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# Probiotic Use in Recurrent Urinary Tract Infection Management: Collective Information on Commercially Available Products

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## Abstract

**Aims:** Emergence of multi-drug resistant organisms with anti-microbial overuse has stimulated interest in alternatives for Recurrent Urinary Tract Infections (rUTIs). Healthy microbial flora is important for disease prevention, and probiotic use is increasingly popular. We investigated probiotics on commercially available markets todetermine products that may offer benefit in rUTI management.

**Methods:** We identified 58 probiotics through Amazon.com, Walmart, Walgreens, and CVS, and evaluated species, Colony Forming Units (CFUs), cost, labelled applications, and labelled side effects. We compared bacterial composition of probiotics with labelled application for genitourinary health, as well as those without, to species with potential efficacy in the literature for rUTIs.

**Results:** *LactoBacillus acidophilus, L. rhamnosus, L. plantarum, L. fermentum, L. crispatus,* and *Bifidobacterium lactis* have demonstrated potential benefit forrUTI management at minimum 10-20 billion-CFUs. All 3 probiotics with labelled genitourinary applications and 34 (61.8%) of the remaining contained ≥3 of these species. Evaluated probiotics contained mean 25.75 billion-CFUs and cost mean $19.42/month. We identified four low-cost products with ≥3 of these species, adequate CFUs, and once/day dosing. "Healthy Origins" was the most cost-effective option ($0.22/billion- CFU), followed by "Nature's Base" ($0.26/billion-CFU), "Nature's Branch 50 Billion" ($0.32/billion-CFU), and "Renew Life Women's" ($0.68/billion-CFU).

**Conclusions:** Providers should be prepared to discuss probiotics with patients given increased popularity/potential benefit in rUTI management. If a patient chooses to utilize probiotics, "Healthy Origins," "Nature's Base," "Nature's Branch 50 Billion," and "Renew Life Women's" are products with minimum 1-20 billion-CFUs, few labelled sideeffects, once/day dosing, and reasonable cost for use in rUTIs.

**Keywords:** Genitourinary; Probiotics; Urinary tractinfection

## Introduction

Probiotics are living, non-pathogenic, bacterial organisms that mimic thenaturally occurring, healthy flora within the human microbiota [1]. They may play a role in disease prevention through promoting mucosal barrier maintenance, inhibiting colonization of pathogenic bacterial organisms, and inactivating virulence factors produced bythese organisms [1]. Probiotics have become increasingly popular for commercial use throughout the last decade. Recent data demonstrated that probiotic salesexceeded 1.1 billion dollars in the United States (US) and 25 billion dollars worldwide [2], with almost 3 million adults and 300,000 children currently using probiotics for a host of medical conditions [3]. Most studies regarding probiotic use in disease prevention have been performed for Gastrointestinal (GI) conditions. Probiotic efficacy for the prevention of infectious diarrhea, antibiotic-associated diarrhea, irritable bowel syndrome, and functional GI disorders have been demonstrated [4]. These findings have led to the investigation of probiotic use for several medical conditions, and published reports havedemonstrated that alterations in the healthy microbial flora may play a role in a host ofgenitourinary conditions including

interstitial cystitis/bladder pain syndrome [5], chronic pelvic pain [6], vaginitis [7], urge incontinence [8], and urinary tract infections (UTIs) [9]. Urinary tract infections are highly prevalent, with an annual cost of treatment reaching approximately 2 billion dollars in US healthcare costs [10]. An estimated 60% of US women are affected by a symptomatic UTI at least once in their lifetime, and of those affected, up to 40% will experience at least one symptomatic recurrence [11]. Several antimicrobial therapies are available for management of symptomatic, uncomplicated UTIs. However, with overuse of these agents, most notably in patients with recurrent UTIs, defined as at least three uncomplicated UTIs in a twelve month period [12], several multi-drug resistant microbial organisms have emerged, resulting in significant difficulty in managing these infections [13]. This has led to a dramatically increased interest in alternative, non-antimicrobial therapeutic strategies for recurrent UTI management.

