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The probiotic *Bacillus clausii* is an effective treatment of acute diarrhea in children

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A systematic review and meta-analysis confirms that the probiotic *Bacillus clausii* is an effective treatment for acute diarrhea in childhood. It shortens the duration of diarrhea and associated hospitalization. New studies shed light on the mechanisms underlying these beneficial effects.

Acute diarrhea in children is a global health challenge. It causes considerable suffering of affected children and their parents and is a major cause of death in developing countries. Rotavirus infection is the most frequent cause of acute diarrhea in children. In 2010, the Cochrane Collaboration reported that probiotics as a class, used alongside rehydration therapy, appear to be a safe and beneficial treatment of childhood diarrhea by shortening the duration of the condition and improving other endpoints; however, it was emphasized that more research is needed to guide the use of particular probiotic regimens [1].

B. clausii is a non-pathogenic, Gram-positive bacterium that can temporarily colonize the intestine following oral ingestion [2]. Ianiro et al. performed a systematic review and meta-analysis of randomized controlled trials testing the efficacy of *B. clausii* in the treatment of childhood diarrhea [3]. They identified 6 randomized controlled trials including 1298 patients and found in their meta-analysis that *B. clausii* reduced the duration of diarrhea by 9.12 h (95% confidence interval –16.49 to –0.15; **Figure 1**) and the duration of hospitalization by 0.85 days (–1.56 to –0.15). None of the 6 studies reported serious side effects. Similar findings were obtained in a more recent controlled clinical trial in 65 children [5].

Additional clinical and experimental studies support the mechanistic plausibility of the beneficial clinical effects reported in the meta-analysis. In a placebo-controlled study [5], children with rotavirus infection had lower levels

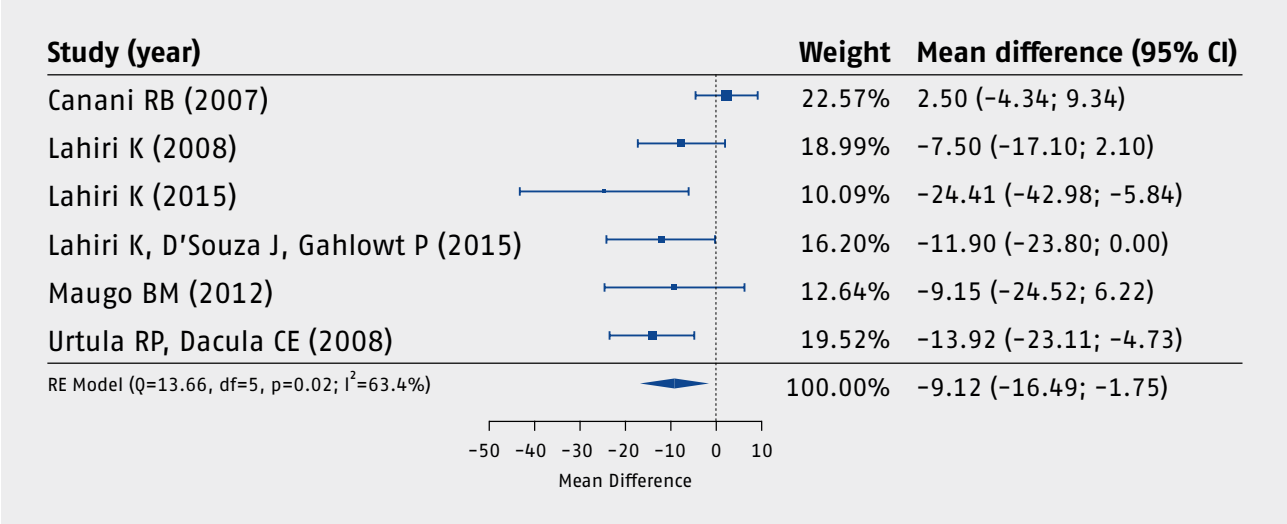

Fig. 1. Forest plot showing effect of *B. clausii* on mean duration of diarrhea in a random effect (RE) model. Reproduced with permission from [3].

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of circulating IgA and increased levels of IgG and IgM compared to children without rotavirus infection. IgA levels increased after treatment and even more after addition of *B. clausii*, whereas IgG and IgM levels returned closer to healthy values with *B. clausii*. In vitro studies in Caco-2 cells, a human enterocyte cell line, found that *B. clausii* protected gut enterocytes against rotavirus-induced decrease in trans-epithelial resistance, apparently by up-regulating the expression of mucin 5AC and the tight junction proteins occludin and zonula occludens-1 [4]. Moreover, *B. clausii* inhibited reactive oxygen species production and release of the pro-inflammatory cytokines, interleukin-8 and interferon-β in rotavirus-infected cells, and down-regulated pro-inflammatory Toll-like receptor 3 pathway gene expression. Thus, *B. clausii* has protective effects and stimulates various non-immune mucosal barrier and innate immune system defense mechanisms.

In conclusion, *B. clausii* is effective and well tolerated in the treatment of childhood diarrhea, apparently by improving intestinal barrier function and innate immunity.

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