

# The Potential of Probiotics to Prevent *Clostridium difficile* Infection



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## KEYWORDS

- *C difficile* diarrhea • Probiotic • Lactobacilli • *Bifidobacteria*
- *Saccharomyces boulardii*

## KEY POINTS

- In this article, the familiar term probiotic is used for microbial preparations being evaluated in clinical trials rather than for organisms with a proven health benefit.
- Probiotics evaluated in the prevention of *Clostridium difficile* diarrhea (CDD) have included bacteria (mostly lactobacilli and *Bifidobacteria*) either as single strains or as blends of strains and/or species, in variable doses (number of organisms) and in variable formulations, and the yeast *Saccharomyces boulardii*.
- The interpretation of the findings of meta-analysis of probiotic trials is complicated by the difficulty in pooling results for different probiotic preparations. As a result, there is insufficient evidence to recommend the use of any specific probiotic preparation.
- The falling incidence of CDD among the older people in hospitals because of control measures complicates the further evaluation of probiotics for CDD prevention.

## INTRODUCTION

*C difficile* has been the major cause of nosocomial infection in the hospital environment accounting for 15% to 39% of diarrhea that is associated with antibiotic treatment. Asymptomatic carriage results in new admissions constantly bringing *C difficile* into the hospital environment. The highly resistant nature of *C difficile* spores results in persistent contamination of the health care environment facilitating person-to-person spread by the fecal-oral route and requiring intensive control measures to prevent

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transmission. Although disease severity varies, CDD can be severe and complicated by toxic megacolon, intestinal perforation, and death.<sup>1,2</sup>

The 3 main risk factors for CDD, age greater than 65 years, admission to hospital, and exposure to antibiotics, have been recognized for many years.<sup>1,2</sup> A prospective study of adults (age >18 years) admitted to hospitals in Canada reported that increasing age, exposure to antibiotics, treatment with proton pump inhibitors (PPIs), and prior recent hospital admission predicted CDD.<sup>3</sup> A retrospective study of patients admitted to hospitals in Europe identified age greater than or equal to 65 years, severe comorbidity, and recent treatment with cephalosporins and aminopenicillin- $\beta$ -lactamase inhibitor combinations as risk factors for CDD.<sup>4</sup> A large, randomized controlled trial of a probiotic in the prevention of CDD found that both increased age (>77 years) and longer duration of antibiotic treatment (>8 days) were associated with an increased risk of CDD.<sup>5</sup>

### WHAT ARE PROBIOTICS?

Probiotics are defined as “live microbial organisms which, when administered in adequate numbers, are beneficial to health.”<sup>6</sup> However, the term probiotic is used more generally in research studies for microbial preparations that are being evaluated for health benefits, and it is this broader meaning that is used here.

The characteristics of microbial strains classified as probiotics are listed in **Box 1**.<sup>6,7</sup> Organisms that have been evaluated for the prevention of CDD include single strains and blends of bacteria (*Lactobacillus* spp, *Bifidobacteria* spp, *Streptococcus thermophilus*) and the yeast *S boulardii* (not of human origin).<sup>8</sup>

*Lactobacilli* and *Bifidobacteria*, bacteria commonly used as probiotics, are generally regarded as safe by the Food and Agriculture Organization of the United Nations.<sup>6</sup> Probiotics have been administered without short-term adverse effects to many vulnerable groups of people, such as preterm infants and people with human immunodeficiency virus infection. Systematic reviews of trials of mainly single strains or mixtures of

#### Box 1

##### Characteristics of probiotic organisms

- Human origin
- Live
- Safe/non-pathogenic
- Resistant to gastric acid, bile, and pancreatic juice to survive transit through the gastrointestinal tract
- Able to withstand technological processes and remain viable during shelf life
- Induce a host response once ingested
- Result in a functional or clinical benefit to the host
- Characterized using phenotypic and genotypic techniques
- Deposited in an internationally recognized culture collection

(Data from Food and Agriculture Organization of the UN and WHO. Report of a joint FAO/WHO working group on drafting guidelines for the evaluation of probiotics in food. Geneva (Switzerland): World Health Organization; 2002. Available at: [http://www.who.int/entity/foodsafety/fs\\_management/en/probiotic\\_guidelines.pdf](http://www.who.int/entity/foodsafety/fs_management/en/probiotic_guidelines.pdf). Accessed July 8, 2014; and Parkes GC, Sanderson JD, Whelan K. The mechanisms and efficacy of probiotics in the prevention of *Clostridium difficile*-associated diarrhoea. *Lancet Infect Dis* 2009;9:237–44.)

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