The American Urological Association (AUA) published guidelines on the management of uncomplicated, recurrent UTIs in 2019, which state that given currently available evidence, probiotic use for recurrent UTI management cannot be recommended for or against, calling for additional studies to assess therapeutic efficacy [14].Despite contradictory data on probiotic efficacy in recurrent UTI management, consumption of probiotics continues to increase drastically amongst consumers, and patients may purchase probiotics over the counter without sufficient counseling or recommendations from healthcare providers. Herein, we performed a detailed analysis of probiotics available on popular, commercially available consumer markets. We determined products that would potentially be effective with low-cost and minimal side effects for use in recurrent UTI management.

## Materials and Methods

### Commercially Available Data Collection

We investigated commercially available probiotics that are directly available to consumers for over the counter purchase as of April 2020 through Amazon.com, Walmart, CVS, and Walgreens. The search term used in all consumer markets was "Probiotic Supplements" and for each source of commercially available probiotics the "best rated" filter was applied. Commercially labelled information from a total of 58 probiotics was evaluated in this study. Bacterial species contained within each probiotic were evaluated, as well as the total bacterial Colony Forming Units (CFUs) within one dose of each product. We determined the cost in US dollars per month, the targeted patient demographic, the recommended applications for use on labelling, and all labelled adverse effects reported for each probiotic evaluated.

### Determining Probiotics for Use in Recurrent UTIs

A detailed evaluation of the available scientific literature on probiotic efficacy in genitourinary health was performed. We compared bacterial species listed on labelling for probiotics with labelled applications for use in genitourinary health with the bacterial species that have been reported in the literature to have potential benefit for use in recurrent UTI management. We additionally determined probiotics that do not list an application for use in genitourinary health in labelling but contain bacterial species with reported efficacy in recurrent UTI management.

### Cost-effective Product Analysis

For all evaluated probiotics with at least three bacterial species listed on labelling with reported efficacy in recurrent UTI management and at least 10 to 20 billion CFUs, we determined the associated monthly cost and total CFUs. To evaluate cost-effectiveness, we divided the monthly price by the total CFUs to define the cost of one CFU for each product. We then identified products with the lowest cost per CFU.

## Results

### Bacterial Species

The five most prevalent bacterial genera within the 58 evaluated probiotics were *LactoBacillus* (N = 53, 91.4%), *Bifidobacterium* (N = 41, 70.7%), *Streptococcus* (N = 12, 20.7%), *Saccharomyces* (N = 7, 12.1%), and *Bacillus* (N = 5, 8.6%) (Figure 1A). The most prevalent bacterial species were *L. acidophilus* (N = 49, 84.5%), *B. lactis* (N =34 58.6%), *L. rhamnosus* (N = 32, 55.2%), *L plantarum* (N = 30, 51.7%), and *L. casei* (N= 28, 48.3%) (Figure 1B). There were over 10 unique species of *LactoBacillus* represented, including *L. acidophilus*, *L. rhamnosus*, *L. plantarum, L. casei*, *L. paracasei, L. salivarius, L. bulgaricus, L. brevis,* and *L. reuteri* (Figure 2A). More than 5 unique species of *Bifidobacterium* were also represented including *B. lactis, B. longum*, *B. bifidum*, *B. breve*, and *B. infantis* (Figure 2B). All *Streptococcus* species were *S. thermophilus*, the most common *Saccharomyces* species was *S. boulardii*, and all *Bacillus* species were *B. coagulans*.

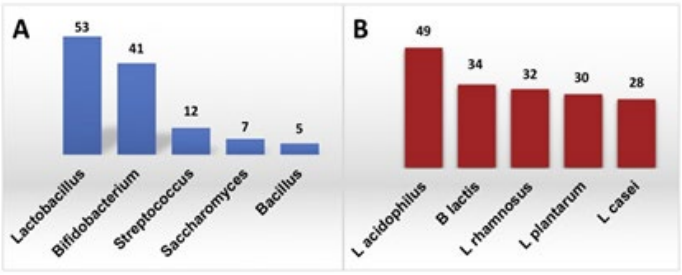


**Figure 1:** The most prevalent bacterial genera (Part 1A) and species (Part 1B) contained within the commercial probiotics.

