

## JAMA Pediatrics Clinical Evidence Synopsis

## Probiotics for Children With Recurrent Abdominal Pain

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**CLINICAL QUESTION** Do dietary interventions, such as probiotics, improve pain in children with recurrent abdominal pain?

**CLINICAL APPLICATION** Compared with placebo, children who were treated with probiotic preparations were more likely to experience improvement in pain in the short term (odds ratio, 1.63; 95% CI, 1.07-2.47), suggesting that clinicians could consider probiotics as part of a holistic management strategy in recurrent abdominal pain.

### Introduction

Recurrent abdominal pain (RAP) is a significant problem in pediatric practice and is associated with emotional disorders, school absence, and hospital admissions.<sup>1,2</sup> It is estimated to affect up to 25% of school-aged children at some point.<sup>1,3</sup> Recurrent abdominal pain refers to a group of functional gastrointestinal disorders that have an unclear etiology that are diagnosed according to Rome Foundation criteria.<sup>4</sup> We use RAP as an umbrella term to refer to the Rome III category of childhood abdominal pain-related functional gastrointestinal disorders, which include functional dyspepsia, irritable bowel syndrome, abdominal migraine, functional abdominal pain, and functional abdominal pain syndrome. Different treatment approaches have been taken for RAP that can be grouped as pharmacological, dietary, or psychosocial. Our Cochrane systematic review<sup>5</sup> (updating a 2009 review<sup>6</sup>) focused on any intervention with dietary changes that was intended to improve the symptoms of RAP. We used standard Cochrane methods, including the Grading of Recommendations Assessment, Development, and Evaluation approach, to assess the overall quality of the body of evidence for each specific outcome.

### Summary of Findings

We found 19 eligible studies, 15 (78.9%) of which were not included in the previous review. Fourteen trials recruited children with a diagnosis under the umbrella of RAP or functional gastrointestinal disorders; 5 recruited children with irritable bowel syndrome. Thirteen trials used differing probiotic-based interventions (the most commonly used strain being *Lactobacillus rhamnosus* GG in 5 trials). Four trials examined fiber interventions. We found only 2 studies of different exclusion/restriction diets.

At 0 to 3 months postintervention, children who were treated with probiotics were more likely to experience improvement in pain than those who were given placebo based on moderate-quality evidence (odds ratio [OR], 1.63; 95%CI, 1.07-2.47; 7 studies; 772 children). The number needed to treat for an additional beneficial outcome was 8. Children who were treated with probiotics also reported a greater reduction in pain frequency (standardized mean difference, -0.55; 95% CI, -0.98 to -0.12; 6 trials; 523 children) and intensity at the same point (standardized mean difference, -0.50; 95% CI, -0.85 to -0.15; 7 trials; 575 children). However, we judged the evidence for these outcomes to be of low quality. Only 2 studies reported outcomes 3 to 6 months postintervention, finding that those treated with probiotics were more likely to experience an improve-

### Evidence Profile

No. of randomized clinical trials: 19

Study years: 1985-2014; original literature search, June 2016

No. of participants: 1453

Male:female: Girls outnumbered boys in most included trials

Race/ethnicity: Unavailable

Age, mean (range): Between 6.3 and 13.1 years (4-18 years)

Settings: Pediatric gastroenterology clinics

Countries: Italy, Iran, United States, Canada, Poland, Germany, Israel, and India

Comparison: Dietary intervention (including probiotic-based interventions, fiber-based interventions, and exclusion/restriction diets) against a placebo comparison. One study used standard diet as the comparator.

#### Primary outcomes:

- Pain improvement (usually defined as a percentage or number of points improved from baseline, or being pain-free)
- Pain severity or intensity
- Pain frequency

#### Secondary outcomes:

- School performance
- Social or psychological functioning
- Quality of daily life

This was an update of the original 2009 review<sup>6</sup>

ment in pain (OR, 1.94; 95% CI, 1.10-3.43; 2 studies; 224 children; moderate-quality evidence). Please see our Cochrane systematic review<sup>5</sup> for the full details of all meta-analyses that were performed.

Children who were treated with fiber-based interventions were no more likely to experience an improvement in pain at 0 to 3 months postintervention than children who were given placebo (OR, 1.83; 95% CI, 0.92-3.65; 2 studies; 136 children) based on low-quality evidence.

### Discussion

The review provides low-quality to moderate-quality evidence that probiotics may be effective in the shorter term in improving pain in children with RAP. There was no convincing evidence suggesting that fiber supplements or other diets (eg, low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) are effective in

RAP. Our updated search in November 2017 found 2 additional trials of probiotics; adding these studies did not alter these findings.<sup>7</sup>

### Limitations

The review's limitations include the quality of evidence available, which was low to moderate, and the variation in the definition and scales that were used to assess pain outcomes. It was not possible to judge the extent of the clinical significance of improvement. Post hoc subgroup analyses of outcomes according to probiotic strain showed that there is currently insufficient evidence to guide clinical practices associated with the choice of strain, as dosages and regimes were different.<sup>7</sup> Only 2 included studies measured outcomes at 12 weeks or more.

### Areas in Need of Future Study

Future trials should assess outcomes over the longer term and use validated and consistent outcome scales that are agreed on by research leaders in this area. Few studies reported on school absences, social or psychological functioning, and quality of life, which are highly significant outcomes for families. Future research should also examine the optimal strain and dosage for probiotic interventions and consider effectiveness in different settings. It has been suggested that distinct subtypes of RAP could guide treatment choice<sup>4</sup>; this needs further investigation to allow tailored management. Finally, further high-quality randomized clinical trials are needed to examine the effectiveness of fiber-based interventions and exclusion diets.

### ARTICLE INFORMATION

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