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## **Probiotics reduce symptoms of antibiotic use in a hospital setting: A randomized dose response study**

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### **Abstract**

Probiotics are known to reduce antibiotic associated diarrhea (AAD) and Clostridium difficile associated diarrhea (CDAD) risk in a strain-specific manner. The aim of this study was to determine the dose-response effect of a four strain probiotic combination (HOWARU® Restore) on the incidence of AAD and CDAD and severity of gastrointestinal symptoms in adult in-patients requiring antibiotic therapy. Patients (n = 503) were randomized among three study groups: HOWARU® Restore probiotic  $1.70 \times 10^{10}$  CFU (high-dose, n = 168), HOWARU® Restore probiotic  $4.17 \times 10^9$  CFU (low-dose, n = 168), or placebo (n = 167). Subjects were stratified by gender, age, and duration of antibiotic treatment. Study products were administered daily up to 7 days after the final antibiotic dose. The primary endpoint of the study was the incidence of AAD. Secondary endpoints included incidence of CDAD, diarrhea duration, stools per day, bloody stools, fever, abdominal cramping, and bloating. A significant dose-response effect on AAD was observed with incidences of 12.5, 19.6, and 24.6% with high-dose, low-dose, and placebo, respectively ( $p = 0.02$ ). CDAD was the same in both probiotic groups (1.8%) but different from the placebo group (4.8%;  $p = 0.04$ ). Incidences of fever, abdominal pain, and bloating were lower with increasing probiotic dose. The number of daily liquid stools and average duration of diarrhea decreased with higher probiotic dosage. The tested four strain probiotic combination appears to lower the risk of AAD, CDAD, and gastrointestinal symptoms in a dose-dependent manner in adult in-patients.

**Keywords:** Antibiotic associated diarrhea, Probiotics, Dose response, Lactobacillus acidophilus, Lactobacillus paracasei, Bifidobacterium lactis