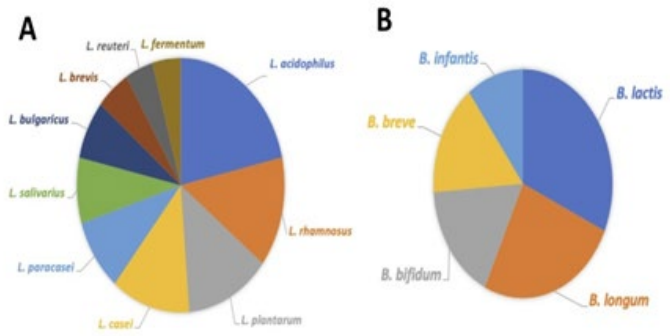


**Figure 2:** Bacterial species contained within the two most prevalent genera: *LactoBacillus* (Part 2A) and *Bifidobacterium* (Part 2B).

**Commercially Available Product Data**

The 58 probiotics evaluated contained a mean of 8.31 ± 5.92 individual bacterial species listed on labelling, ranging from 1 to 21 species, and a mean of 25 ± 25.95 billion total CFU's in each dose, ranging from 0.01 to 100 billion CFU's. Probioticswere most commonly dosed as one pill taken once daily (N = 37, 63.8%), followed by twice daily (N = 17, 29.3%) and three times daily (N = 2, 3.4%) for an indefinite time period. Evaluated probiotics cost a mean of 19.43 ± 9.89 US dollars per month, ranging from $3.10 to $44.99 per month. The most commonly targeted consumer demographics were adults of both sexes (N = 43, 74.1%). Only 8 probiotics (13.8%) were targeted towards adult women and 7 (12.1%) were targeted towards both adults and children. The top clinical applications listed on labelling for probiotic use were gastrointestinal health (N = 55, 94.8%) and immune support (N = 40, 69.0%), followed by vaginal health (N = 8, 13.8%), genitourinary health (N = 3, 5.2%), and mood stabilization (N = 3, 5.2%). The most frequently labelled adverse effects associated with these probiotics were abdominal pain (N = 54, 93.1%), flatulence (N = 52, 89.7%) and bloating (N = 48, 82.8%). Bowel irregularities (N = 16, 27.6%), headache (N = 7, 12.1%), increased thirst (N = 6, 10.3%), and appetite loss (N = 4, 6.9%) were also less frequently included on labelling.

**Analysis of Genitourinary Probiotics**

Three of the evaluated probiotics were specifically labelled for use in genitourinary health: "Renew Life Ultimate Flora Women's," "Omni Recipe Women's," and "Probiotic Pearls Acidophilus" (Table 1). These products contained an average of 25.33 ± 2.01 billion CFUs, ranging from 1 to 50 billion CFUs and cost an average of 14.53 ± 2.78 US dollars per month, ranging from 10.64 to 16.98 US dollars per month. All three of these probiotics were targeted towards an adult female demographic. Upon review of the current scientific data, *L. acidophilus, L. rhamnosus, L. fermentum, L. crispatus, L. plantarum,* and *B. lactis* have demonstrated potential efficacy for use in recurrent UTI management, [15-18] and were used for the subsequent analyses performed. All three of the probiotics with a genitourinary listed application contained *L. acidophilus, L. rhamnosus,* and *L. plantarum.* Two products, ("Renew Life Ultimate Flora Women's" and "Omni Recipe Women's"), contained *B. lactis* and one product, ("Omni Recipe Women's"), contained *L. fermentum* and *L. crispatus* (Table 1). Additionally, 34 of the 55 (61.8%) evaluated probiotics without a listed application for genitourinary health also contained at least three of these species with potential efficacy for use in recurrent UTI management based on current reported data in the literature.

