

# Review: Probiotics are effective in preventing antibiotic-associated diarrhea

D'Souza AL, Rajkumar C, Cooke J, Bulpitt CJ. **Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis.** *BMJ*. 2002 Jun 8;324:1361-4.

## QUESTION

In patients being treated with antibiotics, does coadministration of probiotics reduce the incidence of diarrhea?

## DATA SOURCES

Studies in any language (with English abstracts) were identified by searching MEDLINE (1966 to 2000) with the terms probiotics, biotherapeutic agents, lactobacilli, antibiotic associated diarrhea, and *Clostridium difficile*, the Cochrane Controlled Trials Register; and the Cochrane Database of Systematic Reviews.

## STUDY SELECTION

Studies were selected if they were randomized, double-blind, placebo-controlled trials of probiotic therapy given in combination with antibiotics and diarrhea prevention was reported.

## DATA EXTRACTION

Data were extracted on sample size; type, dose, and duration of probiotic treatment; and antibiotic studied. The outcome of inter-

est was prevention of diarrhea. Diarrhea was defined as a change from the normal bowel habit with  $\geq 2$  loose or watery stools for  $\geq 2$  days.

## MAIN RESULTS

9 trials (1214 patients) met the selection criteria. 2 of the trials studied children. No statistical heterogeneity or publication bias was detected among the 9 trials. The pooled odds ratio (OR) showed that probiotic treatment was more effective than placebo in the prevention of diarrhea (0.37, 95% CI 0.26 to 0.53) (Table). 4 trials that used *Saccharomyces boulardii* (yeast trials) also

avored probiotic treatment (OR 0.39, CI 0.25 to 0.62) as did 5 that used lactobacilli or enterococci (nonyeast trials) (OR 0.34, CI 0.19 to 0.61).

## CONCLUSION

In patients being treated with antibiotics, coadministration of probiotics reduces the incidence of diarrhea.

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*For correspondence: Dr. A.L. D'Souza, Hammer-smith Hospital, London, England, UK. E-mail aloysius.dsouza@ic.ac.uk.* ■

### Probiotics vs placebo to prevent antibiotic-associated diarrhea\*

Outcome	Weighted event rates		RBI (95% CI)	NNT (CI)
	Probiotics	Placebo		
Proportion of patients without diarrhea	90%	78%	15% (9 to 20)	9 (7 to 13)

\*Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data provided by author using a fixed-effects model.

## COMMENTARY

The incidence of antibiotic-associated diarrhea in hospitals ranges from 3.2% to 29% (1). Antibiotic-associated diarrhea has been associated with an increased number of days of hospitalization and higher medical costs. Probiotics are becoming increasingly available, and their lack of side effects makes them a particularly attractive option for preventing antibiotic-associated diarrhea.

The well-done review by D'Souza and colleagues addresses whether coadministration of probiotics with antibiotics reduces the incidence of antibiotic-associated diarrhea. Their analysis yields impressive ORs that show that probiotics seem to decrease the incidence of antibiotic-associated diarrhea.

However, several points should be considered when interpreting the results. First, clinical heterogeneity limits the potential generalizability of the results. The 9 studies had differences in probiotic agents administered, dosages, duration of administration of probiotic agents, and antibiotics. Second, the confidence intervals in this review may be too narrow because the authors used a fixed-effects model for analysis instead of the more conservative random-effects model; the latter may be more appropriate because statistical tests of heterogeneity in meta-analyses may have low statistical power (2).

Does this review provide strong enough evidence to integrate the use of probiotics into practice? My answer would be "no," mainly because of the clinical heterogeneity of the agents used thus far in published studies. The authors have appropriately written a conservative concluding statement in their review. I hope that future clinical trials will give a more definitive answer as probiotics undergo increasing scrutiny and standardization (3). Future trials need to be characterized with the same scientific rigor that is applied to standard drugs.

*Anthony D. Harris, MD, MPH  
University of Maryland  
Baltimore, Maryland, USA*

### References

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