrictions. This study found that women in the fluid restricted group were at a significantly higher risk of UTI ($p = 0.0002$) than women in the latter group [21]. A separate study of 1,613 women evaluated the frequency of voiding as a factor in the development of UTI [22]. Results of this study demonstrated that women aged 20–25 had a higher rate of low voiding frequency, compared to women aged 30–35 or 40–45. In all 3 groups, women who voided 3 times or less per day had significantly more urinary infections than those with 4 or more voids per day. Several other nonrandomized studies have reported that low fluid intake or reduced number of daily voids were associated with an increased risk of recurrent infections in women having a history of UTI [23–27]. Conversely, 3 studies found no difference in fluid intake between women with recurrent infections and controls; also, no association was observed between fluid intake and UTI [28–30]. Thus, the interpretation of the results is inconclusive due to the lack of randomization, small sample sizes, and the fact that none of these studies were designed as interventions to assess the effect of increased water intake on UTIs.

To this date, the only published interventional study showed that optimal hydration assessed by self-measurement of urine specific gravity resulted in a reduced frequency of cystitis [31]. However, because fluid intake was not assessed in this study, these results are not definitive.

Women who consume a low volume of total fluid each day are usually reluctant to increase their water intake due to the consequent increase in the number of voids. In the sample of teachers observed in 1997 (see above), Nygaard and Linder [21] showed that 25% of women voluntarily self-imposed fluid restriction to decrease their voiding frequency. Similarly, Su et al. [26] showed that cleanroom workers limited their water intake and avoided the bathroom because of a short break-time, and the special toilet procedures required to maintain a clean workplace environment. Increased fluid intake seems to be perceived as a burden for women even in an unrestricted work environment. An increased number of voids and nocturia is perceived as a barrier to normal daily activities and as impediments to developing healthy lifestyle habits. However, the quality of life of women with a high fluid intake has never been assessed systematically and should be further evaluated.

In conclusion, relevant and accurate information about the prevention of cystitis is lacking in the scientific literature and well-designed intervention studies are needed. Given this unmet need, we stress the necessity of

a well-designed randomized controlled trial, powered to assess the effects of increased water intake on cystitis. Water, which is widely available and unassociated with adverse effects, may someday provide doctors with further motivation to strongly encourage increased water intake for the prevention of recurrent cystitis in women.

## Disclosure Statement

The authors are employees of Danone Nutricia Research, Palaiseau, France. The results of the first RCT on hydration and cystitis were under review for publication at the time of this printing, and were not available to be included in the 9th Hydration for Health Conference proceedings.

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