| Product | Bacterial Species | CFUs *billions* | Cost *monthly* | Dosing *per day* | Route | Demographic | Adverse Effects |
|---|---|---|---|---|---|---|---|
| Renew Life Ultimate Flora | *L. acidophilus, L. rhamnosus, L. plantarum, L. gasseri, L casei, L. salivarius, L. paracasei, L. brevis, B. lactis, B. longum* | 25 | 16.98 | Once | Oral | Women | Flatulence Bloating Abdominal Pain Increased Thirst |
| Omni Recipes Women's | *L. acidophilus, L. rhamnosus, L. plantarum, L. reuteri, L. crispatus, L. fermentum, L. gasseri, L. paracasei, L. helveticus, L. casei, B. lactis, B. longus, B bifidum, B infantis, B. breve, B. adolescentis* | 50 | 15.97 | Twice | Oral | Women | Flatulence Bloating Abdominal Pain |
| Probiotic Pearls Acidophilus | *L. acidophilus, L. rhamnosus, L. plantarum* | 1 | 10.64 | Once | Oral | Women | Flatulence Abdominal Pain |

**Table 1:** Probiotics labeled for genitourinary use.

**Cost Effective Product Analysis**

We identified ten low cost products that contained at least three of these bacterial species and 10 to 20 billion CFUs minimum (Table 2). Of these, the "Healthy Origins" probiotic was the most cost-effective product identified with monthly cost of $6.74 and 30 billion CFUs, or $0.22 per billion CFU. The "Nature's Base" Probiotic was the next most cost-effective product identified, ($0.26 per billion CFU), followed by "Nature's Branch 50 Billion" ($0.32 per billion CFU) and "Renew Life Ultimate Flora Women's" ($0.68 per billion CFU) (Table 2).

| Product | Bacterial Species | CFUs billions | Cost monthly | Dosing per day | Route | Demographic | Side Effects labelled |
|---|---|---|---|---|---|---|---|
| Nutrition Now PBS | *L. acidophilus, L. rhamnosus, L. plantarum, B. lactis* | 14 | 6.56 | Twice | Oral | Adult men and women | Flatulence Bloating Constipation Increased thirst |
| Healthy Origins | *L. acidophilus, L. rhamnosus, L. plantarum, B. lactis* | 30 | 6.74 | Once | Oral | Adult men and women | Flatulence Bloating Abdominal pain |
| Nature's Bounty Ultra | *L. acidophilus, L. plantarum, B. lactis* | 20 | 11.87 | Twice | Oral | Adult men and women | Flatulence Bloating Abdominal Pain |
| Nature's Branch 50 Billion | *L. acidophilus, L. rhamnosus, L. fermentum* | 50 | 15.95 | Once | Oral | Adult men and women | Abdominal pain |
| Omni Recipes Women's | *L. acidophilus, L. rhamnosus, L. plantarum, L. crispatus, L. fermentum, B lactis* | 50 | 15.97 | Twice | Oral | Adult women | Flatulence Bloating Abdominal Pain |
| Vitalitown | *L. acidophilus, L. rhamnosus, L. plantarum, L. crispatus, B. lactis* | 60 | 15.99 | Twice | Oral | Adult men and women | Flatulence Bloating Abdominal Pain |
| Renew Life Ultimate Flora Women's | *L. acidophilus, L. rhamnosus, L. plantarum, B. lactis* | 25 | 16.98 | Once | Oral | Adult women | Flatulence Bloating Abdominal Pain Increased Thirst |
| New Rhythm | *L. acidophilus, L. rhamnosus, L. plantarum, L crispatus, B. lactis* | 50 | 16.99 | Twice | Oral | Adult men and women | Flatulence Bloating Abdominal Pain Diarrhea |
| Nature's Base | *L. acidophilus, L. rhamnosus, L. plantarum, L. fermentum, B. lactis* | 70 | 17.95 | Once | Oral | Adult men and women | Flatulence Bloating Abdominal Pain Increased Thirst |
| Terranics | *L. acidophilus, L. rhamnosus, L. plantarum, L. crispatus, B. lactis* | 60 | 17.99 | Twice | Oral | Adult men and women | Flatulence Bloating Abdominal Pain Headache |

