

# Probiotics for the Prevention of Recurrent Urinary Tract Infections in Women: A Systematic Review



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## BACKGROUND

incidence of 250 million cases per year and incur billions of dollars in healthcare costs (Chapman, 2014). Recurrent UTI (rUTI) is defined by 3 or more in one year and affects 20-30% of women. Microbiological research has associated healthy urogenital tracts with high levels of lactobacilli in vaginal flora. Those with recurrent UTI have lower levels of lactobacilli. Multi-strain probiotics have also been shown to inhibit the growth of *E. coli*, the pathogen responsible for a large number of UTIs (Chapman, 2014). Current guidelines for the treatment of rUTIs include the use of low dose antimicrobial agents. Pathogens are showing a rise in resistance to these antibiotics, supporting the need to develop a prevention strategy that does not include antibiotics.



## PURPOSE

review the literature and evaluate the effectiveness of lactobacillus in preventing rUTI in women. There is some evidence to suggest that use of lactobacillus may provide protective effects against bacteria commonly associated with urinary tract infections. Findings from a current literature review will be used to provide further support for this intervention and develop recommendations for its use in clinical practice.

## METHODS

process leading to high quality healthcare and best patient outcomes outlined by Ciliska, et al. (2011). Specifically, we 1) cultivated a spirit of inquiry, 2) asked a burning clinical question in PICOT format, 3) searched for the best evidence to answer the PICOT question, 4) conducted a rapid critical appraisal of the studies found from the search, 5) evaluated and synthesized the evidence, and 6) determined if there was enough valid and reliable evidence to make a recommended practice change in clinical practice.

## RESULTS

sources for the review; all searches were limited to articles published in English between the years 2004-2014.

SEARCH RESULTS		
Search Engine	Keywords	# Yielded
CINHAL Plus	"Urinary tract infections" and "probiotics"; "urinary tract infections" and "lactobacillus"	6; 6
Medline	"Urinary tract infections" and "lactobacillus"	47
PubMed	"Probiotics in prevention of urinary tract infections", "Lactobacillus in prevention of urinary tract infections"	98; 90
The Cochrane Library	"Probiotics in preventing urinary tract infections"	3
EBSCOhost	"Probiotics" and "urinary tract infection"	2

After rapid critical appraisal to examine the reliability, validity, and usefulness of the sources, the following nine articles were kept for evaluation and synthesis.

