

# Meta-Analysis of Probiotics for the Prevention of Antibiotic Associated Diarrhea and the Treatment of *Clostridium difficile* Disease

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## ABSTRACT

**CONTEXT:** Antibiotic-associated diarrhea (AAD) is a common complication of most antibiotics and *Clostridium difficile* disease (CDD), which also is incited by antibiotics, is a leading cause of nosocomial outbreaks of diarrhea and colitis. The use of probiotics for these two related diseases remains controversial.

**OBJECTIVE:** To compare the efficacy of probiotics for the prevention of AAD and the treatment of CDD based on the published randomized, controlled clinical trials.

**DATA SOURCES:** PubMed, Medline, Google Scholar, NIH registry of clinical trials, metaRegister, and Cochrane Central Register of Controlled Trials were searched from 1977 to 2005, unrestricted by language. Secondary searches of reference lists, authors, reviews, commentaries, associated diseases, books, and meeting abstracts.

**STUDY SELECTION:** Trials were included in which specific probiotics given to either prevent or treat the diseases of interest. Trials were required to be randomized, controlled, blinded efficacy trials in humans published in peer-reviewed journals. Trials that were excluded were pre-clinical, safety, Phase 1 studies in volunteers, reviews, duplicate reports, trials of unspecified probiotics, trials of prebiotics, not the disease being studied, or inconsistent outcome measures. Thirty-one of 180 screened studies (totally 3,164 subjects) met the inclusion and exclusion criteria.

**DATA EXTRACTION:** One reviewer identified studies and abstracted data on sample size, population characteristics, treatments, and outcomes.

**DATA SYNTHESIS:** From 25 randomized controlled trials (RCTs), probiotics significantly reduced the relative risk of AAD (RR = 0.43, 95% CI 0.31, 0.58,  $p < 0.001$ ). From six randomized trials, probiotics had significant efficacy for CDD (RR = 0.59, 95% CI 0.41, 0.85,  $p = 0.005$ ).

**CONCLUSION:** A variety of different types of probiotics show promise as effective therapies for these two diseases. Using meta-analyses, three types of probiotics (*Saccharomyces boulardii*, *Lactobacillus rhamnosus* GG, and probiotic mixtures) significantly reduced the development of antibiotic-associated diarrhea. Only *S. boulardii* was effective for CDD.