**Table 2:** The ten most cost-effective probiotics containing at least three bacterial species with potential efficacy for recurrent urinary tract infection management and at least 10 to 20 Colony Forming Units (CFUs).

## Discussion

Published reports assessing probiotic efficacy for use in recurrent UTI management demonstrate mixed results. Beerepoot et al (2012) compared the efficacy of *L. rhamnosus* and *L. reuteri*-containing probiotics verses Trimethoprim-Sulfamethoxazole (TMP-SMX) for prevention of UTI recurrence and found no significant difference in UTI recurrence between groups [19].However, they also demonstrated that there was significantly increased bacterial resistance development in patients taking TMP-SMX when compared to those taking *LactoBacillus* probiotics [20]. A Cochrane Database Review in 2015 analyzed the compiled data from current published reports regarding probiotics for recurrent UTI management and concluded that a significant benefitcould not be demonstrated [20]. A number of blinded, placebo-controlled, clinical trials, however, have demonstrated that certain *LactoBacillus* probiotics are potentially efficacious for recurrent UTI management [15-18]. In 2003, Reid et al. demonstrated that probiotics containing *L. rhamnosus* and *L. fermentum* significantly altered vaginal flora and reduced UTI recurrence in female patients [15]. Stapleton et al. also demonstrated in 2011 that a vaginal suppository formulation of a probiotic containing *L. crispatus* was associated with a significant reduction in UTI recurrence in female patients when compared to placebo-group controls [16]. Additionally, in 2019, Koradia et al demonstrated that probiotics containing *L. acidophilus* and *L. plantarum*, in combination with cranberry extract, were associated with a significant reduction in UTI recurrence whencompared to placebo-group controls [17]. Some reports have also demonstrated efficacy of probiotics to prevent recurrent UTIs in children. In 2013, Mohseni et al. demonstrated that probiotics containing *L. acidophilus* and *B. lactis*, in combination withnitrofurantoin, were associated with a significant reduction in febrile UTI recurrence comparing to nitrofurantoin alone [18].

All six of these bacterial species that demonstrate potential efficacy for use in recurrent UTI management were present on labeling for the probiotics evaluated inthis study. *L. acidophilus* was the most common species represented (84.5%), followed by *B. lactis* (58.6%), *L. rhamnosus* (55.2%), *L. plantarum* (51.7%), *L. fermentum* (17.2%), and *L. crispatus* (6.9%) (Figure 3). All three of the probiotics with a labelled genitourinary application contained at least three of these, and 34 (61.8%) of the remaining probiotics without a listed application for genitourinary health also contained at least three of these species. For example, the "Healthy Origins" probiotic lists applications for use in gastrointestinal health and immune support on labelling, but contains *L. acidophilus, L. rhamnosus, L. plantarum,* and *B. lactis* and would potentially be an effective option for use in recurrent UTI management.

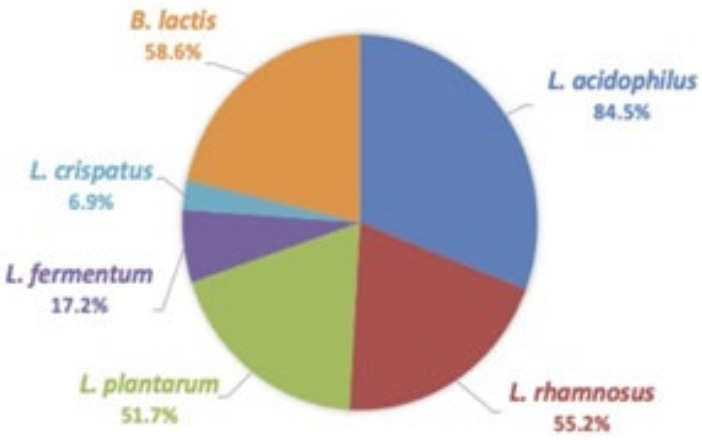


**Figure 3:** Prevalence of strains with evidence of efficacy in the literature for recurrent urinary tract infection management in all evaluated probiotics.