STUDY FINDINGS				
Author, Year	Study Design	Intervention	Results	Level of Evidence
Barrons & Tassone, 2008	Systematic review of 4 RCTs	Lactobacillus vaginal suppository or oral suspension vs. placebo; sterile milk, lactobacillus growth factor (LGF) or cranberry	No statistical significance between the lactobacilli and placebo. Observed incidence rate ratio over 26 weeks was 1.41 (95% CI 0.88 to 1.98). Non-significant difference of rates of rUTI over 6 months in the antimicrobial-plus-lactobacillus group (21%) compared with antimicrobial-plus-placebo group (47%). Non-significant results between lactobacilli vaginal suppository and LGF (mean incidence of UTIs: 1.6 and 1.3). Both rates were 73% lower when compared to previous year without prophylaxis. At 6 months, more UTIs were noted in the lactobacilli species and no intervention group than cranberry-lingonberry group (39%, 36%, 8%, respectively. At 12 months, p=0.048, cranberry-lingonberry vs. lactobacillus.	Level I
Beereport, et al., 2012	Double blind RCT	127 women received 1 tablet of trimethoprim/sulfamethoxazole (TMP/SMX) and 1 placebo capsule twice daily. 125 women received 1 capsule of a 2 species combination of lactobacillus twice daily and 1 placebo capsule daily.	Rate of rUTI: TMP/SMX - 2.9 with 95% CI of 2.3-3.6; Lactobacillus - 3.3 with 95% CI of 2.7-4.0. Between group difference in mean rUTI was 0.4 with 95% CI of -0.4-1.5, p=0.42. Percentage of at least 1 rUTI in 12 months: TMP/SMX - 69.3%, Lactobacillus - 79.1%. Median time to rUTI: TMP/SMX - 6 months, Lactobacillus – 3 months. Antibacterial resistance: TMP/SMX – increased from 20-40% to 80-95%, no change in resistance of lactobacillus group. Complicated rUTIs: TMP/SMX – 4.4, 95% CI 3.4-5.7; Lactobacillus – 3.4, 95% CI 2.6-4.5 (p<0.001 on t-test). TMP/SMX more effective in preventing uncomplicated rUTI. Lactobacillus more effective in preventing complicated rUTIs.	Level II
Cave, J., 2013	Systematic review of trials	Lactobacilli vaginal suppository or oral lactobacilli vs. TMP/SMX or control	Lactobacilli showed to reduce UTIs (RR 0.42, 95% CI, 0.22 to 0.67, p< 0.001). No statistical significance between women receiving lactobacilli and control; however, after ineffective strains and studies testing for safety were excluded, there was a marginally statistical significant decrease in recurrent UTI (RR 0.51, 95% CI, 0.26 to 0.99, p= 0.05). After 12 months of lactobacilli, mean number of CR was 2.9 (95% CI, 2.3 to 3.6) in TMX/SM and 3.3 (95% CI, 2.7 to 4.0) in lactobacilli group, with a difference of 0.4 (95% CI, -0.4 to 1.5).	Level I
Czaja, et al., 2007	Double blind RCT	Vaginal suppository of either placebo or lactobacillus, daily for 5 days	Lactobacillus is well tolerated, may induce an asymptomatic inflammatory response protecting against uropathogen colonization.	Level II
Dwyer & Dwyer, 2012	Double blind RCT	TMP/SMX by mouth daily versus daily oral lactobacillus (2 species)	Mean rUTI for TMP/SMX group was 2.9, and 3.3 in lactobacillus group (p=0.42, non significant). Significant difference in mean microbiological rUTI (TMP/SMX=1.2, Lactobacilli=1.8, p=0.02). Median time to first rUTI was significantly shorter in lactobacillus group. In complicated UTIs, Lactobacillus proved more effective. Mean recurrence: TMP/SMX was 4.4, lactobacillus was 3.4 (p<0.001).	Level II
Falagas, et al., 2006	Meta-Analysis	In 5 of the studies, participants received vaginal lactobacillus alone or compared with a placebo or with sterilized skim milk. One study compared a daily lactobacillus drink vs. daily cranberry drink vs. no treatment. One study compared amount of fresh fruit juices and fermented milk products. The studies lasted anywhere from 1 week up to one year.	In 5 of the studies, rates of rUTI were significantly less with the use of lactobacillus. In 2 of the studies, lactobacillus had no impact and was non-significant. UTI rate decreased by 73% in group receiving vaginal probiotic (6→1.6, p<0.001), and 79% in group receiving vaginal probiotic growth factor (6→1.3, P<0.001). Rate of UTI between treated patients and placebo was 1.41, (95% CI 0.88-1.98), a non-significant result. Recurrence of UTIs over 6 months decreased to 21% for those receiving lactobacillus compared with 47% for the skimmed milk group. 16% of cranberry group had rUTIs and 39% of lactobacillus group. Recurrence was significantly less common in cranberry group (p=.014); lactobacillus had no impact. Fermented milk products consumed 3+ times per week was less commonly associated with UTI when compared with consumption less than 1x/week (OR 0.21, 95% CI: 0.06-0.66)	Level I
Grin, et al., 2012	Meta-Analysis of 5 RCT's	Women received either oral lactobacillus or lactobacillus vaginal suppositories	Use of lactobacillus was associated with trend toward reduction of risk of rUTI (RR 0.85 [95% CI]; p = 0.41; I2 = 19%). A sensitivity analysis of two RCTs showed that use of lactobacillus was associated with significant risk reduction (RR 0.51 [95% CI]; p = 0.05, I2 =0%).	Level I
Stapleton, et al., 2011	RCT	After treatment for UTI, participants received lactobacillus or placebo daily for 5 days, then weekly for 10 weeks	Lactobacillus group had 15% rate of rUTI when placebo had 27%. Those in the lactobacillus group that achieved high level of vaginal colonization with lactobacillus had a significant reduction in rates of rUTI. Lactobacillus species used may prevent rUTI and reduce rate of rUTI by one-half.	Level II
Uehara, et al., 2006	Prospective cohort study	Lactobacillus vaginal suppositories of every 2 days for 1 year; rates of UTI measure before and after	There was a reduction in rate of rUTI from an mean of 5.0 ± 1.6 to a mean of 1.3 ± 1.2 (p=0.0007, significant)	Level IV

The National Guideline Clearinghouse provides guidelines for management of rUTI. Use of probiotics for prevention of rUTIs was considered but not recommended (National Guideline Clearinghouse, 2010). However, detailed information about guideline development is not available. While some results did not reveal significant benefits of use of probiotics, other studies show potential advantages. It is therefore difficult to determine whether evidence is congruent with current practice guidelines.

## CONCLUSION

Lactobacilli probiotics are generally well tolerated among women despite mild adverse effects. While many studies indicate that probiotics may be effective in preventing recurrent UTIs in women, there were several studies that showed antimicrobials were more effective. More research is needed before probiotics can be included in prophylactic recurrent UTI guidelines.

### REFERENCES

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