The total CFUs contained within each dose is also important when choosing a probiotic. Although there are no published studies evaluating the appropriate CFU dose for genitourinary conditions, reports evaluating total CFUs for GI conditions and immune support recommend that at least 10 to 20 billion CFUs are adequate for adults [21]. These findings suggest that patients may benefit from choosing a probiotic supplement, regardless of the listed recommended applications on labels, with multiple of these species with potential efficacy for recurrent UTI management listed on labelling, as well as at least 10 to 20 billion CFUs. Patient compliance is another important criterion when answering questions and counselling patients on product selection. In general, compliance is most optimal with products that have once daily dosing and minimal side effects. The side effects listed on labelling for the evaluated probiotics were generally minor, and most commonly included abdominal pain, bloating, and flatulence. Published data suggest that probiotics are well tolerated by almost all patients, and the incidence of side effects do not differ significantly when compared to placebo controls [22,23]. This point is especially important given the risks associated with problematic, recurrent antimicrobial use, with a variety of serious and potentially life threatening side effects observed in this patient population [24,25].

Cost-effectiveness is another important component of patient compliance given that long-term use is usually necessary for favorable results. We identified four products that would likely maximize patient compliance, with at least three of the previously mentioned bacterial species, adequate CFUs, and once/day dosing. "Healthy Origins" was the most cost-effective option ($0.22/billion-CFU), followed by "Nature's Base" ($0.26/billion-CFU), "Nature's Branch 50 Billion" ($0.32/billion-CFU), and "Renew Life Women's" ($0.68/billion-CFU). Limitations of this study include that all collected data is reliant on package labelling information. These products are typically not regulated by the US Food and Drug Administration (FDA) and subsequently may report inaccurate information on package labelling. Additionally, top-rated products on commercially available consumer markets often change quickly over time with a constant influx of newly marketed products. Despite these limitations, this is the first study to the authors' knowledge that describe the commercially available probiotics in this manner for use in recurrent UTI management, including a comprehensive analysis of over 50 available products across multiple consumer markets. This collective information may be beneficial for providers and patients considering probiotic use to prevent rUTIs.

## Conclusions

Despite non-conclusive evidence regarding efficacy for recurrent UTI management, probiotics are steadily increasing in popularity amongst consumers. Providers may be placed in a situation that warrants counseling patients on which products would be appropriate for use in recurrent UTI management. Providers should counsel patients that probiotics are not currently recommended for or against by the American Urological Association for use in recurrent UTI management. However, if patients still seek to utilize these products, providers should feel comfortable counselling patients that probiotics are generally well tolerated without significant side effects but require long- term usage to maintain microbial flora. Patients seeking probiotics for use in recurrent UTIs should potentially consider the bacterial species listed on package labelling, regardless of the applications listed on labeling, with at least 10-20 billion CFUs when choosing a product. Upon review of the current scientific data, *L. acidophilus, L. rhamnosus, L. fermentum, L. crispatus, L. plantarum,* and *B. lactis* have demonstrated potential efficacy for use in recurrent UTI management. We identified cost-effective probiotic products that may provide potential efficacy for recurrent UTI management. At least four of these products, "Healthy Origins", "Nature's Branch 50 Billion", "Nature's Base Probiotics", and "Renew Life Ultimate Flora Women's" are dosed once daily, contain at least 10 to 20 CFUs, and would potentially be the most effective options for use in recurrent UTI management.

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